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EDITORIAL

Maternal-fetal communication

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The placenta is a temporary organ (40 weeks) and functions as the bridge of maternal-fetal communication. Placentation is a fundamental process that begins with the implantation of the blastocyst in the endometrium, around day 6-7 after fertilization. The trophectoderm of the blastocyst gives rise to cytotrophoblasts, which branch out into structures known as "placental villi," before 12 weeks of pregnancy, the trophoblast differs from the blastocyst in two layers: The syncytiotrophoblast and the cytotrophoblast, as implantation progresses, the syncytiotrophoblast creates vacuoles that form gaps filled with maternal blood, Necessary for communication between the mother and the developing fetus, the syncytiotrophoblast invades the spiral arteries, forming structures known as a column of cytotrophoblast cells that give rise to the trophoblastic plug, whose function is to temporarily block blood flow to create a hypoxic environment, thus promoting vascular remodeling and anchoring between the placenta and the decidua.

Extravillous trophoblasts, which differ from the column of cytotrophoblast cells, migrate to the decidua and superior myometrium (extravillous interstitial trophoblast) or temporarily block the maternal spiral arteries (endovascular extravillous trophoblast), preventing maternal blood flow to the intravillous space, until approximately 12 weeks of gestation, at which time these plugs are detached. Extra-villous trophoblasts and utero-resident immune cells, such as uterine Natural Killer (NK) cells and regulatory T cells (Treg), are actively involved in the remodeling of maternal spiral arteries. The radial arteries of the uterus divide into two or more branches, which end in the myometrium or decidua (basal arteries) or open in the intravellous space, after week 12, the trophoblastic invasion progresses, allowing the plugs to detach, which increases maternal blood flow to the placenta and favors fetal oxygenation. The spiral artery becomes a large-caliber, low-resistance blood vessel, facilitating adequate placental perfusion for fetal growth[1].

Extracellular vesicles are a heterogeneous group of vesicles formed by lipid bilayers, secreted from the cytoplasmic membrane both "*in vivo*" and "*in vitro*" by various cell types, extracellular vesicles according to their size are classified into three groups: (1) Vesicles of 30-100 nm called exosomes, which are derived from the endolysosomal pathway, formed in multivesicular compartments; (2) Vesicles of 0.1-1 μm called microvesicles, which have a greater variability in size and come directly from the cytoplasmic membrane; (3) Apoptotic bodies (1-4 μm), generated during late apoptosis. Extracellular vesicles include proteins, lipids, DNA, RNAs and miRNAs, reflecting the characteristics of the cells from which they originate, likewise molecules typical of the different types of extracellular vesicles have been described that are used as markers, using Alix, TSG101 and flotiline for exosomes, scramblase, cholesterol, flotiline and phosphatidylserine for microvesicles, while for apoptotic bodies annexin and phosphatidylserine are included. The mechanisms by which extracellular vesicles interact with the target cell and how their contents are transferred are not yet fully understood. However, three mechanisms have been proposed: (a) Binding to surface receptors with activation of signal transduction pathways; (b) Internalization, and (c) Membrane fusion[2].

The biological activity of extracellular vesicles is determined by their contents, which are transferred to the target

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cells when the vesicles are internalized by the cells or activate receptors on their surface. However, the role of vesicles in the implantation of the fertilized egg and placental development, as well as in pathological processes, is little studied. The syncytiotrophoblast is the main source of placental-derived vesicles and may constitute the main signaling mechanism between the product and the mother, modifying the physiological activity that allows its presence and satisfies the demands of the developing fetus.

Syncytiotrophoblast-derived vesicles do not express paternal human leukocyte antigen; however, they express minor paternal histocompatibility antigens, such as DDX3Y and HA-1 bound to syncytial nuclear aggregates, which constitute a specific antigen mechanism inducing regulatory T cells that confers maternal immunological tolerance, in the early lacunar stage (1-3 days post-implantation) intervillous blood flow begins. Where the oxygen tension is 1%, while in primary cultures of cytotrophoblast cells it has been shown that under this oxygen tension there is release of vesicles, which transport proteins that lead to proliferation and invasion of cells. Low oxygen tension triggers cytotrophoblast proliferation through mechanisms involving hypoxia-inducible transcription factor 1 alpha (HIF1α), which regulates the expression of genes such as erythropoietin, placental vascular angiogenic factor, and nitric oxide synthase, in the human placenta HIF1α expression is increased during the first trimester and decreases around week 9. When circulation and consequently oxygenation to the fetus increases, the persistence of elevated levels of HIF1α indicates placental stress and announces the development of pathology, such as preeclampsia, in fact, the placenta of women with preeclampsia overexpresses HIF1α and HIF2α, the molecular mechanisms that mediate the remodeling of the spiral arteries are still under debate. During normal placentation, cytotrophoblast differentiates from an epithelial phenotype to an endothelial one, a process called "pseudo-vasculogenesis" or "vascular mimicry," this transition does not take place in pre-eclampsia.

Cytotrophoblast that does not invade maternal spiral arterioles does not express endothelial adhesion markers, such as VE cadherins and $\alpha1\beta1$ and $\alpha V\beta3$ integrins that are expressed by normal invasive cytotrophoblast. Extracellular vesicles of the syncytiotrophoblast in maternal plasma are increased in pre-eclampsia and the increase in their level tends to reflect the severity of the disease[3-5].

Conclusion

– The placenta is a temporary organ that functions as a maternal-fetal communication bridge. Placentation is a process that begins with the implantation of the blastocyst after fertilization.
– The trophoblast differs from the blastocyst in two layers: the syncytiotrophoblast and the cytotrophoblast, the syncytiotrophoblast creates vacuoles that form gaps filled with maternal blood, for communication between mother and fetus, and invades the spiral arteries, forming a column of cytotrophoblast cells originating a trophoblastic plug, blocking blood flow creating hypoxia and promoting vascular remodeling, involving HIF1α, which regulates the expression of genes such as erythropoietin, placental vascular angiogenic factor, and nitric oxide synthase, as well as immune cells (NK and regulatory T).
– Extracellular vesicles of syncytiotrophoblast in maternal plasma are increased in pathologies such as preeclampsia, and the increase in their level tends to reflect the severity of the disease.

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ORIGINAL ARTICLE

Characterization of self-esteem in adolescents according to age, sex, school grade, and body mass index

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†In memoriam

Abstract

Introduction: *Self-esteem is one of the main indicators of psychological well-being. High self-esteem can be considered a protective factor for mental health and diseases of another nature, such as those that affect nutritional status. The study of self-esteem in vulnerable groups, such as adolescents, is important to design strategies that help maintain their overall health.* **Objectives***: The objective of the study was to know the degree of self-esteem in adolescents and its association with age, sex, school grade, and body mass index (BMI).* **Material and methods:** *A cross-sectional design was used in a sample of adolescents from a secondary school located east of Mexico City. Self-esteem was assessed using the Rosenberg instrument; they were weighed and measured to calculate BMI.* **Results:** *Four hundred and sixty adolescents with an average age of 12.6 years were studied, 54.0% were women, and the rest men. The overall frequency of low self-esteem was 18.3% (84), being more frequent in women aged 15 years and with a BMI corresponding to obesity. The frequency of high self-esteem was 81.7% (376), being more frequent in men aged 12 years and with a BMI classified as normal.* **Conclusion:** *It is necessary to plan strategies aimed at reinforcing and increasing self-esteem during adolescence, particularly through physical activity.*

Keywords: *Self-esteem. Adolescents. Body mass index. Schoolchildren. Obesity.*

Introduction

Self-esteem is the extent to which people value themselves according to the perceived success or failure in achieving their goals. It is also an important factor in the development of personality, social, and emotional adaptation. Although self-esteem is formed throughout the life cycle, it is known that childhood and adolescence are the most relevant stages for its formation due to the risk of suffering worse physical and mental health[1].

During adolescence, which runs from 10 to 19 years of age, in addition to the physiological changes of development, other changes occur that is psychosocial, as well as the development of social and cultural expectations, associated with the transition from childhood to adulthood. The adolescent seeks to express his feelings and behavior with an attitude of approval or rejection, this feeling expresses the degree to which he values and trusts himself in decision-making, aspirations, and achievements[2]. Given the great influence that self-esteem can have on people's lives, different instruments have been developed in order to evaluate and classify it mainly as low or high self-esteem[3]. The World Health Organization reports that one in four individuals between 7 and 17 years of age has low self-esteem[4].

When there is high self-esteem, the adolescent seeks personal growth by exercising his abilities to the limit,

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while recognizing his mistakes. Unlike adolescents with low self-esteem who are prone to feel awkward, shy, and unable to express themselves confidently, since they are worried about making a mistake or exposing themselves to ridicule. High self-esteem is related to more active personalities, with feelings of control over circumstances, less anxious, and with better capacities to tolerate internal or external stress, less sensitive to criticism, enjoy their interpersonal relationships, and value their independence; on the other hand, low self-esteem is associated with feelings of apathy, isolation, shyness, and anxiety[5]. Among the health consequences of having low self-esteem is the association with diseases such as eating disorders (anorexia nervosa, bulimia nervosa, among others), depression, or addiction to addictive substances[6].

The main determinants of self-esteem are the family and society. With regard to the family, when violence occurs in the home environment, in particular sexual violence and harassment, or severe parenting by parents, and serious socioeconomic or other problems, there are risks that damage self-esteem. Likewise, today's society has established the slim body as an ideal of beauty and health, leaving people with excess weight (overweight and obesity) vulnerable to social rejection that affects their self-esteem. In vulnerable populations such as adolescents, who are looking for an identity and have the need to feel accepted and integrated into society, fear could lead them to unhealthy eating and exercise practices in their attempt to achieve a healthy and beautiful body[7]. Overweight and obesity are considered risk factors for especially chronic diseases; but also because they have a negative impact on the mental health of the adolescent population, since they feel guilty about their appearance, leading them to avoid situations where they may feel criticized, such as speaking in public, eating in front of other people, wearing clothes that hide their body, adopt a passive, sedentary lifestyle and social isolation, which leads them to have mainly low self-esteem[8,9]. The objective of this study was to determine self-esteem in a sample of adolescents and its association by age, sex, school grade, and body mass index (BMI).

Material and methods

A cross-sectional observational epidemiological study was carried out. The population consisted of high school students from a public school located in the east of Mexico City. The sample was non-probabilistic. All students were invited to participate in the study according to the request of the school authorities; however, only those who so wished and had the informed consent letter signed by their parent or guardian were included in the study.

Each group of the three school grades was visited to request verbal consent to participate in the study, and was given a letter of informed consent for signature by the parents or guardians. If they had this, they were asked to answer the instruments in the computer room electronically. At the end, they were weighed using a previously calibrated Tanita scale, and their height was measured using a wall stadimeter. The BMI was calculated for the corresponding age and sex reported by his parent or guardian. According to the classification World Health Organization: low weight (≤ -2.00), normal weight (-1.99 to 0.99), overweight (1.00 to 1.99) and obesity (≥ 2.00). It is important to clarify that there are other instruments to measure overweight and obesity, such as waist circumference and skinfold thickness[10].

To assess self-esteem, the Rosenberg self-esteem scale (1965) was used[11], which has been adapted to Spanish and validated for Mexican adolescents and young people[12]. The instrument was validated, the results were α 0.77, an intraclass correlation coefficient of 0.77, KMO test 0.68, and Bartlett test 97.49, both significant, and an explained variance of 73.98, so the instrument was valid and reliable for the group studied.

The questionnaire consists of ten scoring questions that allude to global feelings of self-worth, five are written in a positive sense and five in a negative sense. The answer options are on a Likert-type scale with four categories (from strongly disagree with a point value of one to strongly agree with a point value of four). The cutoff point for women was: low self-esteem from 0 to 28 and high self-esteem from 29 to 40; for men, it was: low self-esteem from 0 to 29 and high self-esteem from 30 to 40[11,12].

The statistical program the Statistical Package for the Social Sciences version 20.0 was used for data analysis. The qualitative variables are presented as a percentage and the quantitative variables (age and BMI) are presented with the mean and standard deviation; however, the distribution was not similar to the normal curve according to the Kolmogorov–Smirnov test, so to evaluate the differences between self-esteem and the rest of the variables, the χ^2 test (χ^2) was used, as well as the Mann-Whitney U, considering a level of statistical significance of 0.05[13].

Results

A total of 460 adolescents aged 11-15 years were studied, of which 56.9% (248) were females and the rest were males. The overall mean age was 12.65 years with a standard deviation of 0.96 years. The median was 12 years for males and 13 years for females. No statistically significant differences were found according to sex and age. 50.6% (233) were in the 1st year, 28.5% (131) in the 2nd year, and 20.9% (96) in the 3rd grade. No statistically significant differences were observed in the distribution by sex, according to school grade.

According to the BMI classification, 3.0% (13) of the adolescents were underweight, 55.0% (253) normal weight, 17.0% (78) overweight, and 25.0% (116) obese. No statistical differences were found according to sex or age. The overall frequency of low self-esteem was 18.3% (84). Of these, 58.3% (49) were women and 41.7% (35) men. The difference, however, was not statistically significant. A statistically significant difference was found in the frequency of low self-esteem according to age. A statistically significant difference was found in the frequency of low self-esteem according to school grade. Correspondingly, the highest frequency of low self-esteem was observed in first-grade students with 42.9% (36), being statistically significant ($\chi^2 = 6.4$, $p < 0.05$) (Table 1).

It was observed that most students with high self-esteem had a normal BMI (52.5% males and 58.3% females). On the other hand, among men with low self-esteem, 48.6% (17) were overweight or obese, while in women this percentage was 44.9% (22). No statistically significant differences were observed between self-esteem and BMI (Table 2).

It was also observed that more than 90.0% of the women had responses in which they indicated that they disagreed or strongly disagreed with respect to considering themselves worthy of appreciation, having qualities, or feeling that they did things well (Table 3). In the case of men, more than 90.0% of the responses added to disagree with having a positive attitude and feeling satisfied with themselves (Table 4). Both men and women indicated that 90.0% did not consider themselves failures.

Table 1. Frequency of self-esteem according to school grade of the adolescent population studied

School grade	Low		High	
	No.	%	No.	%
First	36	42.9	197	52.4
Second	22	26.2	109	29.8
Third	26	31	70	18.6
Total	84	100	376	100

$\chi^2 = 6.4$, $p < 0.05$.

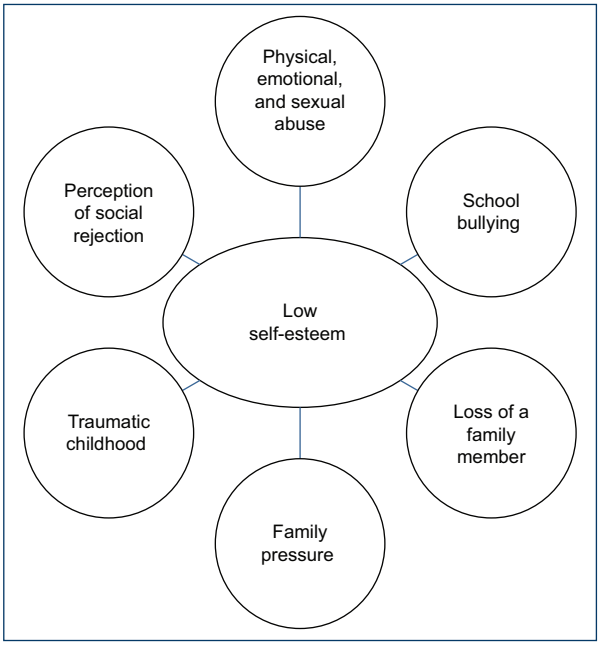

Figure 1. Other factors that influence the occurrence of low self-esteem.

Discussion

In adolescence, the individual faces a physical and emotional development in which he will define and affirm his identity, this can imply the modification of various habits and behaviors, but it can also generate states of emotional instability that prevent him from facing difficulties and effectively facing the changes that the social environment assigns him[14]. The results of this study allow us to measure the frequency and risk groups that have low self-esteem, since it was found in 16.5% of men and 20.0% of women, particularly in younger adolescents, which simultaneously correspond to who were in the first grade of school. It should be considered that this group corresponded to half of the population studied. Sánchez-Rojas et al.[15] reported a prevalence of low self-esteem of 23.3% and 21.3% in 295 children aged 8-13 years (116 overweight or obese and 179 with normal weight, respectively), without statistically significant differences.

Table 2. Self-esteem according to body mass index and sex of the adolescent population studied

Body mass index	Sex							
	Men				Women			
	Self-esteem							
	Low		High		Low		High	
	No.	%	No.	%	No.	%	No.	%
Low	0	0.0	6	3.4	1	2.0	6	3.0
Normal	18	51.4	93	52.5	26	53.1	116	58.3
Overweight and obesity	17	48.6	78	44.0	22	44.9	77	38.7
Total	35	100	177	100	49	100	199	100

χ^2 = no statistical significance.

Table 3. Frequency of responses according to the Rosenberg instrument to assess self-esteem in adolescent women

Questions	Answers No. (%)			
	Strongly agree	I agree	Disagree	Strongly disagree
I feel that I am a person worthy of appreciation at least in the same way as the people around me	1 (0.4)	17 (6.9)	112 (45.2)	118 (47.6)
I think I have a good number of qualities	3 (1.2)	22 (8.9)	133 (53.6)	90 (36.3)
I'm able to do things right like most people	3 (1.2)	11 (4.4)	106 (42.7)	128 (51.6)
I have a positive attitude toward myself	7 (2.8)	27 (10.9)	87 (35.1)	127 (51.2)
Overall, I am satisfied with myself	2 (0.8)	29 (11.7)	103 (41.5)	114 (46)
En general me inclino a pensar que soy una fracasada	4 (1.6)	19 (7.7)	95 (38.3)	130 (52.4)
I feel like I don't have much reason to be proud of myself	30 (12.1)	57 (23.0)	65 (26.2)	96 (38.7)
I wish I valued myself more	90 (36.3)	111 (44.8)	27 (10.9)	20 (8.1)
Sometimes I feel really useless	16 (6.5)	41 (16.5)	74 (29.8)	117 (47.2)
Sometimes I think I'm good for nothing	10 (4.0)	33 (13.3)	74 (29.8)	131 (52.8)

The fact that low self-esteem is found in approximately one in five students affects the personal, school, family, and social spheres (Fig. 1). In the first case, the self-perception of body image, and the state of health, in general, can violate self-esteem. In the present study, overweight or obesity was found in 44.8% of men and 39.9% of women, which constitutes, in itself, a reason for health care. According to the results of the National Health and Nutrition Survey 2020-2022, 23.9% of people between 12 and 19 years of age are overweight and 17.2% obese[16].

On the other hand, secondary education has demands that primary education does not have, in terms of workload, as well as the component that can be added by the participation of several teachers, as opposed to what was the case with basic education, with only one. In the family field, the structure, stability, dynamics, and material resources available are determinants present in the daily life of the adolescent[17]. In the social sphere, for example, although in the present study no statistically significant differences were found in the behavior of self-esteem between men and women, it has been described that these exist, and that they are associated with problems related to gender violence, based on the fact that self-esteem is higher in men. Moreover, it is linked to myths related to romanticism between couples[18].

Table 4. Frequency of responses according to the Rosenberg instrument to assess self-esteem in adolescent men

Questions	Answers No. (%)			
	Strongly agree	I agree	Disagree	Strongly disagree
I feel that I am a person worthy of appreciation at least in the same way as the people around me	4 (1.9)	8 (3.8)	103 (48.6)	97 (45.8)
I think I have a good number of qualities	0 (0.0)	10 (4.7)	89 (42.0)	113 (53.3)
I am able to do things right like most people	1 (0.5)	8 (3.8)	69 (32.5)	134 (63.2)
I have a positive attitude toward myself	5 (2.4)	10 (4.7)	69 (32.5)	128 (60.4)
Overall, I'm satisfied with myself	1 (0.5)	12 (5.7)	76 (35.8)	123 (58.0)
In general, I am inclined to think that I am a failure	8 (3.8)	15 (7.1)	64 (30.2)	125 (59.0)
I feel like I don't have much reason to be proud of myself	33 (15.6)	36 (17.0)	46 (21.7)	97 (45.8)
I wish I valued myself more	1 (0.5)	12 (5.7)	76 (35.8)	123 (58.0)
Sometimes I feel really useless	13 (6.1)	28 (13.2)	65 (30.7)	106 (50.0)
Sometimes I think I'm good for nothing	12 (5.7)	20 (9.4)	56 (26.4)	124 (58.5)

Conclusion

Since adolescents are a vulnerable group, we consider it important to implement a health promotion program, which involves adolescents, parents, and teachers in the biological and psychological areas. The school is considered a key environment where actions are carried out to improve or protect self-esteem, such as workshops on social and emotional skills, increased physical activity, music and arts programs; all of the above would contribute, in addition to increasing self-esteem, to reduce bullying, eating disorders, suicides, or alcohol and tobacco consumption[19,20].

Promoting self-esteem can prevent the development of psychopathological problems mainly associated with depression, so actions such as physical activity have scientifically shown benefits on self-esteem, overweight, and obesity[21]. The treatment of obesity in children and adolescents must have a comprehensive approach: biological, psychological, and social. Rather than seeking the ideal weight or socially accepted weight as a goal[22], it is necessary to seek to achieve healthy lifestyle habits and directly involve the family in treatment; it would be desirable that both friends and peers with whom they live are active members in the process.

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ORIGINAL ARTICLE

WovenEndoBridge embolization versus stent-assisted coiling for the treatment of unruptured wide-neck bifurcation intracranial aneurysms: a retrospective study

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Abstract

Introduction: *Currently, endovascular coil embolization is the first line of treatment for intracranial aneurysms. Over the last decade, several new endovascular devices and techniques have been developed for wide neck aneuryms located at the bifurcation of cerebral arteries, with varying degrees of success.* **Objective:** *To compare the occlusion rates of unruptured wide-neck bifurcation intracranial aneurysms using WovenEndoBridge (WEB) device embolization versus stent-assisted coiling (SAC).* **Materials and methods:** *We performed a retrospective, longitudinal study that included adult patients treated at the National Institute of Neurology and Neurosurgery in Mexico City, between 2020 and 2022. Patients had been previously diagnosed with an unruptured saccular wide-neck bifurcation aneurysm and were assigned to either WEB embolization or SAC. Occlusion rate was assessed using imaging studies performed 90 days after the procedure was completed.* **Results**: *A total of 14 patients were included in the study. Six patients were treated with the WEB device, and eight patients were treated using SAC. No statistically significant differences were observed between the demographic characteristics of the groups. Median aspect/ratio was 1.45 (1.25-1.82) for the WEB group and 1.67 (1.166-2.11) for the SAC group, and bottleneck factor ratios were 1.35 (1.042.42) and 1.26 (1.17-1.77), respectively. Complete occlusion was observed in 6/6 patients for the WEB group and 6/8 patients for the SAC group (p = 0.308). No statistically significant differences were observed in the complication rates, 3-month modified Rankin score, and hospital length of stay between the groups.* **Conclusion:** *The WEB device is a novel treatment that carries the same safety and efficacy profile as SAC. However, more experience with the device is required to fully understand the capabilities of the WEB.*

Keywords: *Intracranial aneurysms. Endovascular treatment. Stent-assisted coiling. WovenEndobridge device. Wide-neck.*

Introduction

Currently, endovascular coil embolization is the first line of treatment for ruptured and unruptured intracranial aneurysms, along with surgical clipping[1,2]. The use of slimmer, more flexible, and better-navigating catheters has led to an improvement in the treatment of aneurysms using endovascular coiling embolization[3-6]. Furthermore, the improvement of current imaging techniques has allowed for better measurements of

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aneurysm size and 3D conformation. The use of endovascular coil embolization is better suited for narrow-neck (< 4 mm) intracranial aneurysms or intracranial aneurysms with a dome-to-neck ratio < 2[7].

On the other hand, there are several cases where, due to the aneurysm location and morphology or the patient's clinical conditions, the patient might be better suited for a surgical approach treatment[8-13]. The study performed by Aydin et al. revealed that bifurcation aneurysms treated with stent-assisted coiling (SAC) using the T approach achieved a complete occlusion in 83.3% of the cases. Complications were observed in 13.7% of patients, of which 1.9% developed a lifelong disability and 1% died[14].

Over the last decade, several new endovascular devices and techniques have been developed for wide-neck aneurysms located at the bifurcation of cerebral arteries, with varying degrees of success[7]. The WovenEndoBridge (WEB) is the most common intrasaccular device currently used for unruptured wide-neck aneurysms in the anterior communicating artery (AComA), middle cerebral artery (MCA), internal carotid artery, and the tip of the basilar artery[12-15].

The WEB is a device built with nitinol threads and a platinum core suitable for aneurysm occlusion and flow diversion[15]. Literature shows that this device has an occlusion rate of 61-84.6%, a complication rate of 5.5-17%, and a mortality rate of 2%[16-19].

Material and methods

Study design

We conducted a retrospective, longitudinal, and analytical study between 2020 and 2022, involving adult patients diagnosed with unruptured intracranial wide-necked saccular aneurysms located at a bifurcation of the MCA and AComA, treated at the National Institute of Neurology and Neurosurgery. Exclusion criteria included prior treatment for the aneurysm and contraindications to dual antiplatelet therapy (DAPT).

Patients were evaluated by a multidisciplinary team and assigned to either the WEB device placement group or the SAC group based on specific criteria. The aneurysms considered for the WEB device placement had a height > 4 mm and < 4 mm for jailing. We also considered, alongside the experience of the endovascular therapist and the availability of institutional resources, particularly since the hospital is a government facility. All decisions made by the multidisciplinary team were in accordance with institutional guidelines.

Patients in both the WEB and SAC groups received DAPT for 10 days before the procedure, consisting of 325 mg of acetylsalicylic acid and 75 mg of clopidogrel once daily. All endovascular procedures were performed through transradial or transfemoral access. An 8 Fr distal access guide catheter was advanced to facilitate diagnostic digital subtraction angiography (DSA). Special projections measuring the aneurysm's size and characteristics, including 3D projections, were completed during the diagnostic DSA.

WEB devices were selected according to the recommended sizing guidelines provided by the manufacturer. The devices were advanced into the aneurysmal fundus using a vascular intervention access microcatheter and a microguide. Adequate device placement and changes in aneurysmal flow were confirmed using 2D projections before detaching the device.

For patients in the SAC group, the length and width of the compromised arteries were measured to select the appropriate stent size. Two microcatheters were advanced to the aneurysm site: the first microcatheter was placed distal to the aneurysm, whereas the second was positioned within the aneurysmal fundus. SAC was achieved by jailing the coils with the deployed stent. After the procedure, patients were instructed to continue DAPT for 6 months.

A cone-beam computed tomography scan was performed within the 1st month following the procedure, and DSA was conducted during the 3rd and 6th months. DSAs were obtained in a biplanar angio suite (Artis Siemens Health) using either a transradial or transfemoral approach. The DSAs were then evaluated by two experts in endovascular neurosurgery, measuring various characteristics of the treated aneurysms, including occlusion rate, height, length, neck, aspect ratio, bottleneck ratio, and the length and width of the compromised vessels and aortic arch.

Results from the web occlusion score were categorized into complete or incomplete occlusion. Patients treated with SAC were assessed using the Raymond–Roy Scale and were similarly classified into complete or incomplete occlusion.

Complications were defined as any neurological symptoms or signs of focalization that developed after the procedure or the absence of contrast passage through any major arterial vessel upon completion of the procedure.

Other outcomes analyzed during the study included hospital length of stay, mortality rate, modified Rankin score at the 3-and 6-month assessments, and intraprocedural and post-procedural complications.

Statistical analysis

Results underwent descriptive statistical analysis. Variables with normal distribution were analyzed with mean and standard deviation, whereas variables without normal distribution were analyzed using median and interquartile ranges. Inferential statistics were carried out to assess statistical significance between the occlusion rates of the WEB device and SAC using the Fisher Exact Test, using $p < 0.05$ as significant. Statistical analysis was performed using the STATA software v16.1.

Results

A total of 14 patients were included in the study. Six patients were treated with the WEB device (Fig. 1), whereas eight patients were treated with SAC (Fig. 2) from January 2020 to May 2022. Eight of the patients were male (57%). Whole patients and aneurysm characteristics are shown in table 1.

The most common aneurysm location was in the MCA bifurcation (eight cases: four in the WEB group and four in the SAC group), and the AComA (six cases: two in the WEB group and four in the SAC group).

Regarding safety and efficacy, 12 cases were completely occluded (87%). No fatalities were reported (0%). One complication involved the WEB device, which experienced partial migration during follow-up, leading to thrombosis of the parent vessel. The aneurysm was at the bifurcation of the MCA, and the partial migration caused thrombosis of the dorsal branch, resulting in motor deficits. The remaining cases had no complications. Table 2 includes outcomes of WEB devices and SAC-treated patients.

Table 1. Characteristics of patients treated with the WEB device and SAC

Characteristics	WEB device (%)	SAC (%)	p
Patient characteristics			
Male sex	5 (83)	3 (37)	0.12
Age (years)	61 (50-64)	61 (60-63)	0.59
Hypertension	3 (50)	5 (62)	0.52
Tobacco use	1 (16)	2 (25)	0.61
Hyperlipidemia	0 (0)	1 (12)	0.57
Type 2 diabetes	2 (33)	2 (25)	0.59
Obesity	1 (16)	2 (25)	0.62
Alcohol consumption	1 (16)	1 (12)	0.69
Aneurysms characteristics			
Dome-neck	6 (6-7)	4.7 (2.5-6.2)	0.243
Width	6 (5.1-7.5)	3.8 (2.8-4.7)	0.023
Neck	4.5 (3.3-5.0)	2.3 (2.2-3.0)	0.039
Aspect ratio	1.45 (1.25-1.82)	1.67 (1.16-2.11)	0.755
Bottleneck	1.35 (1.04-2.42)	1.26 (1.17-1.77)	1.00

SAC: stent-assisted coiling, WEB: WovenEndoBridge.

Table 2. Outcomes of WEB device and SAC-treated patients

Outcomes evaluated	WEB device (%)	SAC (%)	p
Complete occlusion	6 (100)	6 (75)	0.308
Complications	1 (16)	0 (0)	0.429
mRs 0-1 at 3 months	5 (83)	8 (100)	0.429
Length of hospital stay (days)	3 (2-4)	3 (3-3)	1.00

SAC: stent-assisted coiling, WEB: WovenEndoBridge.

Discussion

Wide-necked bifurcation intracranial aneurysms have always proven a challenge for interventional neuroradiology. While most aneurysms undergo open surgical clipping, many are now treated using endovascular approaches, thanks partly due to the availability of new technologies such as SAC or intrasaccular devices.

The safety and efficacy of these new technologies have been demonstrated by recent studies. The prospective WEBCAST and WEBCAST 2 studies were performed in Europe, whereas the WEB-intrasaccular therapy study took place in the United States. All studies confirmed the safety and efficacy of the device[16,20,21]. In addition, several early experiences and systematic reviews have continued to add information regarding the effectiveness of the WEB device[22].

The review by Laurent Pierot[22] compared the safety profiles of different endovascular techniques, including primary coiling, SAC, flow diverters, and the WEB device. The study found a lower mortality rate and similar occlusion and morbidity rates between the WEB device and the other techniques. Furthermore, no statistically significant differences were observed in secondary outcomes. These findings correlate with those observed in the studies by Kabbasch et al.[23,24] and Kashkoush et al.[25] On the contrary, the paper published

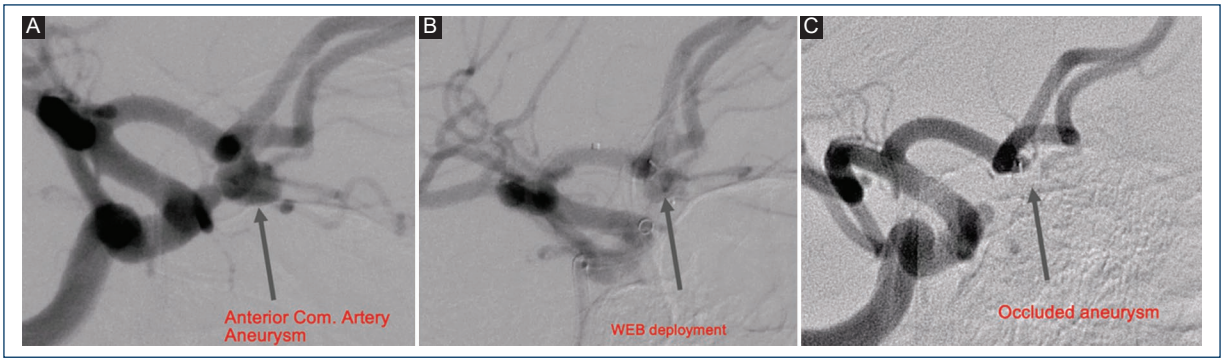

Figure 1. Digital subtraction angiography demonstrating the treatment of an anterior communicating artery aneurysm. **A:** initial angiogram shows the aneurysm. **B:** WovenEndobridge device deployment within the aneurysm sac. **C:** follow-up angiogram confirming complete occlusion of the aneurysm.

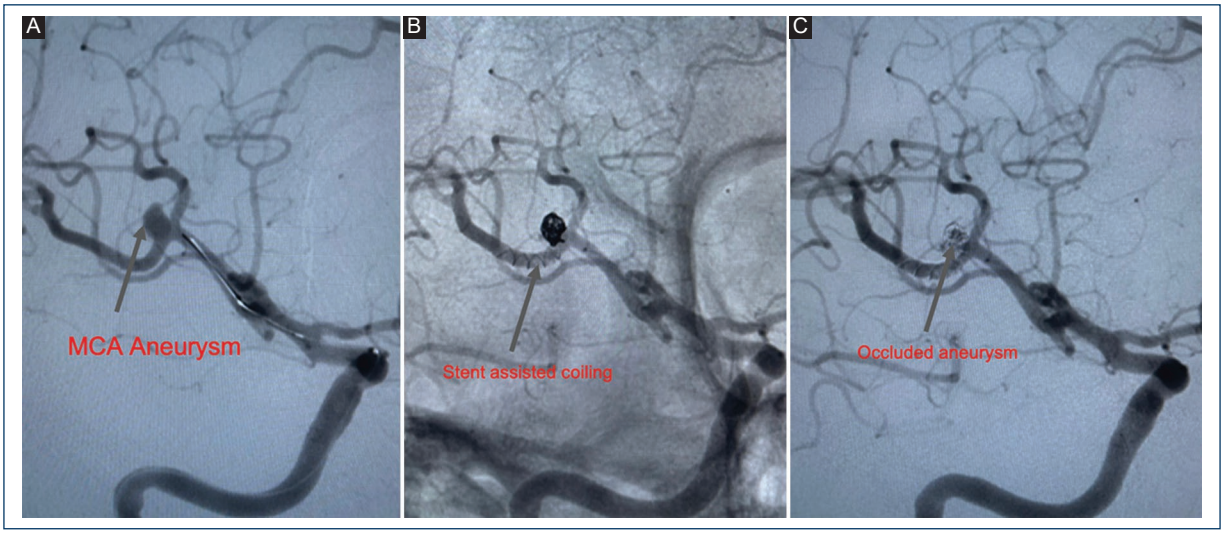

Figure 2. Digital subtraction angiography illustrating the endovascular treatment of a middle cerebral artery (MCA) aneurysm. **A:** initial angiogram shows an MCA aneurysm. **B:** stent-assisted coiling procedure. **C:** follow-up angiogram confirming complete occlusion of the aneurysm.

by El Naamani et al.[26], mentions that the WEB-device-treated patients had a higher occlusion rate in the 6-month assessment. Overall, most of the studies affirm that the WEB device is comparable to SAC in terms of safety and efficacy.

The WEB device may well replace SAC and other coiling techniques in the future. However, the costs of the device and the training should decrease significantly first to become a first-line treatment in places with limited resources. This includes subsidized healthcare systems and underfunded systems.

In addition, time considerations should be considered when deciding on an endovascular treatment for unruptured aneurysms. While the use of SAC can confirm an immediate occlusion of the aneurysm, the use of intrasaccular devices requires at least a follow-up for 3 months to confirm successful occlusion[12,15].

In contrast, the SAC requires a longer use of DAPT than the WEB device. At least 6 months of anti-aggregation therapy must be completed after SAC to effectively reduce post-treatment thrombotic complications[12]. This carries an inherent risk of unintended bleeding, yet most of the patients who present this complication suffer from minor episodes, as was the case in our study.

We consider that the WEB device deployment technique requires a lower number of repetitions to achieve procedure mastery than SAC. More specifically, the jailing technique for SAC involves a higher-level

complexity that requires a higher number of cases to completely develop. The use of a technique that requires a lower number of cases to learn implies a lower exposure to radiation during training, hence becoming a safer technique.

A future approach to treating wide-necked bifurcation intracranial aneurysms with intrasaccular devices such as the WEB system faces several limitations. One of the primary challenges is the high cost of the device, which restricts its widespread adoption, particularly in health-care systems with limited resources or those reliant on public funding. In addition, the requirement for specialized training in its deployment remains a barrier, as widespread proficiency among interventional neuroradiologists has yet to be achieved. Another limitation is the necessity for follow-up imaging to confirm aneurysm occlusion, unlike SAC, which provides immediate confirmation. This follow-up requirement may lead to delays in treatment adjustments if needed. Furthermore, while the WEB device reduces the need for DAPT, its long-term durability and effectiveness compared to SAC or flow diverters require further investigation through larger, long-term studies.

Moreover, the small sample size in this study limits the generalizability of the results. The findings, while promising, should be viewed as preliminary, and larger studies with higher statistical power are necessary to confirm these results and provide a more robust comparison between treatment approaches. Overcoming these limitations will be essential for intrasaccular devices to become a standard first-line treatment in the future.

Conclusion

In our institution, intracranial wide-neck aneurysms located at the AComA and MCA bifurcation demonstrated a high occlusion rate and a low complication rate, regardless of the device used for endovascular therapy. No statistically significant differences were observed between the WEB and SAC groups. Both techniques offer distinct advantages, and an individualized approach should guide the choice of technique used.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that this study was carried out according to the guidelines stated by the Helsinki Declaration and the Mexican General Law of Health. This study was assessed as a class I study under the National Regulations for Research in Healthcare. The research protocol was approved by the IRB of the National Institute of Neurology and Neurosurgery under Resolution #115/22.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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ORIGINAL ARTICLE

Prevalence of palliative care consultation in hematologic and oncologic patients admitted to the intensive care unit

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Abstract

Introduction: *Palliative care should currently be integrated into the treatment of a patient with terminal or progressive disease from the time of diagnosis, including patients who may require admission to the intensive care unit (ICU). Incorporating palliative care in ICU patients improves patient and caregiver satisfaction, reduces days of stay in the unit, and redirects treatment objectives toward guidelines such as "do not intubate/do not resuscitate" or discharge of patients to palliative care centers.* **Objective:** *The primary objective was to determine the proportion of hematologic and oncologic patients with advanced disease at admission to the ICU who had a palliative care consultation early or before admission.* **Material and methods:** *Cross-sectional, observational, descriptive study. Records of patients over 18 years of age, with advanced oncological and/or hematological disease who were admitted to the central ICU and Oncology of the Hospital General de México Dr. Eduardo Liceaga in 2023 were studied.* **Results:** *Of 40 records studied, 15% received a palliative consultation, of which only 5% were generated within the ICU.* **Conclusion:** *This study showed that 15% of patients admitted to the ICU received a palliative consultation, showing a need to integrate palliative care into the standard of patient care in the ICU.*

Keywords: *Palliative care. Hematology. Oncology. Intensive care unit.*

Introduction

The World Health Organization (WHO) defines palliative care as "an approach that improves the quality of life of patients and their families facing problems associated with life-threatening diseases, through the prevention and alleviation of suffering through early identification, impeccable assessment, and treatment of pain and other problems: physical, psychological, social, and spiritual"[1]. The term "palliative care" is popular, but it is often mistakenly considered identical to "end-of-life care" without any treatment. Up to 75% of patients admitted to the intensive care unit (ICU) experience distressing symptoms, derived from the critical state of the disease, invasive treatments, and the uncertainty of the prognosis, which make the ICU a "hell" for critical patients and their families[2]. Currently, about 10-30% of the world's deceased patients die in the ICU. Many symptoms commonly found in palliative care practice, such as pain, thirst, anxiety, sleep disturbances, and dyspnea, develop in critically ill patients and persist even after discharge from the ICU.

It is important to mention that the family member or primary caregiver may develop symptoms such as psychological and physical distress, including depression, fear, anxiety, fatigue, anorexia, and early symptoms of

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post-traumatic stress, resulting in a post-intensive care syndrome of the family member. In addition, the ICU physician is at risk of emotional and psychological distress when faced with these scenarios[3]. In the recent past, cancer patients were discouraged from being admitted to the ICU due to the risk of unfavorable outcomes. However, the number of patients who may benefit from ICU support has increased, with improved survival rates increasing in several subgroups of patients who were assumed to have adverse outcomes, such as hematopoietic stem cell transplant patients, acute respiratory failure, acute kidney failure, and even patients who received urgent chemotherapy while in the ICU[4].

In hematological patients, there are recommendations in which patients require admission to the ICU, such as the presence of sepsis, respiratory failure, tumor lysis, neutropenic fever, and complications secondary to acute promyelocytic leukemia[5,6]. The ICU environment is affected by high mortality and great suffering, so providing palliative care to critically ill patients and their families is an important goal of care in this setting. Palliative care aims to maintain and improve the quality of life of all patients and their families at any stage of a life-threatening illness[3,7]. The cornerstone of palliative care is patient-centered decision-making. In the case of acute clinical deterioration of ICU patients, which is usually unexpected and with unpredictable results, the role of palliative care becomes less clear, with particular challenges in its implementation[8,9].

A dilemma to consider, both for the patient inside or outside the ICU, is to determine the ideal time to start palliative care. There are three models of care to provide palliative care: (1) the traditional model in which palliative care begins once it has been determined that the disease is out of curative treatment; (2) the early and progressive model in which the transition from curative to palliative care is usually gradual, rather than a specific moment in time, starting as the objective of treatment ceases to be the prolongation of life at any cost and becomes the quality of life; (3) the dynamic model in which palliative care begins at any time of the disease, including moments of crisis in the early stages of the disease[10]. With current models of palliative care, we must understand that palliative care is not the result of failed attempts at care to prolong life, but rather a component of comprehensive care for critically ill patients from the moment they are admitted to the ICU[11]. Around 10-30% of the world's deceased patients die in the ICU[12], so all patients receiving curative treatment should receive palliative care simultaneously and individualized according to the needs and preferences of the patient and their family, as well as discussions of changes in care objectives and adjustments in treatment early in the ICU[3].

Limiting palliative care to "end-of-life" issues is insufficient[13]. The American Society of Clinical Oncology recommends that the combination of standard cancer care and palliative care be considered early in the course of the disease for any patient with metastatic cancer and/or a high symptom burden, i.e., from the time of initial diagnosis, including patients with treatment options in whom life expectancy may still be several years[14]. Despite advances in the field of palliative care and critical medicine, the role of palliative care in the ICU is still not recognized, and there is no consensus on the fundamentals of ICU palliative care practice. The goal of palliative care in the ICU is to foster the development of better-quality care centered on the patient and family from the moment of admission to the ICU[15].

In 2017, Ma et al.[16] conducted a randomized clinical trial at a center in the United States to evaluate whether early palliative care consultation in the ICU could improve patient outcomes and positively impact care compared to standard care. It was intuited that palliative care consultation would increase the decision toward do-not-resuscitate/intubation orders, decrease ICU stay, and use of post-ICU resources. A total of 242 patients were studied, of which 117 patients were assigned to the intervention group and 116 were assigned to the usual treatment group. The first result was that the transition to a do-not-resuscitate/intubation order was significantly greater in the intervention group (50.5%) compared to standard management (23.4%), with a risk difference of +27% (95% confidence interval, 13.6-39.1%; $p < 0.0001$). The secondary outcomes obtained were: discharge to a hospice was higher in the intervention group with 18.6% versus 4.9%; $p = 0.0026$; the duration of mechanical ventilation was shorter by 2 days in the intervention group (4 vs. 6 days; $p = 0.0415$); Tracheostomy during hospitalization was lower in the intervention group (1.0% vs. 7.8%; $p = 0.0354$). In terms of operating costs, care was found in the intervention group of $37,310 USD compared to the control group of $45,790 USD, which was not significantly different ($p = 0.1353$). This study concluded that early palliative care intervention led by experienced and certified palliative care clinicians significantly influenced the decision of a no-resuscitation/intubation guideline, hospice referrals, and the use of medical resources.

In 2022, Rao et al.[17] conducted a systematic review in which they sought to answer what is known about the provision of palliative care in ICUs in low- and middle-income countries. A total of 30 studies, mainly from South Asia and Africa, were included in this review. The areas that were commonly studied were the suspension and withdrawal of treatment; professional knowledge and skills in palliative care, opinions of patients and relatives; culture and context, as well as costs of care. The authors conclude that palliative care in ICUs in low- and middle-income countries is understudied, so research focused on the specific needs of the units is required to ensure optimal outcomes for patients. Helgeson et al. in 2023[18] conducted a prospective, randomized, unblinded clinical trial in a center in the United States that aimed to demonstrate that early palliative consultation (within the first 24 h) would increase patient or caregiver satisfaction as a primary endpoint. In addition, as secondary objectives, ICU stay, code change to do not resuscitate/intubate, admission to a palliative care center, ICU, and hospital mortality. The study included 91 patients, of whom 50 patients were assigned to receive early palliative care and 41 were assigned to receive standard of care, of which 11 patients received palliative consultation 8 days after admission to the ICU. To measure the degree of satisfaction, the family satisfaction 24-ICU survey was applied, obtaining a mean score of 92 points compared to 69 points, with a difference of 23 points and a $p < 0.001$, indicating greater satisfaction in patients who received early palliative care. Secondary outcomes included fewer days of stay in the intervention group (3 days vs. 8 days; $p = 0.018$), greater caregiver satisfaction (93 points vs. 69 points; $p = 0.001$), greater referral to a palliative care center (21% vs. 6%; $p = 0.04$), and greater decisions not to resuscitate/not to intubate (28% vs. 14%; $p = 0.037$); no significance was obtained in terms of lower mortality in the ICU (14% vs. 18% $p = 0.11$). The authors of this study conclude that palliative medicine consultation within 24 h of ICU admission significantly decreased the length of ICU stay and improved patient satisfaction.

Currently, there are no data in Mexico on how many palliative care consultations patients admitted to the ICU receive and whether these impact the course of stay within this unit, so starting to generate data and evidence is necessary to substantiate the need to include palliative care in the care of critical patients within the ICU, since the development of techniques for early detection and the treatment of cancer patients has led to a significant increase in survival rates and the need for ICU admission. Our hospital is no exception; however, it is extremely important to document how many patients with oncological or hematological disease who are admitted to the ICU receive prior consultation for palliative care or an early assessment.

The main objective of this study was to determine the proportion of hematological and oncological patients admitted to the ICU who had an early Palliative Care assessment or consultation before admission.

Materials and methods

An observational, cross-sectional, and descriptive study was carried out with records of patients admitted to the intensive medical care or oncology ICU of the *Hospital General de México Dr. Eduardo Liceaga* during 2023. Adult patients over 18 years of age, with a diagnosis of oncological and/or hematological disease in clinical stage III or IV, and who have been admitted to the aforementioned units during the year 2023, were considered for inclusion criteria. The exclusion criteria were taken into account: (a) records of patients with readmission to the intensive medical unit or oncology intensive care, (b) patients without a biopsy result that confirmed the diagnosis of the disease, (c) death in the first 24 h of admission. This study protocol was approved by the Research Protocol Evaluation Committee of the *Hospital General de México Dr. Eduardo Liceaga,* with approval number DECS/UPO-CT-2555-2024 under the ethical and confidentiality principles of data contemplated by said committee. The data from the files was obtained with information provided by the statistics department and the electronic file software of the *Hospital General de México Dr. Eduardo Liceaga*.

Results

A total of 40 files of patients admitted during 2023 to the Central ICU and Oncology ICU of the *Hospital General de México Dr. Eduardo Liceaga* were studied. Within the demographic characteristics, it was found that the most frequent sex was female with 21 patients (52.5 %) and male 19 patients (47.5 %); The age of the patients studied ranged from 21 to 76 years (mean of 49.4 years). Regarding the basic diagnosis, 25 patients (62.5%) had oncological diseases, that is, solid tumors, and 15 patients (37.5%) had hematological diseases. The average score of the APACHE II scale at the time of admission was 17.8 (range of 12 to 35 points).

Of the types of oncological or hematological diseases with the highest prevalence found, breast, thyroid, and cervical cancer stand out, which together accounted for 40% of the cases studied, followed by intestinal tumors with 20% and acute lymphoblastic leukemia with 15% (Table 1). It is important to mention that although the patients in this study had an oncological or hematological diagnosis as the basis, the reason why they needed care in an ICU was not due in the first instance to the underlying condition, so the main causes that motivated admission to the units were described, which were septic shock in 37.5%. Sepsis of any focus in 20% and hypovolemic shock in 12.5% (Table 2 and Fig. 1). Regarding the main objective of this study, which is to describe the prevalence of palliative consultation in these units, it was obtained that of the 40 files studied, 6 (15 %) received a palliative consultation. Of these, 2 (5 %) patients received an early consultation, and 4 (10 %) patients had received a previous palliative consultation.

Table 1. Oncological or hematological diagnosis

Cancer site	Frequency	%
Brain	3	7.5
ALL	6	15
AML	3	7.5
Ovary	1	2.5
Pancreas	2	5.0
Retroperitoneum	1	2.5
Intestinal	8	20.0
Other	16	40.0
Total	40	100.0

ALL: acute lymphoblastic leukemia; AML: acute myeloid leukemia. In the other section, it includes breast, thyroid, and cervical cancer.

Table 2. Admission diagnoses (reason for admission to the intensive care unit)

Diagnosis	Frequency	%
Septic Shock	15	37.5
Sepsis	8	20
Hypovolemic shock	5	12.5
Exploratory laparotomy	1	2.5
Status epilepticus	1	2.5
Gastrectomy	1	2.5
Acute kidney injury	1	2.5
Tumour lysis	1	2.5
Post-surgical abdominal	1	2.5
Post-surgical bowel resection	1	2.5
Post-surgical craniotomy	1	2.5
Post-surgical hemicolectomy	1	2.5
Post-surgical Whipple	1	2.5
Colon resection	1	2.5
Cardiorenal syndrome	1	2.5
Total	40	100

Discussion

This is the first study of its kind to be carried out in Mexico, since even at the international level, the way in which palliative care can enter ICUs has not been solidly established. When looking for literature on palliative care in the ICUs of the country, it is practically non-existent, which is a good contribution that is made here.

During the performance of this study, one of the inclusion criteria was redirected, which included patients with high mortality, as measured by the APACHE II scale, however, it is difficult to have this criterion given that although the oncological or hematological diagnosis should not be a reason to deny admission to the ICU, it is logical that a high mortality score is a conditioning factor for admission to the ICU in any situation and not only in cancer, so the vast majority of the files studied show a reason for admission due to a critical condition but whose mortality did not reach more than 85%. Sepsis and septic shock continue to have the highest prevalence of ICU admission, even in this study. Hypovolemic shock followed the prevalence of conditions that needed intensive care. It is important to mention that most hypovolemic shocks were of hemorrhagic origin during surgical procedures in most cases.

It is noteworthy that only 15% of the patients studied received palliative consultation; however, when analyzing this figure, it is even more important to note that only 5% of these consultations were carried out early (< 24 h of stay) during the ICU hospitalization, since 10% of the palliative consultations were prior, that is, at some point in the course of the disease, palliative consultation was received; the cases to which palliative care was granted in this study are described in table 3.

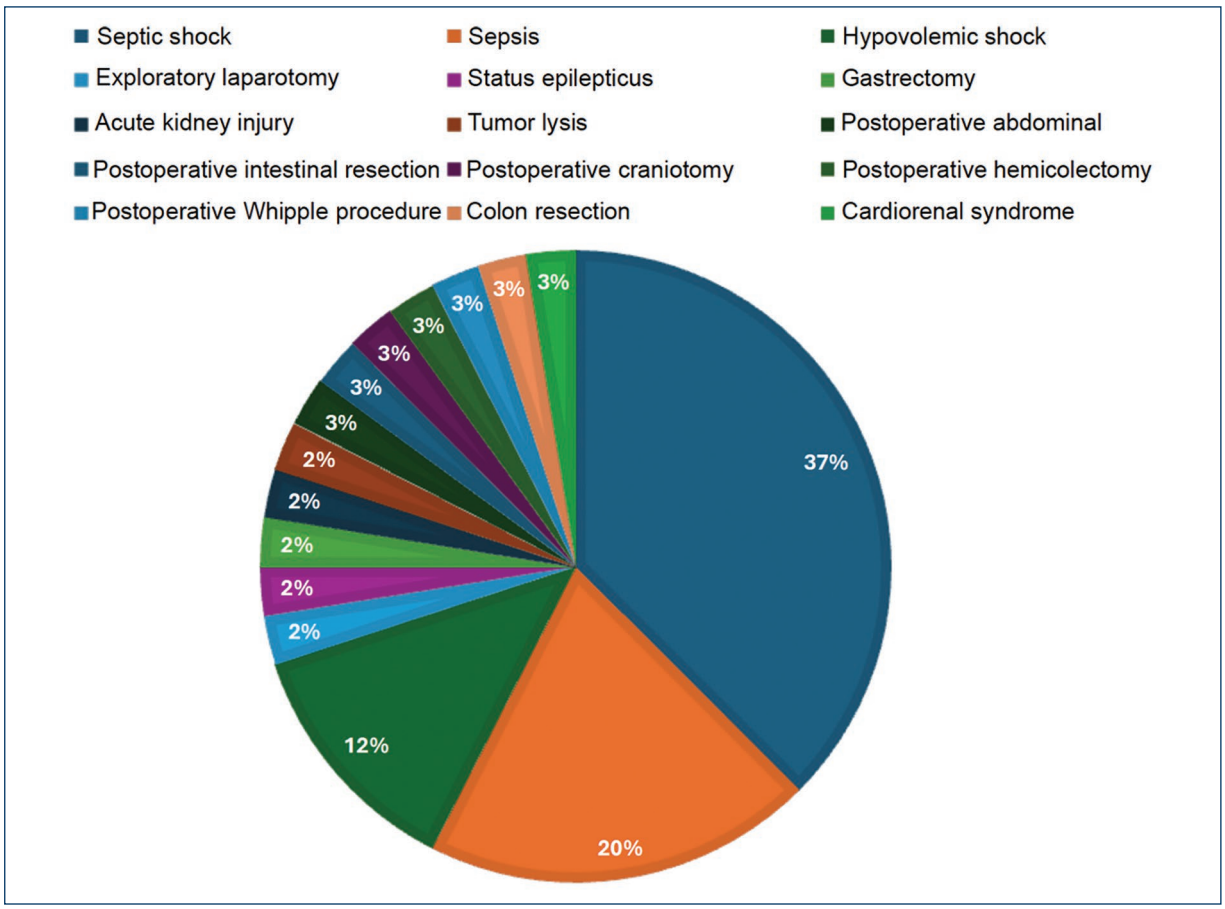

Figure 1. Diagnosis of admission to the intensive care unit.

Table 3. Patients who were granted palliative care

Patient	Gender	Age (years)	Diagnosis	Reason for admission to the ICU	Palliative assessment scales	Palliative treatment
CP_005	Woman	55	Ileocecal valve tumor with lung metastasis	Sepsis	Karnofsky index 30%, PPS 30, ECOG 4	Analgesia, treatment of dyspnea
CP_009	Man	53	Colon adenocarcinoma/ Gastric adenocarcinoma	Post-surgical colectomy	Karnofsky index 80%	Analgesia, information on palliative care philosophy, and thanatological consultation
CP_018	Woman	31	Acute lymphoblastic leukemia/Down syndrome/ Tracheostomy status/Absence seizures/Hypothyroidism	Septic shock	Karnofsky index 50%, ECOG 2	Analgesia, constipation treatment, nausea and vomiting treatment, and home care plan
CP_026	Man	21	Acute lymphoblastic leukemia	Septic shock	Karnofsky index 50%, PAP score 6.5 points, PPI 6 points	Analgesia, delirium treatment, dyspnea treatment
CP_031	Woman	39	Colon cancer	Post-surgical hemicolectomy/ Sepsis	Karnofsky index 50%, PAP Score 10 points, ECOG 3	Analgesia, treatment of opioid side effects
CP_032	Man	44	Acute lymphoblastic leukemia	Sepsis	Karnofsky index 60%, ECOG 2	Analgesia, mucositis treatment

PPS: palliative performance scale; ECOG: Eastern Cooperative Oncology Group; PAP: palliative prognostic score; PPI: palliative prognostic index, ICU: intensive care unit.

This result is consistent with the one provided by the WHO[19] in 2018, which takes into account the global population and not specifically ICU care, reporting that only 14% of people who need palliative care receive it. However, the prevalence of palliative care in this study is lower than that found in other articles that report the need for palliative care within ICUs; the studies are referred to in table 4[1,20-23].

An important fact to mention in this section is that the request for ICU consultation to the Pain Clinic of the *Hospital General de México Dr. Eduardo Liceaga* is made more frequently; however, generally the request is for analgesic treatment. Here, an area of opportunity opens up for ICU staff to request palliative assistance more frequently, and for the pain clinic staff to address not only the analgesic part, but also the patient as an integral being with psychological and spiritual needs, in addition to the physical ones.

Continue with this type of research in other centers or in a multicenter way, also studying other results that the evidence shows as benefits for patients who receive palliative consultation within the ICU, such as greater patient and family satisfaction, fewer days of stay, decision to adequate therapeutic efforts, and greater decisions for orders not to resuscitate or intubate. It is important to continue adding palliative care as a standard of care within ICUs.

Another important aspect to mention is that palliative care should not be limited to the population with oncological/hematological disease, since even at the global level, the WHO[19] refers that the diseases that most require palliative care are cardiovascular conditions in up to 38.5%, followed by conditions such as chronic respiratory diseases in 10.3%. Acquired immunodeficiency syndrome in 5.7% and diabetes in 4.6%; cancer has a demand for care of 34%. The clinical entities referred to above have serious complications that at some point may require attention within an ICU, which further reinforces the idea that palliative care and intensive care must work more closely to provide comprehensive care to the patient.

This can be compared with recent publications, such as the one by Salins et al. in 2024[24], reporting that the need for palliative and end-of-life care in ICUs around the world is often overlooked, mentioning that about 88% of older people have at least one need for palliative care, and patients in the neurological ICU have need rates of up to 62%. This group concludes that comprehensive ICU care planning includes ethical consultation, family education, proactive participation of the palliative care team, discussions about goals of care, and advance planning; it is also recommended that ICU professional teams should have experience in the management of terminal symptoms, as most patients in ICUs experience distressing symptoms such as delirium.

Table 4. Palliative care in the ICU

Author	Year	Type of study	Number of patients	Need for palliative care (%)
Puntillo et al.[20]	2010	Prospective, observational	171	27 a 75
Baldwin et al.[21]	2013	Retrospective cohort	442	88
Hua et al.[22]	2014	Retrospective cohort	53,124	13.3 a 15.8
Creutzfeldt et al.[23]	2015	Prospective cohort	130	62
Neukirchen et al.[1]	2023	Literature review	NA	14 a 20

NA: not applicable; ICU: intensive care unit. Hua et al.[22], Creutzfeldt et al.[23], Neukirchen et al.[1], Salins et al.[24], Chung et al.[25].

Another important aspect to consider when incorporating a non-usual service into the standard care of another unit, such as the ICU, is costs, and in this area, another recent publication was the one carried out by Chung et al. in 2025 in Texas[25] in which patients who receive palliative care reduce the total cost of care by 21% compared to patients who receive usual care. Leaving an opportunity for resource efficiency by incorporating palliative care into routine ICU care.

Little by little, some opinion leading societies in intensive care medicine have addressed the issue, such as the Society of Medicine and Critical Care in the United States, as mentioned above, and the European Society of Medicine and Intensive Care, who in 2024 published guidelines for end-of-life care and palliative care in the ICU[26], who issued different recommendations, two of which are of high level of evidence: (1) implement written communication tools such as brochures or flyers designed for families of ICU patients in all ICUs as a complement to standard oral communication, (2) propose brochures or flyers about grief, combined with structured family meetings before death, to the families of patients at the end of life. With these examples, we can see that palliative care should not be alien to care within the ICU. Providing palliative care to patients who deserve it is not only an indicator of quality, but also that medical practice is carried out with humanity, and it is that as health professionals and mainly in the

medical branch we focus on curing the disease and relieving physical symptoms; the lack of incursion into palliative care makes us put aside psychological needs, emotional and spiritual aspects of patients.

Conclusion

This study shows that of 40 patients admitted to the ICU of our hospital (central or oncology), only 15% received a palliative consultation, and of these, only 5% were requested in the ICU. This study opens the opportunity to carry out more research on the impact that palliative care can generate in patients hospitalized in the ICU.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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REVIEW ARTICLE

Patient blood management program: individualized approach and strategies for optimization based on three pillars

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Abstract

Implementing the patient blood management (PBM) program is a new concept in our country. It is responsible for optimizing the use of blood components, minimizing their administration, and replacing them with other agents, such as thrombopoietin receptor analogs. However, the main objective is to improve the patient's outcome. The PBM addresses three main pillars, the first includes the comprehensive evaluation of the patient, a situation that involves the anesthesiologist and physicians related to the program. The second pillar is to reduce blood loss through minimally invasive methods, antifibrinolytics, and blood recovery systems. The third is based on the patient's tolerance to anemia, increasing oxemia, and maintaining operative volemia. The relevance of these initiatives in Mexico is to improve the management of blood resources, causing a considerable impact on public health and its sustainability.

Keywords: *Transfusion. Blood Management Program. Blood component. Blood derivative. Hemorrhage.*

Introduction

The concept of a patient blood management (PBM) program was created by the Australian hematologist James Isbister in 2005, whose objective is to optimize the use of blood components, minimizing their administration by replacing them with some other agents, such as erythropoiesis stimulants and, more recently, the use of thrombopoietin receptor analogs[1]. Within the definitions established by the Society for Advanced Blood Management, it is considered that, although reducing transfusion requirements is one of the objectives, the main one is to improve patient outcome[2]. This concept is novel since it focuses attention on the patient, prioritizing hemostatic resuscitation through tools such as viscoelastic tests, patient tolerance to anemia, instituting the autotransfusion policy, and the timely intervention of a multidisciplinary team that includes medical, surgical, and laboratory personnel[1].

The blood management program addresses three main concepts, the first includes the comprehensive evaluation of the patient, a situation that involves the anesthesiologist and physicians familiar with the program, the second pillar is to reduce blood loss through minimally invasive methods, antifibrinolytics and blood recovery systems and the third that is based on the patient's tolerance to anemia, increase oxemia and maintain operative volume[3]. Although the blood management program is based on three fundamental pillars, the second of them is the one that is most frequently

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applied by the surgical teams, made up of the surgeon and the anesthesiologist. In our hospital, being a national reference center, the implementation of the blood management program has demonstrated several challenges, the main ones being the acceptance and use of the different blood derivatives and replacing all the components, followed by the incorporation of a multidisciplinary team for the comprehensive assessment of the patient. At the moment, PBM remains an alternative, with a view to constituting a new health policy to reduce costs and complications around any surgical event.

Although the strategy considers a comprehensive approach based on three pillars, to a greater or lesser extent, each one is applied in routine surgical practice. The ultimate goal of the strategy is to have a coordinated strategy whose objective is not only to save blood components, but also to prevent complications associated with the administration of the different components, reducing hospital stay and morbidity.

First pillar. Anemia: comprehensive patient assessment

Patient assessment is essential to reduce the different risks in both surgical patients and patients under any medical situation. This pillar is implemented by a multidisciplinary group that includes specialist doctors familiar with iron supplementation (internists or hematologists). Anemia is the most common perioperative situation (25-40%). It should be detected and managed before the surgical procedure, and transfusion should be avoided only by the hemoglobin level (e.g., 7 g/dL)[4]. The importance of detecting and correcting anemia is due to the fact that it is significantly associated with an increase in mortality (odds ratio [OR], 2.09; 95% confidence interval [CI], 1.48-2.95) as well as an increase in morbidity[5]. Globally, the World Health Organization considers perioperative anemia when the hemoglobin level is < 13 g/dL in men and 12 g/dL in women, but figures below 11 g/dL are associated with higher in-hospital mortality and a longer length of stay. On this, the most frequent cause of anemia is iron deficiency; its diagnosis is based on the abnormality in iron dynamics (the binding capacity of iron to transferrin, the percentage of saturation, and ferritin)[6]. This evaluation should be made in those individuals who are expected to lose more than 500cc or with a 10% risk of requiring transfusion support during the operative procedure. Despite this, not all patients have anemia, since there are states of iron depletion that can increase hospital morbidity. Ferritin is the parameter of choice for the diagnosis of iron deficiency (< 15 μg/L in adults and < 12 μg/L in children) and in states of iron depletion, but other circumstances such as chronic anemia may cause a significant increase in ferritin (> 100 μg/L), requiring the use of other parameters of iron dynamics for diagnosis (e.g, the percentage of transferrin saturation < 20%)[7]. After diagnosis, it is important to initiate replacement orally or by parenteral formulations. Ng et al. in their review of six randomized clinical trials identified that, although oral iron administration did not reduce blood component administration, parenteral formulations achieved a more rapid improvement in both hemoglobin and iron reserve[8].

Most studies evaluating perioperative management include intravenous formulations and agree on the benefits of pre-operative administration, both for increasing hemoglobin and reducing transfusion requirements. However, due to the heterogeneity of the studies in terms of type of surgery, estimated losses, and time of administration, it is difficult to establish robust recommendations[9]. Another option includes the combination of parenteral iron in conjunction with erythropoietin, on this Donat Spahn and collaborators in a randomized double-blind trial in patients who would undergo elective cardiac surgery (505 patients with anemia or iron depletion) reported the benefit of the administration of reduced doses of parenteral iron in conjunction with erythropoietin (20 mg/kg ferric carboxymaltolate, 40,000 U of subcutaneous erythropoietin alpha), subcutaneous Vitamin B12, and folates on hemoglobin levels, reticulocytes, and reduction in erythrocyte unit transfusion requirements[10].

This has been replicated in several series where the combination of iron, erythropoietin, or other hematins is useful for the management of perioperative anemia. In this regard, in cardiovascular surgery, Weltert et al. reported the benefit of erythropoietin administration (80,000 units of recombinant erythropoietin) 2 days before surgery, identifying that individuals with a figure < 13 g/dL are the ones who benefited the most, significantly reducing transfusion needs ($p < 0.0005$)[11]. The combination of carboxymaltose iron with erythropoietin has been tested in other types of surgeries. Bernabeu et al.[12] analyzed its benefit in patients undergoing hip surgery, demonstrating a benefit on hemoglobin recovery in the post-operative period (10.2 g/L vs. 9.7 g/L) as well as at 60 days, but without an impact on transfusion needs compared to the placebo group. This finding has also been replicated in other series where, despite the fact that the administration of iron before

Table 1. Useful strategies for the evaluation and management of perioperative anemia

Pillars	Intravenous iron	Drug	Presentation	Iron elemental	Infusion time (min)	Dose
First		Iron sucrose	100 mg/5 mL	100 mg	15 a 30	200 a 500 mg/day
		Ferric oxide saccharate	100 mg/5 mL	100 mg	30	100-200 mg
		Hierro dextran	100 mg/2 mL	50 mg/L	60	100-200 mg c/72 h
		Ferric carboxymaltose	500 mg/10 mL	50 mg/mL	15	500-1000 mg/day
	Erythropoietin	**Drug**	**Presentation**	**Route of administration**	**Half-life (hours)**	**Dose**
		Erythropoietin alfa	2000 UI/0.3 mL	SC, IV, IP	19	50-150 UI/kg 1-3 dose/week
		Erythropoietin beta	5000 UI/0.3 mL	SC, IV, IP	20	20-80 IU/kg 1-3 dose/week
		Darbepoetin alfa	300 µg/0.6 mL 500 µg/mL	SC, IV	73	0.45 µg/kg/weekly or c/2 weeks
Second	**Drug**	**Presentation**	**Route of administration**	**Latency (min)**	**Dose**	
	Prothrombin complex concentrate (FII, FVII, FIX, FX, Protein C and S)	500 UI/vial 1000 UI/vial	IV	5	25 IU/kg, maximum 5000 IU, at 8 mL/h	
	Tranexamic acid (Lysine analog)	650 mg 100 mg/mL	VO IV	10	1300 mg c/8 h 1g IV, infusion every 8 h	
	Human fibrinogen	1.5 g/100 mL	IV	60-90	2-4 g 25-50 mg/kg	
	Desmopressin	15 ug/mL Spray 10 µg/dose	IV	30	0.3 µg/kg maximum 20 µg 0.3 µg 2 h before the procedure	
	Cryoprecipitates (FVII, Fibrinogen, FXIII, Vwf)	Unit 5-15 mL	IV	4-12 h	1 unit/5 kg or 10 units	
	Fresh frozen plasma (Fibrinogen, albumin, protein C and S, antithrombin, tissue factor)	Unit 200-250 mL	IV	2-6 h	15-20 mL/kg each/6 h	

SC: subcutaneous; IV: intravenous; PI: intraperitoneal.

surgery improves hemoglobin levels in the post-operative period, it has not been possible to reduce the need for transfusion[13], emphasizing that this requires minimization of blood loss and improvement of hemostatic resuscitation.

The administration of parenteral iron remains an inexpensive and accessible option in most Latin American countries. However, the main challenge lies in implementing effective strategies for its administration, which includes establishing adequate infusion areas and having trained personnel to monitor and manage potential adverse events. Table 1 presents some of the useful strategies for the evaluation and management of perioperative anemia.

Second pillar. Optimizing hemostasis, minimizing blood loss

Optimizing hemostasis is one of the key strategies for reducing blood loss during a surgical procedure. This measure, considered the second pillar of the blood management program, is implemented more frequently than is commonly recognized, both by the surgical team and by the anesthesiologist in its intraoperative

management. In Mexico, hemostatic resuscitation is performed primarily through the use of blood components. The most significant challenge lies in knowing and effectively applying the various types of blood products available (industrialized products) to optimize hemostasis and reduce blood loss.

Normally, the most frequently used blood components are fresh frozen plasma and cryoprecipitates, but there are currently different industrialized derivatives that can replace these blood components. Among the main ones is the concentration of activated prothrombin complex, fibrinogen, Von Willebrand factor, and tranexamic acid as antifibrinolytic therapy. The first is prothrombin complex concentrates (PCCs), which contain coagulation factors (II, IX, X or II, VII, IX, and X) whose hemostatic power is 25 times more potent than fresh frozen plasma, while it can contain heparin, protein C, and protein S[14]. van den Brink et al. in a meta-analysis identified that, although the use of prothrombin complex concentrates (PCC) reduces the need for the use of blood components, its administration does not impact mortality except for patients with trauma (OR = 0.64; CI, 0.46-0.88; p = 0.007)[15]. PCC was originally developed for the treatment of hemophilia B, but with different purified compounds of factor IX, the indications were reduced to the reversal of anticoagulation or congenital deficiency of other less frequent factors[16].

On this aspect, CCP has been analyzed as an option to replace the use of fresh frozen plasma, Ortmann et al. compared its use in patients undergoing endarctectomy, in the group in which CCP was used, a lower blood loss was shown (650 mL [325-1075] vs. 277 mL [175-608], p = 0.008), but without impact with the administration of erythrocyte packages[17]. Recently, Li et al. in a meta-analysis evaluating the benefit of the use of CCP in cardiac surgery agree that although there is no direct impact on mortality (relative risk [RR] = 1.18, 95% CI = 0.86-1.60, p = 0.30), electrical complications or hospital stay, a benefit was demonstrated in the length of stay in the intensive care unit and total bleeding (Mean difference = −248.67 mL, 95% CI = −465.36-−31.97, p = 0.02, I^2 = 84%)[18]. Although plasma can provide coagulation factors, the use of CCP shows certain advantages, such as its quick and easy administration, not requiring cross-referencing or the risk of adverse reaction, but still being limited by the lack of management algorithms outside of cardiac surgery or trauma[19]. For Latin America, the use of this derivative is an option, especially in those cases where rapid resolution of bleeding is required.

The second derivative is fibrinogen, which, similar to PCC, the blood component that provides the highest amount of fibrinogen is cryoprecipitates. This component is very useful in situations where fibrinogen is low or dysfunctional. Fibrinogen is a plasma glycoprotein that is synthesized at the hepatic level. It is the main substrate for the formation of fibrin, and its deficiency can be both congenital and acquired. Similar to other derivatives, the greatest evidence derives from trauma protocols; its benefit can be extended to other types of surgical scenarios[20]. In trauma, the dose is highly variable (2-9 g), as in cardiac surgery (25-50 mg/kg) and even in liver transplantation (50 mg/kg), emphasizing that its consumption is almost immediate for the formation of a clot, and the efficacy of this intervention must be carried out through different viscoelastic tests[21]. In the absence of fibrinogen supplements, the blood component that contains the highest amount is cryoprecipitates (10-20 g/L), but other components, such as fresh plasma (400 mg in 200-250 mL) or platelets (300 mg in 200-250 mL), contain minimal amounts[22]. Due to its dynamism and interaction with coagulation activation complexes, the strategy based on thromboelastography (TEG) is superior to a support based on hemostasis tests (prothrombin time, international normalized ratio, and partial thromboplastin time) in various situations, such as trauma or cardiac surgery, and there are even methods for calculating fibrinogen based on the amplitude of the rotational thromboelastometry (ROTEM)/FIBTEM (Fibrinogen thromboelastometry test) maximum clot firmness (MCF in FIBTEM) that are useful for optimizing fibrinogen supplementation[23].

Monitoring through viscoelastic testing

TEG and ROTEM are similar techniques used to assess hemostasis and blood clotting in real time. Both techniques measure the elasticity and stability of the clot formed in a whole blood sample (340 μL), but differ in their principle of operation[24]. TEG uses a piston or needle in the center of a cup that measures the resistance of the clot as the cup is gently rotated, generating a graph showing parameters such as reaction time (R), clot formation time (CFT) (K), α angle, maximum amplitude, and clot lysis at 30 min (LY30). On the other hand, the ROTEM rotates the cup instead of the piston and measures the resistance of the clot generated, providing equivalent parameters such as coagulation time, CFT, α angle, MCF, and clot LY30. ROTEM offers specific tests such as INTEM, EXTEM, FIBTEM, and APTEM, whereas

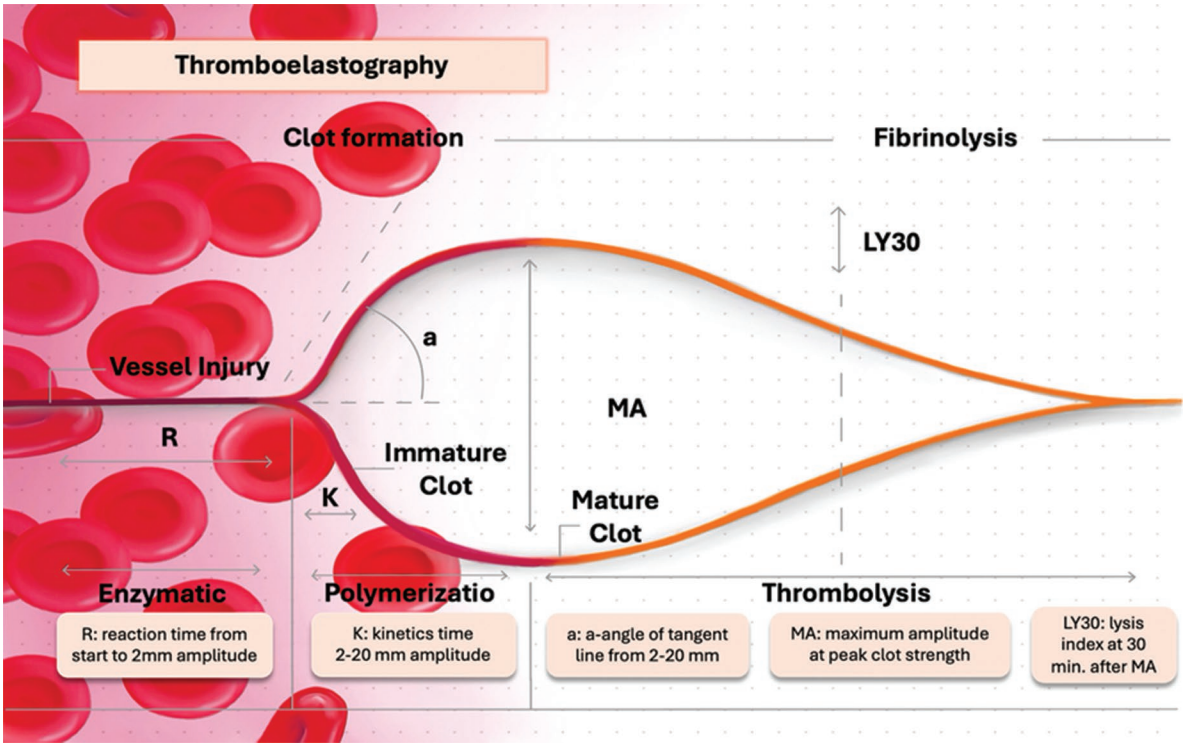

Figure 1. Phases of the thromboelastogram and how it is modified in different perioperative situations.

TEG has variations such as conventional TEG and with coagulation activators[25]. The choice between TEG and ROTEM depends on availability, but both allow for the establishment of guidelines for the transfusion of both components and blood derivatives during surgery, trauma, or situations that alter the stability of a clot, such as liver disease[26]. Various situations can affect the curve generated by the TEG or ROTEM, such as the use of anticoagulants, antiplatelet agents, deficiency of coagulation factors or states of fibrinolysis, giving for example a lengthening of the R time in situations such as severe bleeding or deficiency of coagulation factors, whereas in situations such as hypofibrinogenemia or dysfibrinogenemia the Alpha Angle will be reduced and in very severe states of fibrinolysis the Ly30 will be prolonged. In Mexico, hemostatic evaluation through different viscoelastic tests is becoming more and more common; its use has extended from liver transplantation to resuscitation strategies and, more recently, incorporation into PBM. The implementation of this type of program contributes not only to the saving of blood components but also allows the incorporation of new dynamic hemostatic monitoring strategies, such as viscoelastic tests. Fig. 1 illustrates the phases of the thromboelastogram and how it is modified in different perioperative situations.

Other interventions that optimize hemostatic control

In addition to both correct hemostatic monitoring and the administration of the different components or blood derivatives, there are other drugs that can modify the solidity of the clot, such as antifibrinolytics. Antifibrinolytics are a group of medications that inhibit fibrinolysis, the process by which the body breaks down fibrin clots. Among the best known are tranexamic acid, ε-aminocaproic acid (EACA), and aprotinin. Tranexamic acid works by blocking the binding of plasminogen to fibrin, thus preventing its degradation. It is widely used in surgery and in the treatment of heavy menstrual bleeding[27].

Devereaux et al. in one of the largest studies compared the benefit of tranexamic acid use versus placebo in patients with non-cardiovascular surgery (n = 9535 in total, 4757 treated with tranexamic acid), identifying that bleeding was lower (9.1% vs. 11.7%, RR, 0.76; 95% [CI], 0.67-0.87) in patients treated with tranexamic acid[28]. In civil trauma, the Clinical Randomization of an

Antifibrinolytic in Significant Hemorrhage (CRASH-2) study evaluated 20211 patients, identifying a significant reduction in in-hospital mortality who were administered tranexamic acid (1 g initial dose in 10 min, followed by 1 g every 8 h) compared to those who were administered a placebo (p = 0.0035). A sub-analysis of the CRASH-2 analysis identified that the time to initiation of antifibrinolytic therapy is critical, because early administration (< 1 h) significantly reduced bleeding-associated mortality compared to placebo[29]. This contrasts with the findings of the PATCH-trauma study in which tranexamic acid was administered before arrival at the hospital (1 g before arrival at the hospital and 8 h later), where there was no evidence of an impact on mortality at both 28 days and 6 months after the event[30]. EACA has a similar mechanism of action to tranexamic acid and is used to control bleeding in various clinical contexts, mainly surgical, with similar efficacy[31].

Another drug considered for perioperative loss reduction is desmopressin (DDAVP). This synthetic analog of vasopressin is widely used in mildly expressed congenital coagulation disorders (e.g., hemophilia A or B, Von Willebrand disease), both prophylactically and therapeutically. Outside this scenario, the administration of desmopressin has been evaluated in different surgical scenarios, showing a minimal effect on both the risk of bleeding, the number of blood units transfused, and blood loss, but increasing the risk of hypotension with clinical repercussions. In some clinical situations, such as a history of antiplatelet drug use, the use of DDAVP (0.4 μg/kg × 1 dose) may be beneficial, especially due to the release of factor VIII and von Willebrand factor through the platelet[32].

On this pillar, we can conclude that the timely identification of a bleeding disorder, the selection of the type of blood component, as well as the administration of various derivatives or adjuvants can improve the hemostatic velocity of the individual, reducing the use of blood units and hospital mortality.

Third pillar

The third pillar is based on the patient's tolerance to anemia; it is possibly the least known since it is implemented by the anesthesiology staff to improve the patient's tolerance to blood loss. This principle is based on the ability to release oxygen to each tissue, a situation that is modified by the individual's tolerance to the reduction of their blood volume. This is achieved by improving the individual's cardiovascular performance (avoiding hypotension), increasing arterial oxygen content through increased FiO_2, and preventing a septic process in the post-operative period[33]. Unlike animal models, humans can survive with hemoglobin levels < 2 g/dL, but from levels of 5 g/dL, changes in perfusion can be observed, so for safety reasons, the minimum hemoglobin level for a procedure was postulated between 7 and 8 g/dL. This pillar requires the participation of a multidisciplinary team that contributes to optimizing ventilation methods and resuscitation strategies. Some situations that require a higher hemoglobin level are neurotrauma, as well as in acute coronary syndromes, where the optimal hemoglobin level ranges from 9 g/dL[34]. Some situations that can contribute to greater blood loss are iatrogenic losses, such as taking multiple unnecessary samples, surgical incidents, or the non-use of blood recovery mechanisms.

The management program is a cost-effective option

The fractionation, processing, and storage (activity-based costing method) of blood is one of the parts that generates a constant cost in any hospital[35]. In Europe, Rigal et al. evaluated the cost of this process by establishing a cost of 339.64 euros per unit of blood transfused[36]. In our country, the cost is variable and depends on the type of institution (average of 1750 MXN for a public hospital and 5235 MXN for a private institution)[37]. Another indirect cost derives from the pre-transfusion process (blood typing, cross-testing). In this regard, our institution analyzed the proportion of units transfused over the number of units requested, with only 9.2% of the units requested transfused[38]. This makes any strategy to prevent the use of blood lower the costs of medical care, especially in procedures that require a high consumption of blood components. Roman et al. evaluated 393 randomized controlled trials, which included a total of 54,917 participants, demonstrating that blood management program (PBM) interventions significantly reduce the need for blood component transfusions (RR = 0.60; 95% CI 0.57-0.63; I^2 = 77%). However, no statistically significant impact was observed on mortality at 30 days or during hospitalization (RR = 0.93; 95% CI 0.81-1.07; I^2 = 0%). Although secondary and sensitivity analyses were consistent across clinical settings, intervention types, and study quality, network meta-analysis did not show additional benefits when combining PBM strategies. In addition, the authors concluded that while these interventions reduce transfusions and bleeding, no substantial clinical or economic benefits were achieved[39]. Finally, although the benefit is clear on the

consumption of blood components, more studies are needed in our region to evaluate the economic impact of these strategies.

Conclusion

We consider that the PBM is a useful strategy to save blood components and reduce the different complications related to transfusion. It focuses on the rationalization and optimization of both the components and the different industrialized derivatives in order to reduce morbidity and operative mortality. Despite this, there are still many challenges to implementing this approach in countries with limited resources or without a blood surveillance system. Finally, it should not be forgotten that these policies can generate significant savings in both the short and long term. The relevance of these initiatives is especially critical in Mexico, where improving blood resource management can have a considerable impact on public health and the sustainability of the health system.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

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HISTORY ARTICLE

Color blindness, a scientific perspective on the world of color

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Introduction

John Dalton's curiosity about his unique color perception led to the discovery of color blindness, a condition that affects the way we perceive color and challenged our understanding of human vision. His scientific legacy blazed a trail in the study of color perception and remains key to current research.

Fog drifts through stone and houses. Vines climb fences, and lush greenery blankets the land and hills; this is Eaglesfield, England. The tranquility of the village is disturbed by a piece of news: John Dalton, the chemist, mathematician, and naturalist best known for his work on atomic theory and the law of partial pressure, donated his eyes for scientific study after his death. What secrets did these eyes hold that Dalton was unwilling to reveal until after he left this world?

At the age of 28, Dalton realized that he saw the world in a different way. For him, colors were not the vivid explosions of tones that others described, but he experienced them as shades and indefinite contrasts. Far from being a limitation, this situation awakened in him an irresistible curiosity, a thirst for knowledge that would lead him to explore the darkest corners of his vision.

In 1794, John first described the visual defect he suffered from. He had discovered it by accident 2 years earlier when he gave his mother a pair of deep purple stockings. The color was inappropriate for a conservative woman of the time, so she was puzzled and asked her son why he had chosen that color. It was then that the young scientist realized that people perceive color differently than he does[1].

Dalton's curiosity and the experiments that revealed a new view of color

Following this event, he conducted an experiment in which he observed the color of a geranium flower illuminated by candlelight. In broad daylight, the flower would have appeared blue to him (its color was actually pink), however, under candlelight, he saw it as red. This observation was the beginning of an extensive study of color perception that led him to write "extraordinary facts relating to color vision" (1794), in which he described his experience in detail[2,3].

– "Although I had no doubt that such a change of color would be the same for all, I asked some of my friends to observe the phenomenon; I was surprised to find that they all agreed that the color was not substantially different from what it was in daylight, except in the case of my brother, who perceived the same change of color as I did"[3] (Fig. 1).

To Dalton, his color blindness was a mystery, and to solve it, he discussed it with his friends and students, hoping to find other people who had a vision problem similar to his and his brother's. He met several friends and a family in which all the male children suffered from this condition, which led him to conclude that this was an anomaly found only in males. Thus, he met several friends and a family in which all the male children suffered from this condition, leading him to conclude that it was an anomaly found only in men.

All these observations culminated in the identification of a pathology that would be called color blindness. Since then, the term achromatopsia has been widely used to refer to color blindness.

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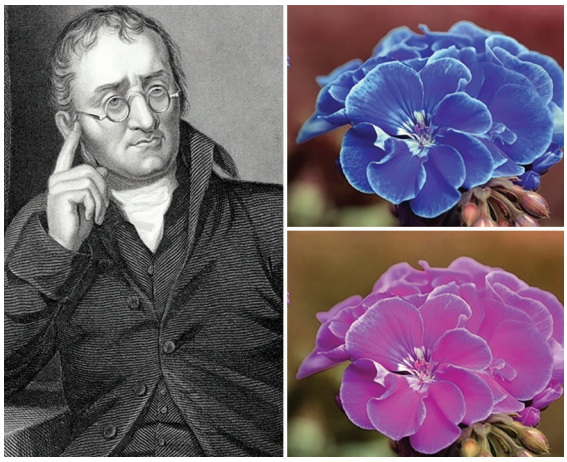

Figure 1. Photograph of John Dalton[8]. The geranium in blue as he perceived it (upper right image), the pink geranium in its original color (lower right image).

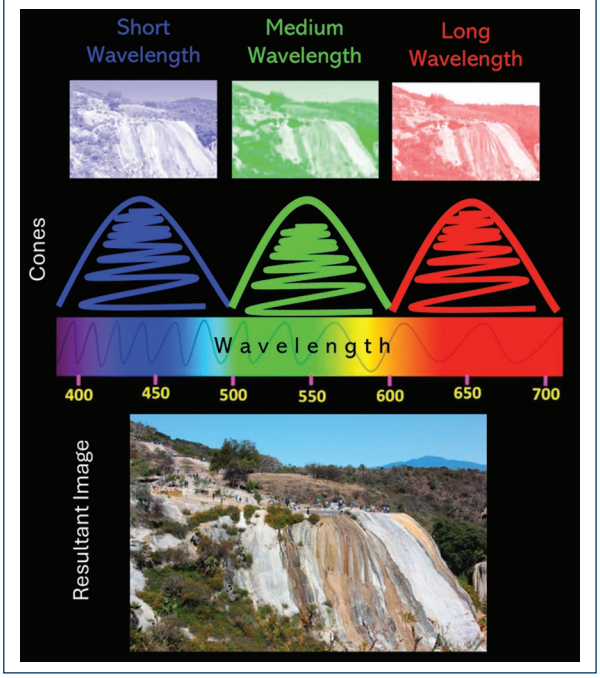

Figure 2. Description of the process in which the wavelengths of light are captured by the cones, generating the final perception of the landscape.

Dalton thought that his color blindness was due to the pigment within his vitreous humor (a clear, gelatinous fluid that fills the space between the inner surface of the retina and the back of the lens inside the eyeball), so he thought it would not be transparent as in a normal eye, but possibly blue and act as a red filter. To test this hypothesis, he would have had to perforate his eye to extract the vitreous, and he definitely did not consider that an option. Therefore, in his will, he directed that his eyes be extracted to test whether the vitreous humor was blue. The person responsible for carrying out this request was Joseph Ransome, his general practitioner[2].

A scientist's eyes: the autopsy that changed the study of color vision

John Dalton died on July 27, 1844, and as agreed, Ransome performed the autopsy the next day. He removed the vitreous humor from one of John's eyes, placed it over a lens, and described it as transparent. He removed the second eye, drilled a hole in it, and found that neither red nor green was distorted when viewed through it[4].

With this experiment, he rejected the hypothesis that color blindness was caused by a "preretinal filter" and concluded that the defect might be in the optic nerve that connects the retina to the brain.

Fortunately, Ransome had the good idea to preserve the eyes for further study. They were placed in a container with a preservative and remained in the custody of the Manchester Philosophical and Literary Society. They were later given to the Manchester Museum of Science and Industry for safekeeping[4].

In 1994, 150 years after Dalton's death, a group of Cambridge geneticists and physiologists resumed the analysis of the scientist's eyes. The researchers took a small sample of the retina to extract and amplify deoxyribonucleic acid to analyze the genes of the three types of retinal cones involved in color vision[4].

Cones are light-sensitive retinal cells responsible for color detection and perception. There are three types of cones, each sensitive to different wavelengths of light. There are cones sensitive to short wavelengths (blue), cones sensitive to medium wavelengths (green), and cones sensitive to long wavelengths (red). The combination of signals from these three types of cones allows the brain to perceive and distinguish a wide range of colors[5,6] (Fig. 2).

Dalton's genetic analysis revealed he was a deuterope, meaning he lacked sensitivity to medium wavelengths of light, critical for distinguishing greens[2].

John Dalton's eyes are much more than a sensory organ: they are a window into the vast and complex universe of human knowledge. His decision to donate them marked a milestone in scientific history, opening new doors to understanding a condition that had baffled mankind for centuries. Dalton's eyes became a

Table 1. Types of color blindness

Red-green color blindness	Blue-yellow color blindness	Complete color blindness
Deuteranomaly: the most common type of red-green color blindness. It causes certain shades of green to appear redder. This type is mild and usually does not interfere with normal activities.	Tritanomaly: makes it difficult to distinguish blue from green, yellow from red.	If you have total color blindness, you cannot see colors at all. This is also called monochromatopsia or achromatopsia and is rare. Depending on the type, you may also have trouble seeing clearly and be more sensitive to light.
Protanomaly: causes certain shades of red to appear greener and less bright. This type is mild and does not usually interfere with normal activities.	Tritanopia: makes it impossible to distinguish between blue and green, purple (violet) and red, and yellow and pink. It also makes colors seem less light.	
Protanopia and deuteranopia: both make you unable to distinguish between red and green.		

symbol of his commitment to the advancement of knowledge and his desire to leave a legacy for future generations.

Color variations: there is no single color blindness

Thanks to Dalton's curiosity and his unique gift, we now know a little more about color blindness. But you may be wondering, what does it mean that Dalton was color blind? isn't there only one type of color blindness, and do all people with this condition perceive colors in the same way?

To answer these questions, we need to know a little more about the cells involved in color perception.

Our eyes have two types of light-sensitive cells in the retina: rods (their function is to allow us to see in the dark) and cones, which require more light and allow us to see in color. As briefly mentioned above, there are three types of cones, and the difference between them is a function of the wavelength of light to which they respond[6].

For example, the short-wavelength (S) cones, known as blue cones, are less numerous than the other two types and are critical for the perception of blue and violet hues.

Mid-wavelength (M) cones, known as green cones, are more numerous than blue cones and play a critical role in the perception of green and yellow tones.

Long wavelength (L) sensitive cones, known as red cones, are the most abundant and are essential for the perception of reds, oranges, and yellows[6].

Color perception occurs by stimulating and combining these different types of cones in the retina. When light strikes the retina, cones sensitive to different wavelengths respond selectively, sending electrical signals to the brain that are interpreted as different colors. The combination of information from the three types of cones allows the brain to interpret a wide range of colors and distinguish between hues[5,6].

In color blindness, the function of the cones is altered due to genetic abnormalities in the light-sensitive pigments. These abnormalities can affect the sensitivity of the cones to certain wavelengths, resulting in difficulty perceiving and distinguishing certain colors. As a result, there are several types of color blindness, each associated with different cone abnormalities[5-7].

Deuteranopia is associated with difficulty distinguishing shades of green. It was the type of color blindness that John Dalton suffered from. Protanopia corresponds to individuals who have difficulty distinguishing reds. Finally, tritanopia, the least common condition, affects the perception of blue tones[5-7].

These are the main types of color blindness, although there are variations and combinations of these types that can affect color perception differently in each person. It is important to note that color blindness can vary in severity, from mild forms in which the individual can distinguish certain colors but with difficulty, to more severe forms in which color perception is severely affected[5,6] (Table 1).

Another important fact is that color blindness is binocular (it is present in a similar way in both eyes), it affects men more than women, since it is transmitted with recessive character associated with the X chromosome, so it is almost always of genetic origin. It can also be acquired as a result of injury or disease of the retina or optic nerve[5-7].

The study of color vision continues, and it is important to continue to support research that will help us better understand this condition and develop solutions that will allow those who suffer from it to fully enjoy a vibrant and colorful world.

From the scientific curiosity that led Dalton to study his own visual defect to the modern advances in genetics that have allowed us to unravel its many facets, the study of color blindness reminds us that perception is

not universal, but a kaleidoscope of individual conditions and experiences. By understanding these differences, we not only advance scientific knowledge but also promote empathy and inclusivity, ensuring diverse perceptions are valued and understood in society.

Conclusion

John Dalton's personal experience of color blindness marked the beginning of a scientific journey that transformed our understanding of color perception. His observations, followed by post-mortem studies and later genetic analysis, laid the foundation for modern vision and genetics research. The ongoing study of color blindness continues to emphasise the importance of recognising sensory diversity, not only to advance scientific knowledge, but also to promote inclusion and awareness in society.

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CLINICAL CASE

Neurogenic orthostatic hypotension after diabetic ketoacidosis in a Mazahua patient

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Abstract

Introduction: *Diabetes is a significant worldwide health issue. In Mexico, it was described as the second major cause of death, affecting 12.8 million individuals. In the Mazahua Indian communities, the incidence of diabetes is 20% higher than in other indigenous communities nationwide. The prevalence of neurogenic orthostatic hypotension (OH) and autonomic failure in these patients is unknown.* **Case description:** *A 56-year-old female with diabetes who developed neurogenic OH after a diabetic ketoacidosis episode.* **Conclusions:** *Recognition of neurogenic OH in hospitalized patients will help address the early diagnosis and assessment of autonomic failure.*

Keywords: *Neurogenic orthostatic hypotension. Diabetes. Autonomic failure. Hospitalized patients.*

Introduction

Diabetes is a common chronic disease worldwide. In Mexico, a recent study by Bello-Chavolla et al.[1] showed that 12 million individuals suffered from the disease. The acute complications related to diabetes received treatment in the emergency department (ED) of the second level of attention hospitals. The naive indigenous populations in Mexico represent 6% of the total population[2]. According to the study of Esparza-Romero et al., the highest prevalence of diabetes was reported among the Mixtec population from Baja California (26.2%) and the Yaquis population from Sonora (18.3%).

Mazahua Indian communities in the north of Mexico State have a notably high incidence of diabetes compared to other indigenous groups nationwide. The study by Conzuelo-González and Vizcarra-Bordi found that 20% of this community had diabetes with chronic complications and frequent acute decompensation episodes, even the most common cause in the emergency rooms of public hospitals in these areas[3].

Neurological complications of diabetes have been well described in Mexican patients; however, the autonomic dysfunction related to small fiber neuropathy has yet to be thoroughly researched in the indigenous Mexican population, and the prevalence of efferent baroreflex failure is unknown[4]. Patients with diabetic autonomic neuropathy exhibit efferent baroreflex failure, deficiency in plasma catecholamine release, and a loss of post-ganglionic sympathetic neurons, resulting in the denervation of the peripheral arterial vasculature and

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showing clinical features such as orthostatic hypotension (OH), supine nocturnal hypertension, and post-prandial hypotension.

Autonomic failure leads to a poor response in blood pressure to the gravidity challenge, such as arising from lying down to a standing position, resulting in OH. OH symptoms vary, with mild and non-significant features as light-headedness, dizziness, and coat-hanger pain to prodromic fainting symptoms or syncope, or in extreme cases, hypovolemic shock[6]. Severe cases often do not respond well to conventional treatments used in hospitalized patients.

Case presentation

A 56-year-old female was admitted to the ED due to 5 days of drowsiness, fever, and back pain. She has been living with diabetes for 20 years, with non-compliance to treatment and poor blood sugar control.

She had dry mouth, confusion, and an elevated respiratory rate (32/min). The blood pressure in lying down was 70/40 mmHg, with a heart rate of 92 bpm, and a temperature of 101.1°F (38.3° ˚C). She was diagnosed with severe diabetic ketoacidosis (DKA) and community-acquired infectious pyelonephritis. She began IV fluids, norepinephrine infusion, electrolyte replacement, insulin infusion, and antibiotic therapy. The DKA resolved in 24 h, and she continued her treatment in the hospital. After 10 days of antibiotics (day 11), her follow-up laboratory serum tests were normal. However, she did not tolerate weaning norepinephrine because her blood pressure dropped to 60/30 mmHg and worsened when she moved from a lying to a sitting position. She had experienced brain fog, blurred vision, profuse sweating, drowsiness, and fainted when attempting to sit up on two occasions. These symptoms persisted while she was lying down, and her blood pressure slowly rose.

Furthermore, she had blurred vision, dizziness, light-headedness, drowsiness, and fainted after she was eating high-carb meals. Her blood pressure dropped to 60/40 mmHg with a heart rate of 55. She received an IV single bolus of Hartman solution (250 cc) and was allocated to the Trendelenburg position. The norepinephrine infusion was increased up to 0.65 mcg/kg/min. She remained on norepinephrine infusion with periodic adjustments according to blood pressure levels. Moreover, she experienced a new episode of mental fog and fainting symptoms after consuming carbohydrate-rich meals, followed by a drop in blood pressure of 70/50 mmHg over the next 120 min. On the following, she experienced constipation, empty fullness after eating, bloating, nausea, vomiting, urinary urgency, frequency, and nocturia. In addition, her blood pressure levels at night showed a marked tendency to rise (Fig. 1).

We decided underwent her to new assessments to rule out differential diagnosis[7,8] (Fig. 2) and essay trials of treatment for improve her blood pressure levels[9] (Fig. 3). After a 48-day hospital stay, her blood pressure levels improved and reached a systolic BP of 90 mm Hg during the day, she was discharged at home.

Conclusion

Autonomic dysfunction in hospitalized patients is feasible using a conventional blood pressure monitor. We provide an assessment of the behavior in the BP using an orthostatic challenge to determine the delta systolic heart rate over systolic blood pressure ratio (ΔHR/SBP), which can help confirm neurogenic OH and guide the etiological approach. The blood pressure and the pulse should be measured every minute for 5 min in the supine position and 10 min in the standing position. Subtracting the last systolic blood pressure in the supine position from the systolic blood pressure at 3 min of upright position. Furthermore, it is necessary to do the same subtraction between the heart rate in supine and the heart rate at 3 min of standing.

The delta ΔHR/SBP ratio will be calculated by dividing the heart rate by the systolic blood pressure results. If the ratio is < 0.5, it strongly suggests a neurogenic OH. In the original study from Norcliffe-Kaufmann et al.[10], the ΔHR/SBP ratio was tested in patients with alpha-synucleinopathies such as multiple system atrophy (MSA), pure autonomic failure (PAF), Parkinson's disease (PD), Lewy bodies Dementia (LBD) in the tilt table testing, showing excellent sensitivity (91.3%) and specificity (88.4%) to distinguish between patients with neurogenic versus non-neurogenic OH (area under the curve = 0.96, $p < 0.0001$). If the delta ratio exceeds 0.5, it should address non-neurogenic causes of OH. Once a neurogenic OH diagnosis has been corroborated, the assessment can be focused, as we labeled in Figure 4. In addition, during the orthostatic challenge, we suggest taking catecholamine levels (norepinephrine, epinephrine, dopamine, vasopressin, and renin) in the supine and standing positions to discriminate pre-ganglionic or post-ganglionic autonomic failure. The algorithm reduces the number of etiologies, as Goldstein and Cheshire described[11]. Neurodegenerative central causes are the main etiology of pre-ganglionic sympathetic failure, such as MSA. Post-ganglionic etiologies are broad since peripheral neuropathies (metabolic, hereditary,

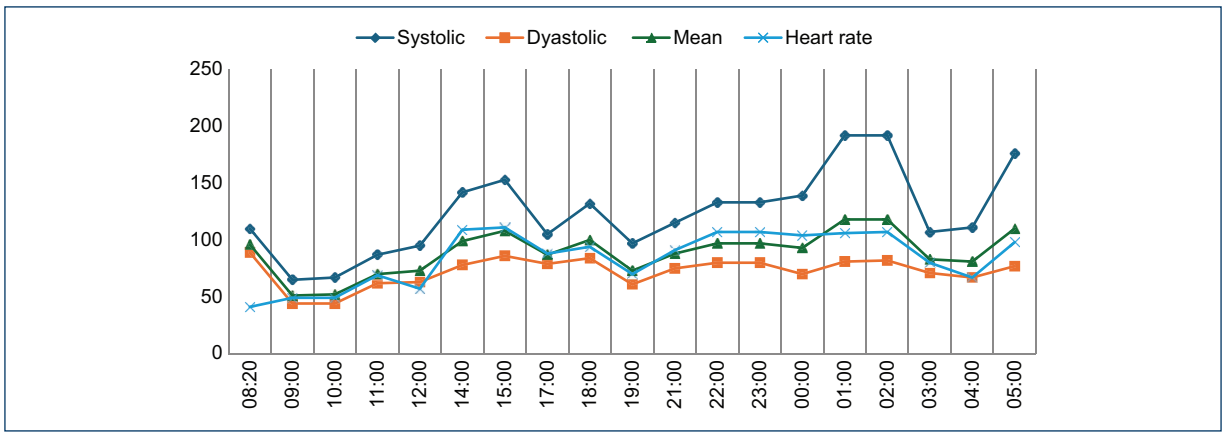

Figure 1. Blood pressure levels with conventional telemetry. The patient exhibited blood pressure lability during the day. She was unable to stand up and remained in supine and sitting down. She had episodes of post-prandial hypotension, supine hypertension, and one episode of fainting (day 15 post-DKA).

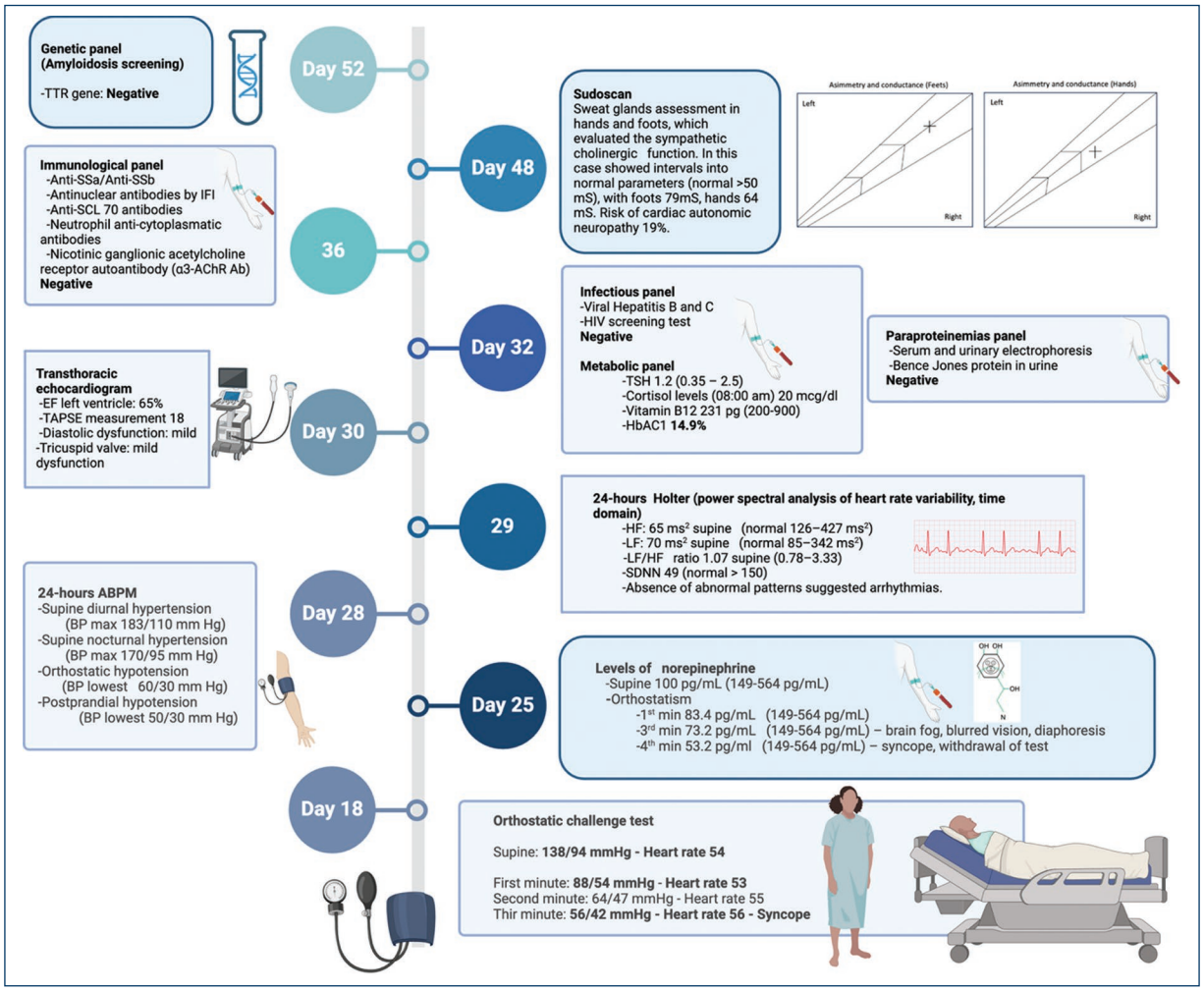

Figure 2. Timeline approach in our case.

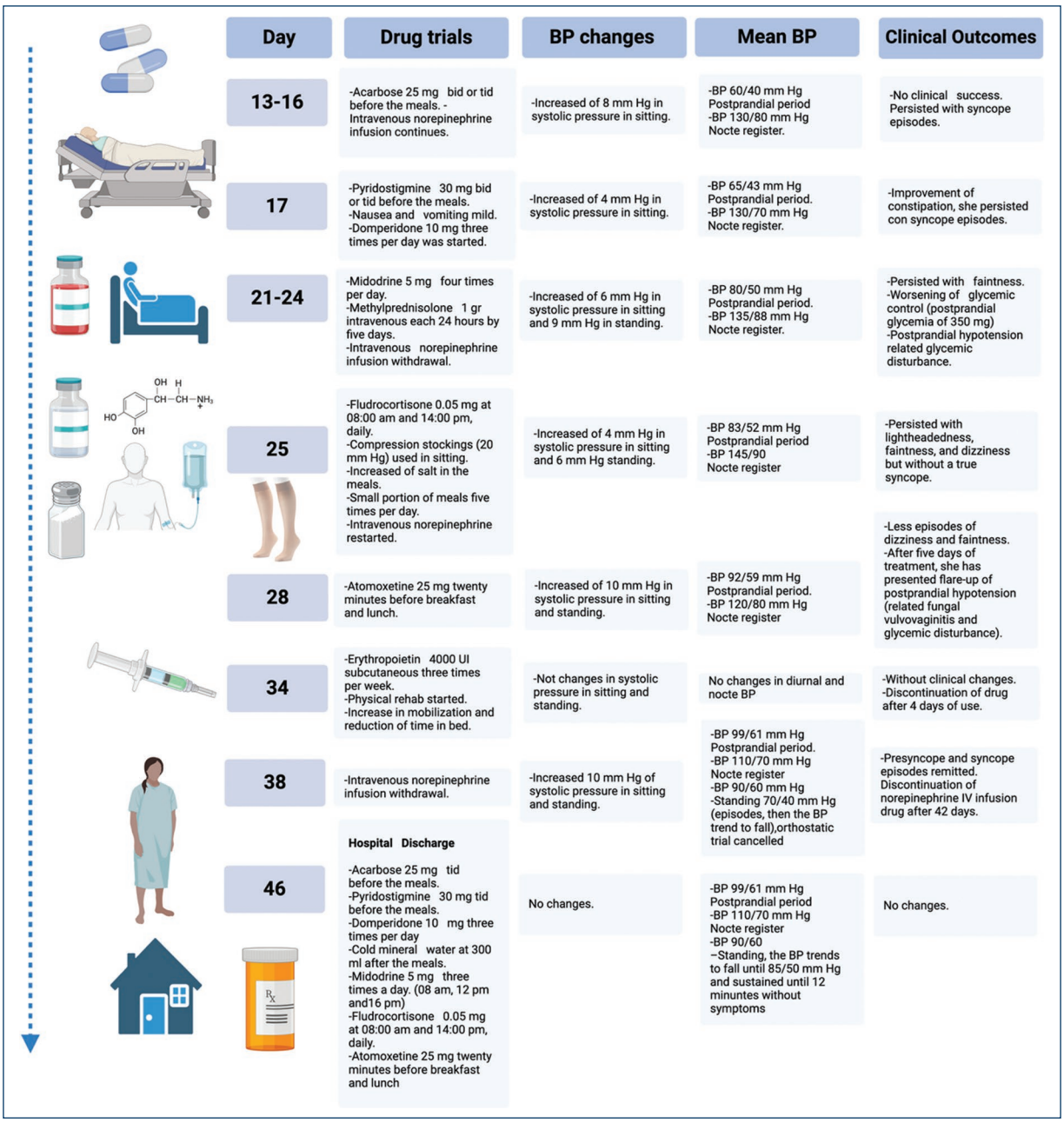

Figure 3. Timeline of medication trials tested in the patient.

autoimmune, paraneoplastic, etc.), or degenerative diseases such as PAF, PD, or LBD[12].

Denervation patterns in autonomic failure are clues for diagnosis. Can affect one, two, or all autonomic system divisions (sympathetic, parasympathetic, and enteric). The complete implication of the autonomic system is denominated pandysautonomia.

One cause of pandysautonomia is the autonomic autoimmune ganglionopathy (AAG), with monoclonal IgG antibodies against the subunit 3 of ganglionic acetylcholine receptors (α3-AChR Ab). The patients have a subacute or acute progression of autonomic symptoms, such as OH, supine hypertension, post-prandial hypotension, constipation, diarrhea, sexual dysfunction, bladder incontinence, frequency, and urinary retention. They can endorse anhidrosis, hyperhidrosis, temperature, skin color changes (limb acrocyanosis, Raynaud phenomenon), pupillary changes (Adie pupil) in weeks or months.

The α3-AChR Ab antibodies were described by Vernino et al in 1998[13]. The original study included

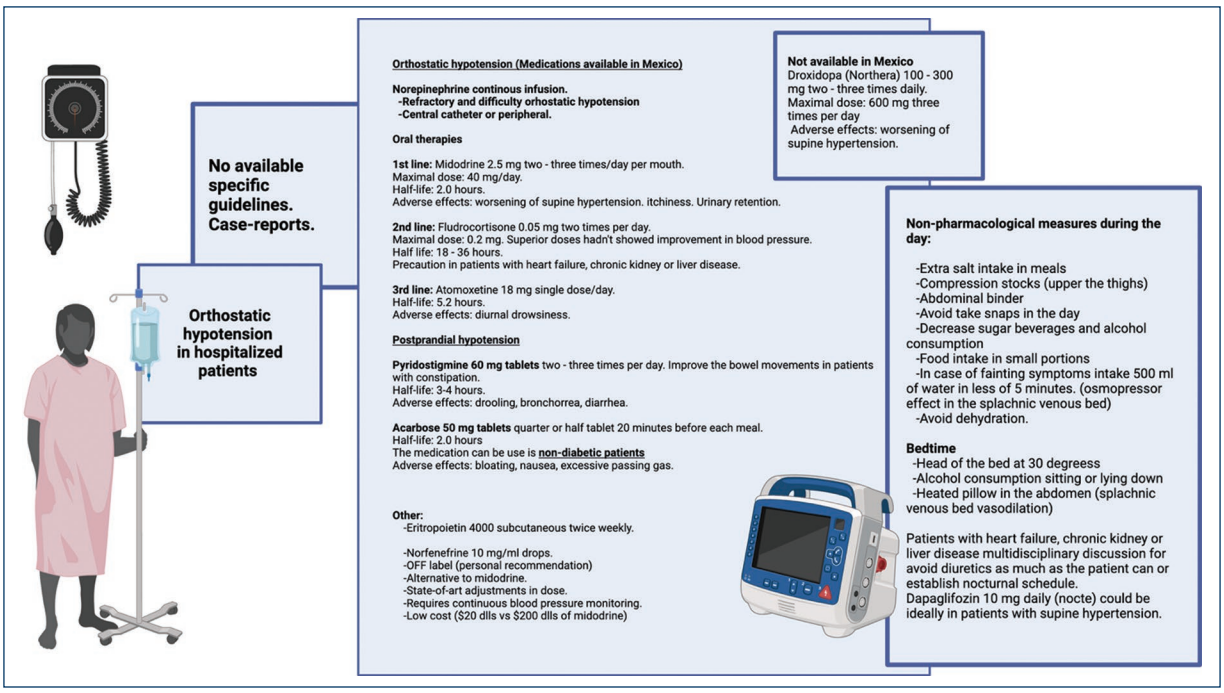

Figure 4. Therapeutic lines in orthostatic hypotension in hospitalized patients.

patients with alpha-synucleinopathies, diabetic neuropathy, idiopathic autonomic neuropathy, postural tachycardia orthostatic syndrome, idiopathic gastrointestinal dysmotility, and paraneoplastic autonomic neuropathy. All the patients exhibited antibody positivity, with the exception of patients with degenerative diseases (MSA, PD, PAF, LBD). That suggests the chronic inflammatory conditions can develop monoclonal antibodies in patients with high risk factors, such as rheumatological diseases (rheumatoid arthritis, systemic erythematosus lupus, myasthenia gravis, pernicious anemia, Sjogren syndrome, inflammatory intestinal disease, and systemic sclerosis). As the AAG has been considered a paraneoplastic syndrome, we should rule out occult neoplasia and follow up for at least 5 years.

There are case reports of AAG with isolated enteric nervous system damage, called gastrointestinal autonomic neuropathy[14]. The patients developed subacute motility disturbances in the upper or lower gastrointestinal tract (oropharyngeal dysphagia, thoracic dysphagia, gastroparesis, chronic intestinal pseudo-obstruction, constipation, and fecal incontinence) with a not clear etiology in the work-up and a positive serology for the α3-AChR Ab. The course of this entity will be monophasic, remission, or relapse-exacerbation (36 months), either or not therapeutic intervention.

There were case reports of patients with clinical features of AAG and negative α3-AChR antibody. In a converse fashion, we favor beginning treatment as soon as possible to stop the pathophysiological mechanism and hopefully avoid the augment. The treatment must be initiated with conventional immunosuppressor therapy described in the literature (high dose of intravenous methylprednisolone, intravenous immunoglobulin, azathioprine, mycophenolic acid, plasma exchange, rituximab, etc.), regardless of the serology status of the α3-AChR antibody[15,16].

We concluded the diagnosis of diabetic autonomic neuropathy for the evolution and improvement during hospitalization and post-discharge. However, the patient continues in vigilance because the seronegative status of the α3-AChR antibody didn't rule out the diagnosis of AAG. Regarding our patient's diagnosis, our discussion was the possible correlation between DKA and acute sympathetic failure. The relationship between acute exacerbations of diabetes (DKA and hyperosmolar hyperglycemic state) and autonomic dysfunction needs to be clarified. One theory suggests that the autonomic denervation could be due to microvascular regulation of the vasa vasorum, loss of myogenic reactivity, endothelial cell dysfunction, reduced high-quality angiogenesis, and a proinflammatory state[17]. This may be associated with the advanced

glycation of proteins on the basal membrane and glycocalyx. Moreover, the hyperglycemic environment may increase the prothrombotic state, leading to vessel obliteration and thrombosis of microcirculation in the sympathetic paravertebral trunks or vagal nerve endings.

Autonomic failure is a challenge for hospitalists, senior physicians, and residents. Neurogenic OH is the early clue of the different baroreflex failures. The subtle disturbances in a patient's blood pressure are related to positional changes (from supine to standing), abnormal circadian variations (where blood pressure does not follow the normal daily rhythm), and abnormal drops in blood pressure levels in the post-prandial period, which are cues to figure out the diagnosis. Multiple factors in critical care patients (adrenal failure, septic shock, heart failure, internal bleeding, antihypertensive medication, acute liver or kidney injury, metabolic acidosis, etc.) dismissed the neurogenic OH diagnosis. However, our threshold should be low to assess the blood pressure fluctuations. In the absence of recognized etiologies of hypotension, it should be attributed to neurogenic causes. We keep in mind that all systemic conditions lead to generalized hypotension and are non-related to position. The combination of OH and supine hypertension strongly suggests neurogenic OH, and we should emphasize the blood pressure and heart rate to address the diagnosis.

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CLINICAL CASE

Splenic abscess secondary to brucellosis: a case report

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Abstract

Brucellosis is a zoonotic infection transmitted to humans by infected animals, through the ingestion of unpasteurized dairy products or by contact with tissues or fluids from infected animals or humans. The symptoms present as an insidious picture, characterized by fever, general malaise, night sweats, and arthralgias. Splenic abscess is an extremely rare complication. The diagnosis of brucellosis is made by immunological means. However, the presence and location of abscesses are detected by ultrasonography, tomography or magnetic resonance imaging. Our manuscript presents the case of a splenic brucelloma in an adult male.

Keywords: *Brucella. Zoonosis. Splenic abscess.*

Introduction

Brucellosis is a zoonotic infection transmitted to humans by infected animals (cattle, sheep, and goats), through the ingestion of unpasteurized dairy products or by contact with tissues or liquids of infected animals or humans. Brucellosis is the most common zoonosis worldwide, with 100-200 cases of human brucellosis reported annually in the United States. In Latin America, Mexico is one of the countries with the highest incidence of brucellosis and is considered a country where the disease is endemic. During the years 2012 to 2017, the disease represented the most important zoonosis in terms of human morbidity with 15,496 cases recorded[1-5].

Unlike other infectious organisms, Brucella does not have virulence factors. However, it uses other mechanisms to infect its host, such as the presence of lipopolysaccharides, outer membrane protein, and type IV secretion systems and BvrR/BvrS (system devoted to the homeostasis of the outer membrane and, therefore in the interface for cell invasion)[6,7]. Four species of Brucella have been described as having the ability to infect humans: *Brucella melitensis*, *Brucella abortus*, *Brucella suis,* and *Brucella canis*. However, most infections identified in humans are caused by *B. melitensis*[8,9].

The symptoms of brucellosis present as an insidious picture, characterized by fever, malaise, night sweats, and arthralgias. Fever may be accompanied by chills, and due to its duration, it may be recurrent, mild, or prolonged. Additional symptoms may include weight loss, arthralgias, low back pain, headache, dizziness, anorexia, dyspepsia, abdominal pain, cough, and psychiatric symptoms such as depression. A characteristic that makes its diagnosis difficult is the frequent finding of hepatosplenomegaly and lymphadenopathy, which suggest myeloproliferative syndromes[10,11].

Diagnosis is made by nucleic acid amplification tests, nucleic acid hybridization tests, or through cultures,

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which are still considered the gold standard for *Brucella* identification. However, serological tests are the most widely used in endemic areas, due to their low cost and accessibility[12,13]. Although brucellosis can affect any organ, the development of splenic abscesses is extremely rare with an estimated frequency of occurrence of 0.05-0.7%. This complication is clinically relevant because if not treated properly it can be life-threatening[14,15]. The objective of this article is to report a case of splenic abscess secondary to human brucellosis.

Clinical case

A 40-year-old male patient, who presented to the emergency department in May 2023 for approximately 21 days, generalized weakness, hyporexia, prolonged fever of more than 15 days of evolution, periodic, of unquantified nocturnal predominance, which subsides with antipyretics transiently and generalized headache. The picture is accompanied by unintentional weight loss of 10 kg in approximately 3 months. As a personal history, smoking since the age of 20, suspended 6 months ago, chronic alcoholism since the age of 30, suspended 6 months ago, and consumption of dairy foods produced in the community allegedly without pasteurization.

On physical examination, he was neurologically intact. Chest with decreased respiratory murmur, voice transmission, and dullness to percussion in the left hemithorax, integrating pleural effusion syndrome. Right hemithorax without pathological alterations. Precordium with rhythmic heart sounds without aggregates. Globose abdomen, palpable hepatosplenomegaly 5 cm below the rib margin, hepatalgia to the palmopercussion, upper and lower limbs without pathological data lower limb with strength and muscle tone without alteration.

Due to the symptoms and the history of consumption of unpasteurized dairy products, laboratory and cabinet studies (blood count, procalcitonin, blood cultures, Rose Bengal staining, standard agglutination tests (SAT), agglutination test in the presence of 2-mercaptoethanol, and a contrasted thoraco-abdominal computed tomography [CT]) are performed to rule out and/or confirm the diagnosis of brucellosis. However, no other studies were conducted to look for brucellosis involvement in other organs and systems. Seventy-two hours later, laboratory results are obtained, which show positivity for Rose Bengal staining, as well as for SAT and agglutination test in the presence of 2-mercaptoethanol, (2-ME) with titers of 1:150 for SAT and 1:80 for 2-ME. Contrasted thoraco-abdominal CT scan shows a hypodense, well-defined, well-defined lesion, without reinforcement with contrast medium located in the lower pole of the spleen (Fig. 1); analytically, it is reported: procalcitonin 1.07 ng/mL, C-reactive protein 154.0 mg/dL, hemoglobin (Hb) 11.50 g/dL with mean corpuscular volume of 86.6 fL, mean corpuscular Hb of 29.7 g/dL, and thrombocytopenia of 95000/mL.

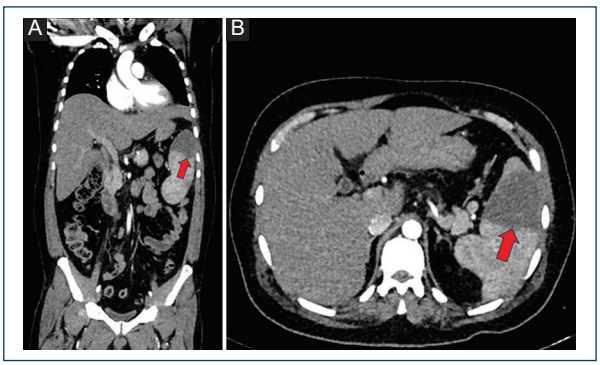

Figure 1. Thoraco-abdominal computed tomography, with the presence of a hyperdense lesion, well-defined and defined in the upper pole of the spleen (red arrows). **A:** axial and **B:** sagittal cutting.

With confirmation of the diagnosis of brucellosis, treatment with doxycycline 100 mg PO every 12 h for 6 weeks + gentamicin at 5 mg/kg/day for 7 days is initiated.

The patient's evolution was favorable, with remission of fever and dyspnea; biochemically, a significant decrease in procalcitonin 0.09 ng/mL versus 1.07 ng/mL, Hb of 12.8 g/dL versus 11.50 g/dL, and 184000 platelets/mm^3 versus 95000/mL was observed with respect to her admission. An appointment was made to the external internal medicine clinic in 1 month for follow-up.

Conclusions

In the case of our patient, several factors favored brucellosis infection, among them, it is worth noting that Mexico is one of the countries with the highest incidence of brucellosis in Latin America as a result of its fragile health system and the poor conditions of the population[3,4]. In addition, our patient had a history of ingestion of unpasteurized dairy products, which represents one of the most important risk factors for the transmission of the disease[16,17], favored by two important factors, on the one hand the deficiency of sanitary

controls of farm animals, especially in rural areas, and on the other the total absence of sanitary controls for food processing by the local population[3,4].

An important aspect that we must highlight about our patient was the fact that the clinical picture with which he was admitted to the emergency department characterized by anemia, weight loss, fever, and splenomegaly suggested the onset of tuberculosis or a myeloproliferative disease, both exclusionary diagnoses in the case of brucellosis. However, without a history of the patient's consumption of supposedly unpasteurized dairy products, they could delay the diagnosis and specific treatment of brucellosis and, thus, increase the risk of severe complications[1]. On the other hand, although systemic brucellosis is rare, there are reports of Brucella infection of the spleen, although this entity is extremely rare[14,15], this could be explained by the ability of Brucella to infect, survive, and replicate within macrophages located in reticuloendothelial organs, which is done through multiple mechanisms including its ability to alter phagocytosis. Prevent apoptosis or modulate the host's innate immune response by directly regulating the elements of the signaling pathway, mediated by the toll-like receptor-4 receptor adapter and MyD88-adapter-like[13,18-20].

In the case of the first-choice treatment for brucellomas, this has not yet been determined; however, several antibiotic treatment guidelines have been suggested, which depend on several factors such as accessibility, costs, adverse reactions, or the coexistence of other infectious diseases such as tuberculosis in the case of double or triple regimens with rifampicin, such as doxycycline-rifampicin-quinolone, doxycycline-rifampicin-aminoglycoside, or rifampicin-aminoglycoside; however, these could be contraindicated in countries with high rates of rifampicin resistance.

Although the scheme recommended by the World Health Organization establishes the triple regimen with doxycycline-rifampicin-streptomycin as the first scheme of choice[21]; in the case of our patient, the lack of adherence, socioeconomic conditions, availability, and accessibility of drugs in our hospital determined the administration of a double scheme consisting of doxycycline at a dose of 100 mg orally for 6 weeks + gentamicin at a dose of 5 mg/kg IV every 24 h/week. However, 7 days after starting the pharmacological treatment, streptomycin was replaced by gentamicin due to the high cost of streptomycin. Finally, it should be noted that in case of severe complications associated with splenic brucelloma, non-surgical drainage should be performed as described by Del Arco et al. due to the lower complication rate and high success rates[22].

Finally, an important limitation of our clinical case was the fact that we could not perform subsequent studies on our patient to evaluate the response to medical treatment, this is common in second-level hospitals where the population living in rural areas is itinerant and, in most cases, does not attend follow-up consultations after the start of any medical treatment.

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Conflicts of interest

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Protection of human subjects and animals. The author declares that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The author has followed their institution's confidentiality protocols, obtained informed consent from patient, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

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CLINICAL CASE

Spermatic cord liposarcoma presented as inguinal hernia: case report

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Abstract

Liposarcomas are the most common malignant soft-tissue tumors in adults, predominantly occurring in the extremities and retroperitoneum. Only 3.6% of these tumors affect the scrotum, including the spermatic cord, testicular tunics, and epididymis. We present the case of a 53-year-old man with iliac fossa pain and increased left scrotal volume. Imaging studies included an inguinal ultrasound under stress and computed tomography (CT), which showed the protrusion of the hernial sac with a well-defined wall and fatty content through the inguinal canal. During laparoscopic hernioplasty, a lipomatous tumor was found in the spermatic cord, leading to testicular lumpectomy and left orchiectomy. Histopathological examination revealed a 13 cm well-differentiated liposarcoma, with no evidence of lymphovascular or perineural invasion. Ultrasound was the first study performed due to its availability and usefulness in diagnosing hernias. However, the atypical appearance of the hernial sac content on ultrasound prompted the performance of a CT scan to better characterize the lesion and rule out other pathologies. In conclusion, spermatic cord liposarcoma is a rare entity that can mimic an inguinal hernia. It is essential to consider it as a differential diagnosis in cases of inguinal hernia. Advanced imaging studies can improve the accuracy of pre-operative diagnosis.

Keywords: *Liposarcoma. Inguinal hernia. Spermatic cord. Ultrasonography. Computed tomography.*

Introduction

Liposarcoma is a group of rare neoplasms with an incidence of < 1/100,000 new cases per year. Despite its rarity, it is the most frequent subtype of soft-tissue sarcomas, accounting for approximately 85% of these tumors[1]. The diagnosis is made predominantly in individuals between 40 and 60 years of age and the most common sites of presentation are the extremities and retroperitoneum, although it can also be found in the scrotum. The incidence of liposarcoma in this location is low (3.6%), within the scrotum it can affect the spermatic cord (76%), the testicular tunica (20%), or the epididymis (4%)[2].

There are genetic risk factors, such as Li-Fraumeni syndrome and neurofibromatosis type 1, as well as environmental factors such as exposure to ionizing radiation or certain chemicals, although their etiology remains largely unknown[3]. The World Health Organization classifies liposarcomas into five histological subtypes: myxoid, well-differentiated, dedifferentiated, round cell, and pleomorphic[4]. Spermatic cord liposarcoma represents a diagnostic challenge due to its silent evolution and its similarity to other more common pathologies, such as inguinal hernia, hydrocele, spermatocele or testicular tumors[5]. The available imaging techniques do not always allow a specific diagnosis[6].

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This article presents a case of well-differentiated liposarcoma of the spermatic cord, initially diagnosed as bilateral inguinal hernia in clinical and imaging studies.

Case presentation

This is a 53-year-old male patient who presented to the emergency department due to pain in the left iliac fossa during physical exertion. In his clinical history, type 2 diabetes controlled with metformin and arterial hypertension under treatment with losartan are reported. The clinical picture had begun a month before the consultation, with pain in the inguinal region after loading efforts. Imaging studies performed included stress inguinal ultrasound and computed tomography (CT), which revealed the presence of a non-reducible left indirect inguinal hernia and a reducible right inguinal hernia with ipsilateral hydrocele (Figs. 1 and 2). Color Doppler ultrasound showed no vascular abnormalities. Ultrasound was the first study performed due to its availability and usefulness in the diagnosis of hernias. However, the atypical appearance of the contents of the hernial sac on ultrasound prompted a CT scan to better characterize the lesion and rule out other pathologies.

The patient underwent surgery for bilateral inguinal hernioplasty with laparoscopic mesh placement. During the intervention, a lipomatous tumor was identified in the spermatic cord, which led to a lumpectomy of the spermatic cord, left orchiectomy, and lymph node dissection. Histopathological analysis revealed a well-differentiated liposarcoma of 13 × 8 × 3 cm in the distal third of the spermatic cord, with no evidence of lymphovascular permeation or perineural invasion. The surgical margins were reported to be free of neoplasia (Fig. 3). Immunohistochemical findings showed positivity for MDM-2, protein P53, CDK-4 and CD34, with a proliferation index of < 10%. The degree of differentiation was 1, according to the French classification of sarcomas (differentiation 1, mitosis 1, and necrosis 0) (Fig. 4).

Discussion

According to the literature, the tomographic findings of liposarcoma can be varied depending on the histological subtype. In the specific case of well-differentiated liposarcoma, CT imaging usually presents as a predominantly lipomatous mass with thick septa or non-lipomatous focal nodules. In this patient, CT showed homogeneous fat attenuation without septa, which is more characteristic of an inguinal hernia. Since inguinal hernias are a common and typically clinically diagnosed pathology, imaging studies play a key role in differentiating them from other pathologies of the inguinal region.

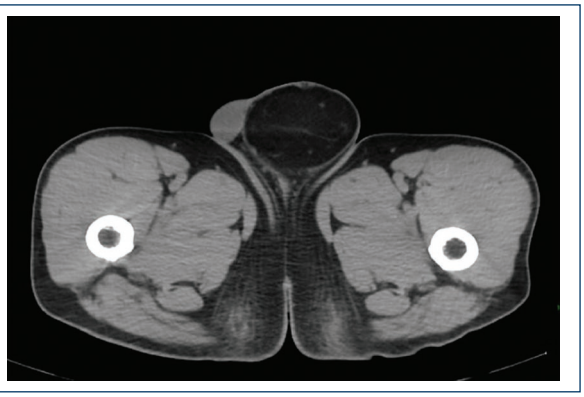

Figure 1. Image of plain tomography of the pelvis at the level of the scrotal pouch, in axial section and with soft-tissue window. An ovoid image with a well-defined contour and a thin hyperdense wall is observed, which is heterogeneous in appearance with a predominance of fat (hypodense on average of –80 UH), as well as isolated hyperdense lines in its interior. It occupies the left scrotal pouch extending from the ipsilateral inguinal canal.

Presentation of soft-tissue tumors in adults is rare. The incidence is estimated to range from 4-5 cases per 100,000 inhabitants per year, of which < 1/100,000 are identified as liposarcomas[1,2]. The different histological subtypes of liposarcomas have prognostic relevance. Well-differentiated liposarcoma is recognized by its low risk of distant metastasis; however, it has a high rate of local recurrence. In the event of recurrence, it may be due to a dedifferentiation event, which is directly associated with increased aggressiveness and a worse prognosis[6,7]. Diagnosis of soft-tissue tumors, including sarcomas, has an inaccuracy rate of 20-30%, due to several factors:

- Its rarity, given its low incidence and the existence of up to 70 subtypes with variable clinical and morphological characteristics.
- The intrinsic complexity of these tumors, since traditional morphological criteria of malignancy, such as the degree of cell differentiation, are not always applicable.
- Technological limitations, since diagnosis requires the combination of microscopic morphology, immunohistochemistry, and molecular genetics.
- The lack of clinical experience with these neoplasms, due to their low prevalence[5].

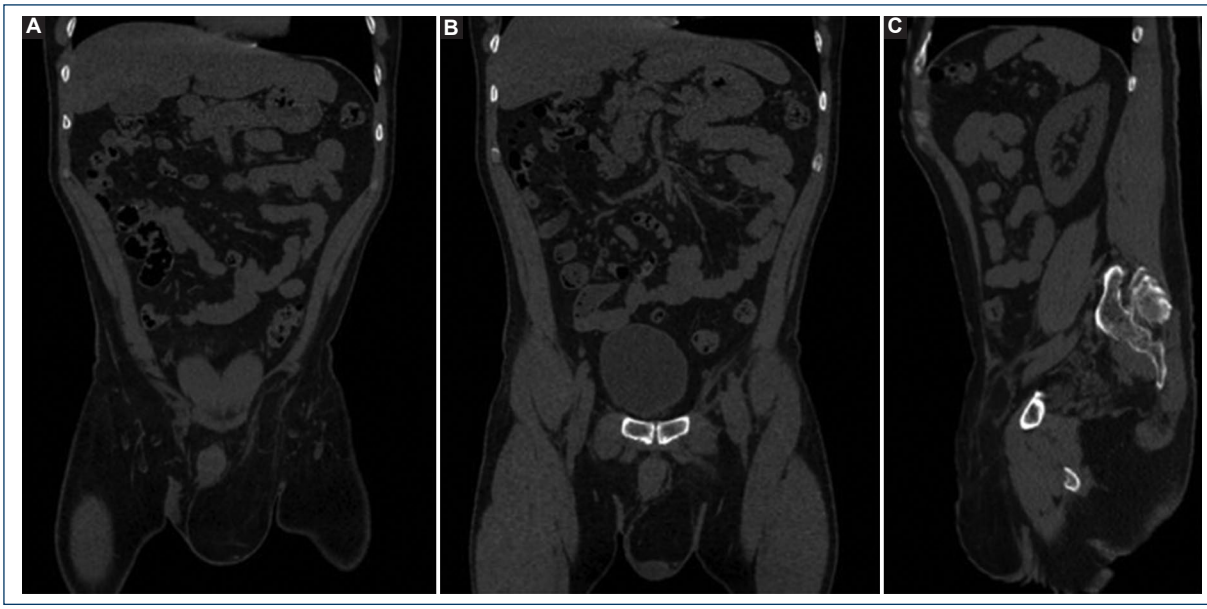

Figure 2. A: coronal plane image of abdominopelvic plain tomography with emphasis on the left inguinal region and with a soft-tissue window. A saccular image with a well-defined contour and a thin hyperdense wall was observed, which is heterogeneous in appearance with a predominance of fat (hypodense on average of –80 HU), as well as isolated hyperdense lines inside. It occupies the left inguinal canal from its upper third to the ipsilateral scrotal pouch. **B:** coronal plane image of abdominopelvic plain tomography with emphasis on the left inguinal region and with a soft tissue window. A saccular image with a well-defined contour, thin wall and fat content was observed, which occupied the left inguinal canal from its upper third to the ipsilateral scrotal pouch, conditioning caudal displacement of the testicle. **C:** computed tomography image with multiplanar reformatting in the oblique plane where a hernial defect of 20 mm is observed in the left inguinal canal, as well as protrusion of the hernial sac of 18 × 5 mm and fat content with poor interface of the spermatic cord and that conditions inguinoscrotal occupation.

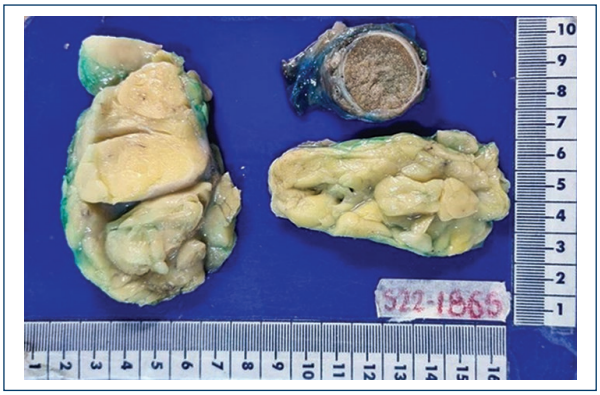

Figure 3. Left testicle and tumor weighing 316 g. Testicle measures 5.0 × 3.5 × 3.0 cm, when cut the testicular parenchyma is solid, light brown, soft, and spongy in appearance without obvious macroscopic lesions. Spermatic cord measuring 10.5 × 1.5 × 0.8 cm. Tumor found in the spermatic cord of 13.0 × 8.0 × 3.0 cm, ovoid and lobed, the capsule is smooth and light yellow; when cut it is solid, light yellow, and soft.

For soft-tissue tumors, especially those located in the extremities, pelvis, or trunk, magnetic resonance imaging (MRI) is the imaging study of choice. However, ultrasound is usually the first study requested in these cases, although it should be complemented with MRI, which provides a better prognostic value in well-differentiated liposarcomas. MRI reveals fatty masses occupying about 75% of the lesion, with low-density features typical of a lipoma. Major prognostic factors include tumor size, the presence of necrosis, and its location. In addition, radiography and CT are useful for ruling out bone tumors, while positron emission tomography is recommended for monitoring and evaluation of the risk of recurrence[8].

The most commonly used immunohistochemical markers in the diagnosis of liposarcomas include MDM2 and CDK4, which are expressed in 100% and 90% of cases of well-differentiated and dedifferentiated liposarcomas, respectively. However, MDM2 has low specificity, which makes it difficult to interpret, especially in the presence of macrophages. On the other hand, CDK4 has limited sensitivity[6]. The treatment of choice is surgical, using high orchiectomy and resection of surrounding tissue to achieve tumor-free margins. However, information on the risk of recurrence and

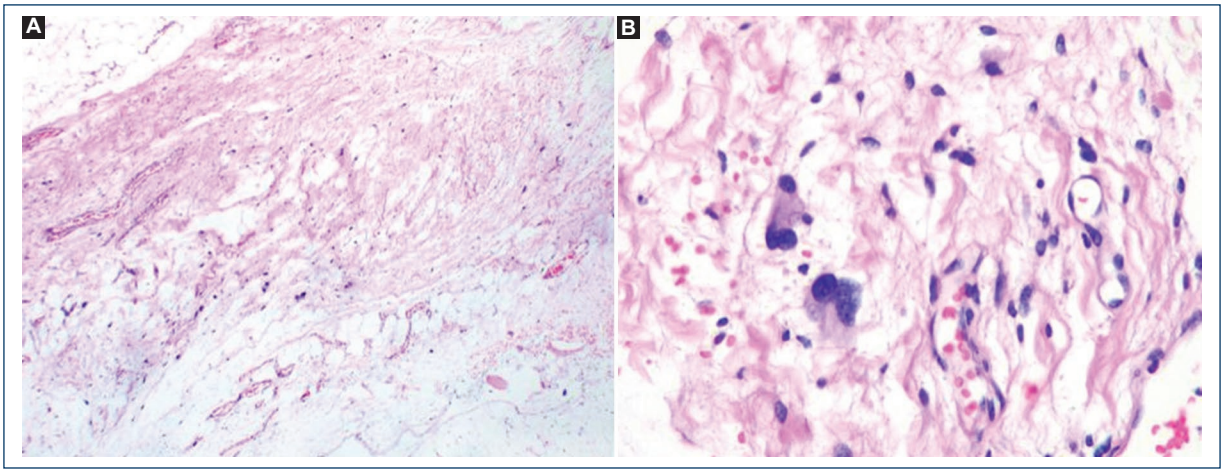

Figure 4. A: histological section with ×10 approach showing malignant mesenchymal neoplasm. **B:** histological section with 40x approach is composed of round-shaped malignant cells with intranuclear vacuoles, stellate, and pleomorphic and hyperchromatic nuclei compatible with lipoblasts, which are identified by immunohistochemistry as MDM2, CDK4, CD34, and P53 positive.

distant metastasis varies depending on the surgical approach (such as reoperation to reduce recurrence or lymphatic dissection). The use of radiotherapy and adjuvant chemotherapy has not shown high effectiveness in these cases[9,10].

Conclusions

The patient was consulted with the oncology service for oncological follow-up and surveillance. Long-term follow-up is recommended due to the risk of local recurrence in this type of tumor. Liposarcoma is a rare neoplasm with a wide variety of clinical presentations. Its silent evolution and the presence of multiple differential diagnoses, together with the lack of a clear etiology, represent a significant challenge for diagnosis. The case presented in this paper exemplifies the management of an unexpected transoperative diagnosis. Currently, the different modalities of imaging studies not only facilitate a more accurate diagnosis but also allow for adequate monitoring of the disease.

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CLINICAL CASE

Primary retroperitoneal mucinous cystic retroperitoneal neoplasm with incidentaloma (adenocarcinoma) in the renal capsule

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Abstract

Primary retroperitoneal mucinous neoplasms (PRMCNs) are infrequent and have a remarkable prevalence in women, with a ratio of 9.4:1 compared to men. This statistic is especially relevant today, as this condition was previously believed to be exclusive to women. We present the clinical case of a 60-year-old male patient with a retroperitoneal tumor. A retroperitoneal tumor resection was performed, revealing a mucinous, lobulated tumor surrounding the ureter and displacing the right renal unit and great vessels. As physicians, it is important to take into account this pathology and not to exclude its incidence in men. According to an article published in 2019, 19 cases of PRMCN have been reported, of which two correspond to men. In conclusion, primary retroperitoneal mucinous cystic neoplasms present a challenge for pre-operative management due to the lack of specific data available on this entity.

Keywords: *Retroperitoneal mucinous neoplasms. Retroperitoneal tumor. Primary neoplasm.*

Introduction

Primary retroperitoneal mucinous neoplasms (PRMCNs) are rare tumors, predominantly in the female population. Most neoplasms are found in the left or right lateral retroperitoneal space[1,2]. Histologically, they resemble ovarian mucinous tumors and are similarly classified into the following three categories: benign mucinous cystadenoma, borderline mucinous cystadenoma, and malignant mucinous cystadenoma[3,4]. Pre-operative diagnosis is often confusing due to vague and non-specific clinical signs and symptoms, and the inability of radiology to determine the exact site of origin[5]. The etiology, biology, pathogenesis, and prognosis of PRMCN are still unclear since there is originally no epithelial tissue in the retroperitoneum[3,5]. Several hypotheses have been formulated with the purpose of clarifying the potential origin of these neoplasms. However, to date, some theories have gained greater acceptance within the community than others, underscoring the continued need for rigorous research and thorough analysis to accurately discern the mechanisms underlying the genesis of these neoplastic diseases.

We report the case of a 60-year-old male patient with a history of previous surgeries, who presented with non-specific and intermittent abdominal pain. Following clinical evaluation and imaging studies, a diagnosis of PRMCNM was made, a rare entity that is

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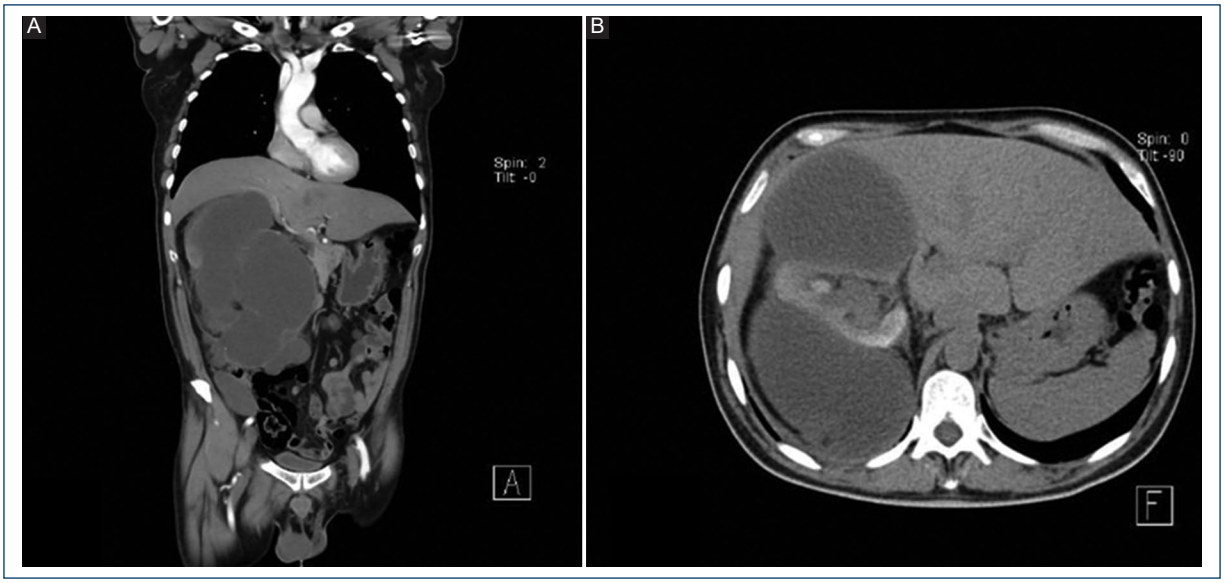

Figure 1. The computed tomography scan reveals a well-defined mass in the right retroperitoneum with a cystic, lobulated, and heterogeneous appearance, likely with mucinous features typical of neoplasms with mass effect. **A:** axial view; **B:** coronal view.

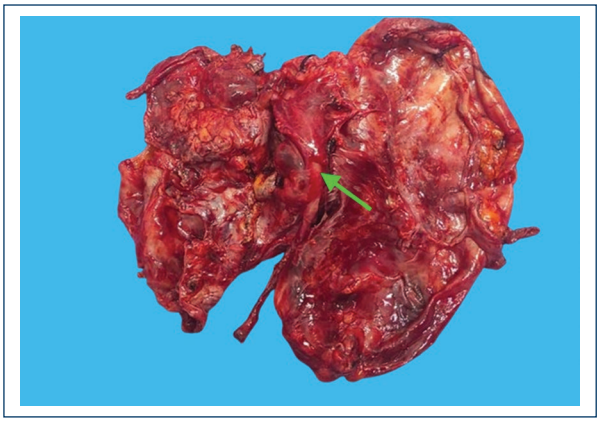

Figure 2. Retroperitoneal tumor capsule. The arrow indicates the ureter attached to the retroperitoneal tumor capsule.

difficult to diagnose due to its vague symptoms and the lack of consensus regarding its origin and pathogenesis.

Clinical case

A 60-year-old male patient with a significant history, open appendectomy secondary to acute appendicitis (2001), left arthroplasty secondary to gonarthrosis (2016); both procedures are reported without complications. The patient began suffering 4 months before surgery, with non-specific and intermittent abdominal pain predominantly in the right hypochondrium, reporting a pain intensity of 4/10 on a Visual Analog Scale, dull type without irradiation or aggravating factors, with increased volume of the right hemiabdomen and data of intestinal pseudo-occlusion, so he went for evaluation. On admission, the patient denied pain, vomiting, fever, hematuria, lithuria, pyuria, or alterations in voiding mechanics. On physical examination, inspection revealed a globular abdomen due to adipose panniculus, with increased volume in the right hemiabdomen without color changes; on auscultation normoactive peristalsis; soft and depressible abdomen, not painful on palpation, reducible, without data of peritoneal irritation, palpable in the right hemiabdomen, non-painful tumor, bilateral Giordano negative. Therefore, a computed tomography (CT) scan was performed, which revealed the right renal unit with contrast medium uptake, failing to visualize the ureter in excretory phase, hypodense retroperitoneal lobulated image of 8.9 × 5.6 × 10.91 cm with altered morphology, displaced toward the ipsilateral diaphragm, with change in situation and anatomy. There is evidence of pyelocaliceal dilatation, and a hypodense, lobulated image in the right ureter topography with dimensions of 19.7 × 8.9 × 20.8 cm with a density of 14.21 HU (Fig. 1). As a complementary diagnostic study, cystoscopy was performed, revealing multiple hypervascularized trabeculations in the bladder that obstructed the

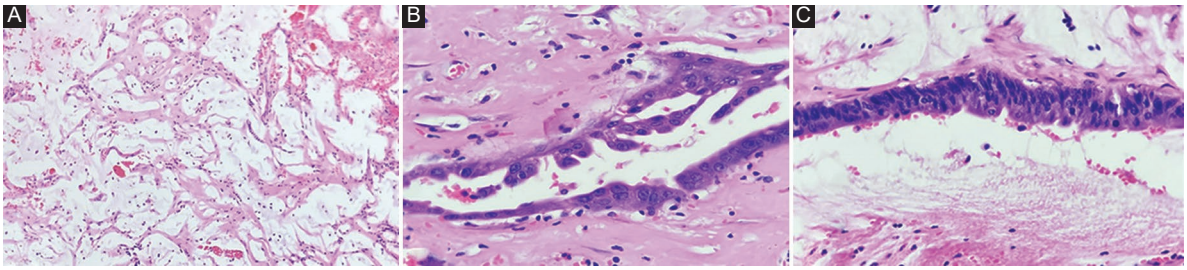

Figure 3. Microphotographs stained with the hematoxylin and eosin method. **A:** fibroconnective tissue with mucin (magnification ×10). **B:** epithelium with high-grade dysplasia (magnification ×40). **C:** dysplastic epithelium (magnification ×40).

visualization of the ureteral meatus. A protocol for surgical treatment of the neoplasm was established in which a simple open right nephrectomy was performed with resection of the tumor with mucinous content (Fig. 2), lobulated, surrounding and adhering to the ureter making its release impossible, displacing the right renal unit and great vessels, approximately 4,000 CC of mucinous material were drained. The patient had an adequate post-operative recovery and was discharged after a 4-day hospital stay, with follow-up care provided at an outpatient clinic. The pathology report describes cystic mucinous neoplasm with high grade dysplasia with focus in a capsule of 5 mm × 4 mm in retroperitoneal space; a peritoneal fluid sample was taken where malignant cells were reported (Fig. 3). Follow-up by the oncology department, where a study protocol was initiated in search of the origin of the primary tumor. Due to the pathological report describing a focus of invasive adenocarcinoma in the capsule of the mucinous neoplasm, a study protocol was initiated, including the evaluation of tumor markers CA 19-9 and carcinoembryonic antigen, both of which were within normal limits. The patient has been under close follow-up by the oncology department for 2 years, undergoing imaging studies (CT scans) every 6 months, along with tumor marker assessments, to detect any potential recurrence or disease progression at an early stage. So far, all results have been negative, and the patient has shown favorable clinical progress with no signs of relapse. Outpatient monitoring will continue as per medical recommendations to ensure long-term disease control.

Discussion

PRMCNs are very rare tumors, are uni or multiloculated cystic tumors with a fibrous capsule and lined by a mucin-producing epithelium, associated with a subepithelial stroma, which was initially described as similar to the ovary[6]. The first case was reported in 1889 by Bassini, where he described a case of cystic adenoma morphologically resembling a mucinous cystadenoma of the ovary[5], and the first male patient with PRMCN was described in 1994. The prevalence of PRMCN among resected retroperitoneal neoplasms was 1.95%[6]. They have a female predominance with a female-to-male ratio of 9.4:1 and are most frequently seen in young adults[5]. The median age at diagnosis was 42.0 years (range 18-86 years), with females being significantly younger than males at diagnosis (42.0 years vs. 62.2 years, p = 0.005)[7]. Despite efforts to understand the pathogenesis of these neoplasms, no definitive conclusion has yet been reached. Several explanatory theories have been proposed, with four of them standing out for their relevance, prominence, and acceptance in the scientific literature. The first explanation is that PRMCs arise from teratomatous lesions, in which columnar epithelium becomes the predominant cell line[8,9]. The second possibility is that they arise from ectopic ovarian tissue[8]; however, ovarian tissue has never been found within a retroperitoneal mucinous cystadenocarcinoma[8,10]. The third hypothesis is that the tumors are remnants of the embryonic urogenital apparatus, in which cysts develop from specialized mesothelial cells of the urogenital ridge. The latest and most widely accepted theory is that PRMCs are produced by invaginations of the peritoneal epithelium during embryonic growth and subsequently undergo metaplasia[8]. An incidentaloma is an unexpected finding. In this case, it was discovered incidentally during the histopathological examination of the renal capsule, revealing a malignant adenocarcinoma localized in this structure. The clinical presentation of this pathology exhibits remarkable specificity and variability, which implies

considerable difficulty in pre-operative diagnosis. The absence of specific laboratory tests, pathognomonic signs, or distinctive radiological findings makes it difficult to discriminate precisely between neoplasms of renal, ovarian (in female patients), or other possible origins. In the different sources consulted, CT of the abdomen is described as the test of choice to evaluate the extension of the tumor, its distribution, and to carry out surgical planning. It has been described that exploratory laparotomy with radical resection without effusion or rupture is the standard therapy and the most important prognostic tool[5,7]. It is definitely important to remove these tumors without rupturing them, and laparoscopic removal should be avoided if the histology of the tumor is unclear[11]. Regarding the application of adjuvant treatment after resection, it is not established due to its limited reported evidence. It is very important to make the diagnosis in time as well as the treatment, since there may be complications such as rupture, infection, and malignant transformation, making the prognosis more unfavorable. The prognosis of patients with these tumors remains uncertain due to their rarity and the fact that most patients were not followed up for 24 months[3].

Myriokefalitaki reported a 5-year overall survival of 75.4% for PRMCs. It should be noted that in the majority of reported cases, follow-up did not exceed 5 years[7,12].

Conclusion

PRMCN is complex to diagnose due to the lack of specific evidence. There are no radiological patterns or serum markers that initially suggest this entity, and biopsy is risky due to the possibility of tumor dissemination. The challenge lies in determining the type of tumor before surgery, which allows for more accurate and less risky surgical planning. This is crucial to avoid complications such as cyst rupture, which occurred in our patient.

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The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patient, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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CLINICAL CASE

Intestinal endometriosis as a cause of intestinal stenosis. A case report

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Abstract

Endometriosis affecting the terminal ileum is a rare condition, appearing in 1-7% of women with endometriosis, with secondary intestinal occlusion estimated in 7-23%. Diagnosis before surgery is difficult and requires a high clinical suspicion; it should be a differential diagnosis in all women with abdominal pain. The clinical case is a 26-year-old female presented with abdominal pain and a lack of bowel movements, with poor response to medical management. A computed tomography scan shows signs suggestive of intestinal obstruction, leading to surgical treatment. A diagnostic laparoscopy was initially planned; however, due to the unavailability of the necessary equipment, a laparotomy was performed. Two areas of stenosis were found in the terminal ileum, managed with a right hemicolectomy and ileocolic anastomosis. Pathology reports revealed endometriotic implants in the areas of obstruction. In conclusion, while there is not established consensus regarding surgical management, a minimally invasive approach is recommended when feasible. Diagnosis can be confirmed only on histopathological examination of the surgically resected specimen. The decrease in abdominal pain, gastrointestinal discomfort, and the improvement in the quality of life are evident following surgical treatment.

Keywords: *Ileal endometriosis. Right hemicolectomy. Occlusion. Intestinal resection. Endometriosis. Stenosis.*

Introduction

Endometriosis is defined as the presence of endometrium in an abnormal or ectopic location. Histologically, it is the presence of endometrial-like tissue or glands outside the uterine cavity. It is a hormone-dependent gynecological disorder that is most often seen in reproductively active women[1,2].

It is a common cause of pain and infertility, but it also negatively affects quality of life, intimate relationships, participation in daily activities, social activity, productivity, and income[2].

In their study, Fuldeore et al. report that the prevalence of diagnosed endometriosis was estimated at 6.1% (2,922 out of 48,020 women surveyed); 52.7% of women were between 18 and 29 years old when they were diagnosed with endometriosis. The majority (86.2%) of women experience symptoms before diagnosis[3]. In Mexico, the incidence of endometriosis in women with primary and secondary infertility diagnoses has been studied, reaching 34.5% in a sample of 197 patients; however, the number of fertile patients with endometriosis is unknown[2].

The main theories about the pathogenesis of endometriosis seek to explain the appearance of endometrial tissue outside the uterus. Among them are: the theory of retrograde menstruation, proposed by Sampson in 1927, suggests that during menstruation, part of the

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flow moves through the fallopian tubes into the peritoneal cavity, carrying with it endometrial cells that adhere and proliferate in ectopic locations. Although it explains the presence in the peritoneal cavity, it fails to justify other locations of the disease. Theory of coelomic metaplasia: states that peritoneal mesothelium cells can transform into endometrial tissue under specific hormonal or inflammatory stimuli. This could explain the presence of endometriosis in more atypical sites, such as the diaphragm, where the phenomenon of retrograde menstruation would not have a direct role. Theory of lymphatic and blood dissemination: It proposes that endometrial cells migrate through the lymphatic system and blood circulation, which would justify the appearance of endometriosis in distant organs such as the lungs, brain, or even in the skin. Immunological theory: Suggests that a dysfunction of the immune system prevents the recognition and elimination of endometrial cells outside the uterus, allowing them to implant and grow. This would help to understand why some women with retrograde menstruation develop the disease, whereas others do not. Theory of genetic predisposition and epigenetics: Recent studies indicate that there are genetic and environmental factors that predispose some women to develop endometriosis, altering the expression of certain genes and favoring the formation of lesions. Together, these theories indicate that the pathogenesis of endometriosis is complex and multifactorial, combining immunological, genetic, hormonal, and anatomical characteristics to different degrees depending on each case[1,4-6].

Endometriosis affecting the gastrointestinal tract (infiltrating deep endometriosis) has been reported in between 3% and 37% of menstruating women. It is seen in the rectum-sigmoid, cecum, small intestine, and appendix in decreasing order of frequency. Involvement of the ileum is quite rare, and obstruction of the small intestine is very rare. Only a few cases have been reported so far, and all required emergency surgery[5,6].

We present the case of a patient with intestinal endometriosis who presented with intestinal pseudocclusion data, requiring emergency surgery. The diagnosis of endometriosis in the ileum was made by histopathology in the resected specimen.

Case presentation

This is a 26-year-old female patient, with no medical or surgical history before admission, date of last period 2 weeks before, regular cycles of 28 × 4 days, active sex life with barrier contraceptive method, dysmenorrhea of more than 5 years of evolution, attended in the emergency department for the presence of abdominal pain of 2 weeks of evolution, intermittent type, located in the right iliac fossa as well as in the hypogastrium, mild-to-moderate intensity, without irradiation to other areas and without apparent attenuation or aggravating factors, as the only accompanying symptom he mentioned absence of bowel movements 6 days before admission but with the presence of flatus, she self-medicated with oral analgesic having partial improvement, two similar previous conditions which were self-limiting.

On arrival at the emergency department, she had vital signs within normal parameters, physical examination with flat abdomen, slight distension, peristalsis present, decreased in frequency, pain on deep palpation generalized without evidence of acute abdomen, rest without alterations. As part of the diagnostic approach, laboratory tests were requested with only an alteration in leukocytosis of 14.08 ($\times 10^9$/L) at the expense of neutrophilia 79.5%. An abdominal X-ray in two positions and an abdominal ultrasound without reporting alterations.

As none of the studies were inconclusive and pain had decreased, strict medical surveillance was decided with bowel rest, defecatory surveillance, and analgesics. 24 h later, she again presented abdominal pain, absence of bowel movements, no fever, nausea or vomiting, demotion in leukocytosis and neutrophilia, for which a tomography of the abdomen and pelvis contrasted with the following findings: thickening of the ileal wall, maximum caliber of 44 mm, discrete striation of fat at the level of the terminal ileum at its junction with the cecum in close relation to the apparent right annex, rest unaltered.

It was decided to perform diagnostic laparoscopy; however, the equipment was not available, so laparotomy was performed, showing 12 areas of stenosis at the level of the terminal ileum, the first at 8 cm from the ileocecal junction, with an occlusion of 100% of its lumen when it rotated on its own axis, the second at 15 cm from the ileocecal junction with occlusion of approximately 60% of its lumen (Fig. 1). A right hemicolectomy was performed with mechanical ileotransverse anastomosis. The histopathological report of the specimen sent was: endometriosis in the muscle wall and serous wall of the ileum (transmural involvement), as well as secondary extrinsic compression in two areas, surgical edges without histological evidence of lesion (Fig. 2).

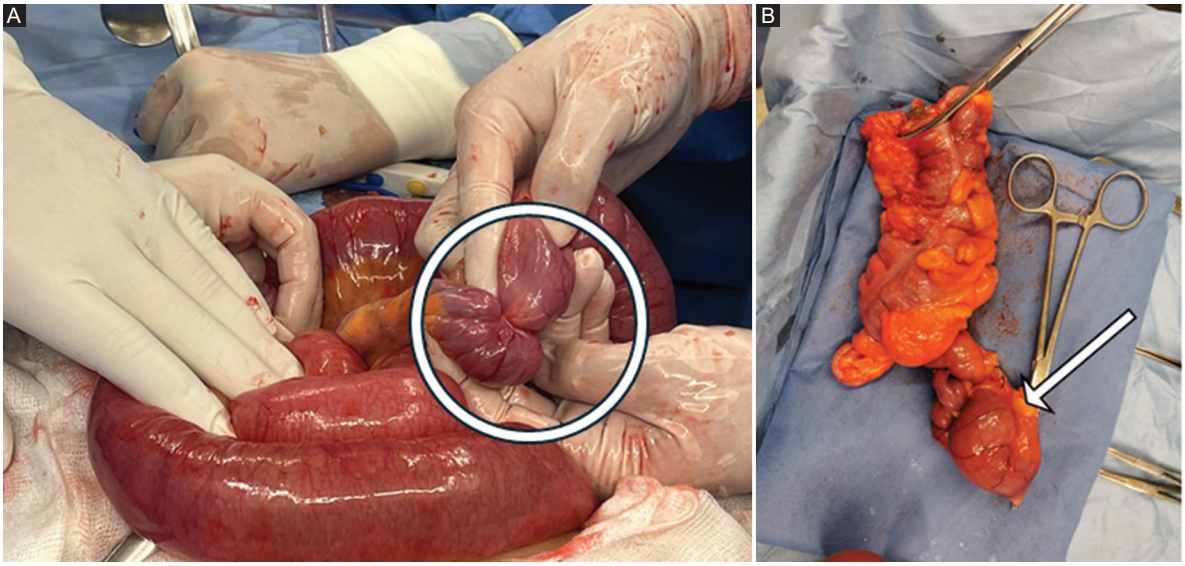

Figure 1. A: the area of stenosis in the terminal ileum (white circle), found as a finding during laparotomy, is appreciated. **B:** specimen resulting from right hemicolectomy with a stenosis area with torsion on its own axis (white arrow).

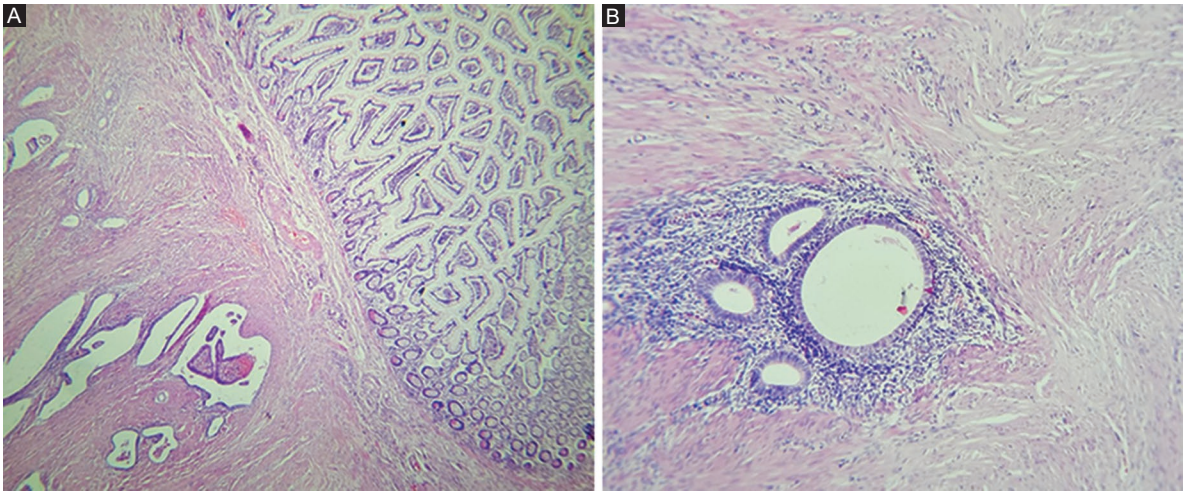

Figure 2. A: photomicrograph shows ileum mucosa. Below in the muscular mucosa, note the presence of glands and stroma with endometrial phenotype. **B:** photomicrograph shows glands and endometrial stroma without atypia, immersed in smooth muscle of the intestinal muscularis propria with transmural involvement.

The patient evolved favorably, tolerating a liquid diet at 24 h postoperatively and a normal diet at 36 h. The patient was discharged on the 6th day and summoned to an outpatient clinic for the removal of stitches, finding a wound in adequate condition. 2 months later, with total remission of symptoms, she was discharged from the General Surgery Service and sent to the Gynecology Service due to histopathological diagnosis of endometriosis.

Discussion

Countless hypotheses and theories have been proposed for the pathogenesis of endometriosis. From the implantation theory, which is currently the most widely accepted, to the stem cell theory. However, it is currently still a question to be resolved[1,2,5,6]. Endometriosis can be asymptomatic, but it also presents a wide variety of clinical manifestations, including pain, dyspareunia,

intermittent bleeding, and infertility. The symptoms that have the greatest impact on the quality of life of patients are those associated with pain, such as dysmenorrhea, profound dyspareunia, cyclic pelvic pain, dysuria, and dyschezia, which occur cyclically according to the menstrual cycle. In addition, intestinal endometriosis can cause irritative functional symptoms, such as diarrhea, intestinal cramps, hematochezia, and mucus expulsion, due to the cyclic release of inflammatory mediators, as well as obstructive mechanical symptoms, such as constipation and abdominal distension, caused by enlarged nodules, intestinal angulation and stenosis, and retraction of fibrotic tissue. Some specific symptoms, such as cyclic dysphasia and tenesmus, are typical of rectal endometriosis[1,2,5-7].

To date, no individual classification system adequately classifies endometriosis. The American Society for Reproductive Medicine's revised criteria for staging endometriosis (revised American Society for Reproductive Medicine) are the most widely used and are useful for clinicians to explain the severity of endometriosis in simple terms to patients. The ENZIAN classification describes in detail infiltrating deep endometriosis (PID) involving retroperitoneal and/or abdominal structures. In addition, the ENZIAN classification is probably most useful when determined using imaging modalities and can be used for surgical planning; however, it has little acceptance worldwide[1,8,9].

Previously, diagnostic imaging modalities were not very successful, but new advances in the field of imaging show promising results for detecting intestinal lesions. In a report, Gillen et al. show that multislice tomography combined with oral contrast located 94.8% of intestinal endometriotic nodules[10]. Magnetic resonance imaging has a high sensitivity for detecting endometriosis, but it has difficulty distinguishing it from other diseases, as well as being expensive[10-12]. Ultrasound, on the other hand, is an inexpensive and efficient means of examining and diagnosing intestinal endometriosis. However, diagnostic accuracy depends significantly on the sonographer's experience[1,13].

Due to the low frequency and non-specific symptoms, multiple differential diagnoses should be considered, such as tuberculous enteritis, yersinia enterocolitis, carcinoid tumors, lymphomas, Behçet's disease, and amoebomas, among others. The final diagnosis is based on histopathology and the presence of endometrial epithelial and stromal cells at ectopic sites[2,5,6,11-13].

The quality of the available evidence on medical treatment for intestinal endometriosis is suboptimal. Most studies were not comparative. There are very few reported cases in which infiltrating deep intestinal endometriosis has been resolved by non-surgical management when symptoms persist or worsen, and with the disadvantage that treatment cannot be interrupted[14].

Medical treatment should not be suggested if the lesion is located above the middle part of the rectum, the degree of lumen stenosis is > 60%, if the lesion infiltrates > 50% of the intestinal circumference, or if the largest diameter of the nodule is > 3 cm, the same rule is followed in the locations in the small intestine[7,14-16].

Surgical treatment depends on the degree of intestinal involvement and the clinical condition of the patient at the time of diagnosis. Ideally, it consists of intestinal resection of the affected ileal segment and primary anastomosis; however, cases have been reported in which right hemicolectomy is performed with or without anastomosis, preferring in either case the minimally invasive approach. When there is doubt of malignancy, resection with oncological criteria is justified and should be considered at the discretion of the surgeon[17-22].

Although successful cases have been presented with medical management, high recurrence rates continue to be shown in contrast to patients who undergo resection, have significant and persistent long-term improvement in pelvic pain, gastrointestinal discomfort, and quality of life, as well as a negligible recurrence rate[14,23,24].

Pharmacological therapy plays a fundamental role as a complement to surgical intervention, both in the pre-operative period and, more significantly, in the post-operative phase. In the pre-surgical context, its use can contribute to the reduction of the size of the lesions, thus facilitating the intervention. Subsequently, in the post-operative period, pharmacological therapy is essential to reduce the size of residual implants, control the progression of the disease in cases where surgical resection has not been able to be carried out completely, as well as to prevent the recurrence of the disease[25-27].

There are multiple therapeutic alternatives available for the management of endometriosis. Non-steroidal anti-inflammatory drugs are a widely used option in the treatment of chronic inflammatory diseases and have been shown to be effective in relieving primary dysmenorrhea. Combined oral contraceptives (COCs) and progestins, which are available in various presentations and routes of administration, represent the first line of hormonal treatment due to their efficacy and safety profile.

In cases where these therapies are not sufficient, the second line is mainly composed of gonadotropin-releasing hormone agonists. Although these agents have shown positive results in women who do not respond to COCs or progestins, it is important to mention that they require the addition of complementary treatments. On the other hand, the use of danazol has decreased significantly due to the availability of hormonal options with a superior safety profile and better tolerability. Since there are few data available on the long-term efficacy and safety of aromatase inhibitors, they should be given only to women with symptoms refractory to other conventional therapies in a clinical research setting[26,28-31].

Studies have shown that vitamin C and vitamin E supplementation is effective in reducing the severity of dysmenorrhea and improving dyspareunia, as well as decreasing the intensity of pelvic pain in patients with endometriosis[32-34].

Conclusion

Endometriosis with terminal ileum involvement is a rare and difficult to diagnose entity that can mimic multiple entities. This pathology should be suspected in all women of childbearing age who show intestinal symptoms without apparent causes traditionally demonstrable as if it were a functional digestive disorder, especially because of the implications that emergency surgery can have. Minimally invasive surgery should be considered the standard of management due to its widely demonstrated benefits, as well as a follow-up in conjunction with the gynecology service.

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LETTER TO THE EDITOR

Review and analysis of the report: *fungal multivalvular endocarditis*

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Dear Editor:

We have read and analyzed the report on "*Fungal multivalvular endocarditis: literature review and case report*" by Herrera-Salgado et al.[1]. The clinical case and its analysis are interesting, on a clinical entity that is difficult to think of and more complicated to confirm by mycological tests. Most of these cases go unnoticed or are confused with bacterial infections, which are the most frequent. In this particular case, however, the identification was not reached due to the morphology presented in the periodic acid-Schiff (PAS) and Grocott stains, which correspond to blastoconidia or yeasts, without the presence of pseudohyphae, which rules out an infection by the various species of *Candida,* with the exception of *Candida glabrata*, which does not form these structures and which has now been classified as *Nakaseomyces glabratus* by phylogeny studies. Because in this case the agent could not be isolated, it is impossible to confirm the species; however, due to the morphology it presents, it is most likely an infection by *Malassezia* yeasts*,* which are integral parts of the microbiota of many parts of the body[2].

In general, *Malassezia* endocarditis is exceptional and complicated to confirm; the two most involved species are *Malassezia furfur* and *Malassezia restricta*, these as well as others are strict lipophilic, that is, they depend on fat sources, hence the culture media that are required, are special media that incorporate lipids such as Sabouraud + olive oil or Modified Dixon medium; both media are not inside of the series that should be done for cases of endocarditis and are only incorporated when the suspicion is high, so an image, such as the one put in the article, is highly suggestive of this infection[2].

It is worth highlighting the issue with a couple of recent publications, Houhamdi-Hammou et al.[3] and Zhang et al.[4], in the first one highlighting the diagnosis of this type of endocarditis, when conventional cultures are negative (as in the case presented), and the second is an analysis of the literature with 86 cases from 37 studies, where most were premature infants (44.2%), followed by adults (31.4%). The fungemia was caused by *M. furfur* in 79.1% and it should be noted that in just over half of the cases, the infection was obtained from blood from the catheter. The report highlights catheter-related infections, pneumonia, peripheral thromboembolism, endocarditis, meningitis, peritonitis, and disseminated infections. Another source that may be the origin of this is parenteral feeding that is rich in lipids, and that can favor *Malassezia* infections; in this analysis, it was associated in 80.2% of cases. In general, *Malassezia* spp. is sensitive to amphotericin B and to triazoles, particularly voriconazole, but not to echinocandins.

We conclude our commentary by indicating that it is good to see this type of report, because it allows us to analyze the problem of diagnosing fungal endocarditis, particularly when fungi and yeasts cannot be isolated by conventional methods, and incorporate *Malassezia* spp. infections into the possible causes.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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