Research Article ISSN 2639-944X

Journal of Medical - Clinical Research & Reviews

Membranous Dysmenorrhea: An Underdiagnosed Condition

Laíssa Gava Altoé Luz*, Rúbia Soares De Sousa Gomes, Jéssica Maria Colnago, Daniel Sossai Altoé, Marina Rangel Reis Monteiro Alves, Fernanda Rosetti Fernandes, Pedro Henrique de Souza Loureiro, Izabella Ahnert Blanco de Moura Magalhães, Isabela Ribeiro Rodrigues, Débora Qualhano Trigo, Ricardo Cristiano Leal Da Costa and Antônio Chambô Filho

Obstetrics and Gynecology department of the Hospital Santa Casa de Misericórdia de Vitória, Espírito Santo, Brazil.

***Correspondence:**

Luz Laíssa Gava Altoé, Obstetrics and Gynecology Resident, Hospital Santa Casa de Misericórdia de Vitória, Street Dr João dos Santos Neves, 143, Vila Rubim, Vitória, Espírito Santo, Brazil, Zip code 29025-023, Tel: +55 27 3212-7200.

Received: 11 Jul 2024; **Accepted:** 25 Aug 2024; **Published:** 03 Sep 2024

Citation: Luz LGA, Gomes RSDS, Colnago JM, et al. Membranous Dysmenorrhea: An Underdiagnosed Condition. J Med - Clin Res & Rev. 2024; 8(9): 1-7.

ABSTRACT

Dysmenorrhea is the most prevalent gynecological symptom in menopausal women. Currently defined as menstrual cramps, it is on the list of the main complaints in gynecological consultations. A sub-classification forgotten in medical dictionaries is membranous dysmenorrhea (MD), which corresponds to the elimination of membranes through the vaginal canal. The definitive diagnosis requires anatomopathological study, and abortion is the main differential diagnosis. As there are few cases in the literature, this study aims to present a series of eight cases, highlighting the pathophysiology and comparing the data with other studies to encourage discussion on the subject. This is an observational, longitudinal, retrospective study including women with clinical membranous dysmenorrhea (spontaneous elimination of fibroelastic material via the vagina). The results show that of the eight patients, seven had used or were using exogenous female hormones; 62.5% of the total had MD in the 2nd - 3rd decade of life, two had had previous abortions, and one was nulliparous. All these facts have been associated in the literature as etiological or contributing factors to MD. However, while diverging from the literature, our article showed that the infection factor is not mandatory for the occurrence of MD. In conclusion, proposing a single pathophysiological and etiological mechanism based on a series of cases and in comparison with other data in the literature is a challenge. However, consistently with what has been published, most of the cases presented were the result of an increased vascular response of the endometrium when exposed to an exogenous source of estrogen and progesterone, and this could be a hypothesis which, of course, requires further studies to establish the exact casuistry, but which contributes greatly as a source of data for future research.

Keywords

Colic, Dysmenorrhea, Membranous dysmenorrhea, Menstruation.

Introduction

Dysmenorrhea is a word of Greek etymology and means difficult menstruation [1,2]. Currently, it can also designate menstrual cramps [1,3,4]. It represents the most prevalent gynecological symptom in women during menacme, with a prevalence rate ranging from 43% to 93%. However, it is still one of the most neglected symptoms by medical professionals and the patients themselves [5-9]. Didactically, it is classified into primary or functional dysmenorrhea and secondary or organic dysmenorrhea [1,8].

Primary dysmenorrhea includes cases when there is no identifiable disease, which means it is a diagnosis of exclusion. It usually affects younger women, one to two years after menarche, and has a cyclical nature [1,5-7]. In organic dysmenorrhea, as the name suggests, it is possible to identify an underlying pathological cause that leads to the clinical picture - such as leiomyomas,

endometriosis, adenomyosis, ovarian cysts, among other causes [4,5,7,10], and it has an acyclic characteristic, affecting women in adulthood, or even occurring with the menarche [1,4,5]. There is also a sub-classification of dysmenorrhea called membranous dysmenorrhea (MD), described in both primary and secondary dysmenorrhea [10].

MD is the elimination of a fibroelastic material, in the shape of a membrane or uterine mold, via the uterine cervix and exteriorized through the vaginal canal [3,6,7,11-14]. Few reports are available in the literature about this etiological entity, mainly published between the 1950s and 1970s, and only a few recent papers based on these older studies. Besides, epidemiologically, no data is available on the prevalence and incidence of MD in the literature [9,10]. Therefore, the clinical-pathological entity has been little discussed in academic circles, perhaps due to underdiagnosis and misinformation by healthcare professionals. Thus, there is a clear need for more research into the subject to elucidate the etiology and pathophysiology and to detail the clinical picture and predisposing factors that can help define the propaedeutics [7,10]. For this reason, it is necessary to introduce new reports into the literature to promote a discussion on this subject, acting as a vehicle for spreading the word about a condition that, although common, is forgotten by health professionals [3,4,6,9,12].

Methods

The present study is a quantitative, descriptive, observational, longitudinal, retrospective case series study of MD. Patients were selected from the electronic medical records of eight patients seen at the Gynecology Outpatient Clinic and Gynecology Emergency Room of the Santa Casa de Misericórdia de Vitória Hospital (HSCMV). The report was based on articles on the subject, using the indexing databases Lilacs, Scielo, and BVS. PubMed and Google Scholar were also used as databases, although only a few articles found could serve as a theoretical basis.

As this is a study that includes the exposure of data relating to civilians, the entire process that preceded the preparation of the work was approved by the platform of the Extension and Research Center (NEP, in Portuguese), by the National Research Ethics Commission (CONEP, in Portuguese) and by the Research Ethics Committee of the Santa Casa de Misericórdia Hospital in Vitória (CEP/HSCMV, in Portuguese). In addition, the subjects were informed about the ethical process and their rights were clarified through the Free and Informed Consent Form and the Free and Informed Assent Form for minors.

Based on studies already published and available in digital and physical forms, the theoretical foundation aims to provide a scientific basis for the work and help identify the current stage of knowledge on the subject [15]. The articles used in this research included case reports on MD and its consequences, causal and precipitating factors, diagnosis, prognosis, and treatment. Studies that did not meet the inclusion criteria were excluded.

Case Series

Case 1: B.O.V., 22 years old, single, nulliparous, with no comorbidities, currently taking levonorgestrel 0.15 mg + ethinylestradiol 0.03 mg (Ciclo 21 ®), with interruptions due to moderate to severe primary dysmenorrhea. She reported using oral contraceptives since menarche. The patient was admitted to the Emergency Department of the HSCMV complaining of vaginal bleeding with a slightly larger volume than usual since the start of menstruation, as well as its frequency, which had lasted for nine days so far but was compatible with her menstrual period. She reported cyclical menstrual cycles. She described that on the ninth day, in addition to the bleeding, she had moderate pelvic pain associated with a membranous, pinkish material coming out of the vagina (Figure 1). She denied any previous similar conditions. On physical examination, the patient was in good general condition with no pain on abdominal palpation. On speculum examination, there was slight malodorous bleeding from the external orifice of the cervix. The beta-human chorionic gonadotropin (BHCG) test was negative, the white and red blood count was unchanged, and the histopathology result of the specimen was compatible with MD (decidual remnants).

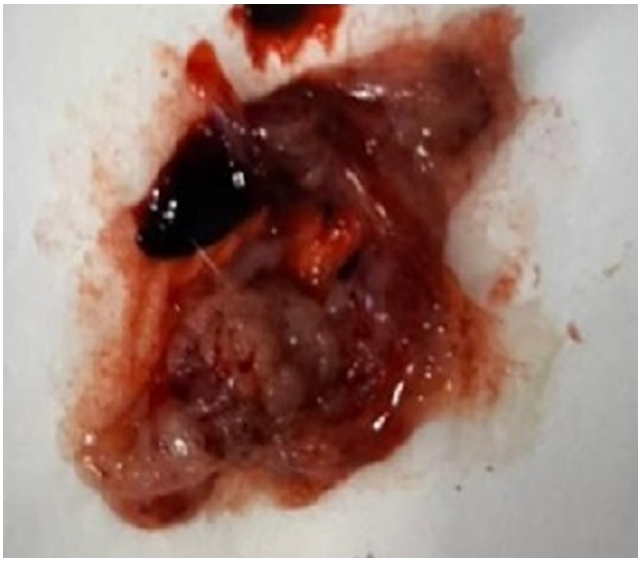

Figure 1: Membranous product eliminated via the vagina.

Case 2: L.M.S., 43 years old, multigravida, using monthly injectable contraceptives since menarche: norethisterone enanthate 50mg/ml + estradiol valerate 5mg/ml (Noregyna ®). The patient was seen in the emergency department due to vaginal bleeding for six days, associated with moderate pelvic pain, which eased with the use of a common analgesic, and the elimination of pinkish vaginal membranes. She said it was the first time this had happened. Physical examination was unremarkable, the BHCG test was negative, and the histopathology report said: membranous dysmenorrhea. Microscopy - 30x objective, hyperplastic secretory endometrium compatible with membranous dysmenorrhea (Figure 2). The patient continued the follow-up and kept using the same contraceptive, with no recurrence of the pathology.

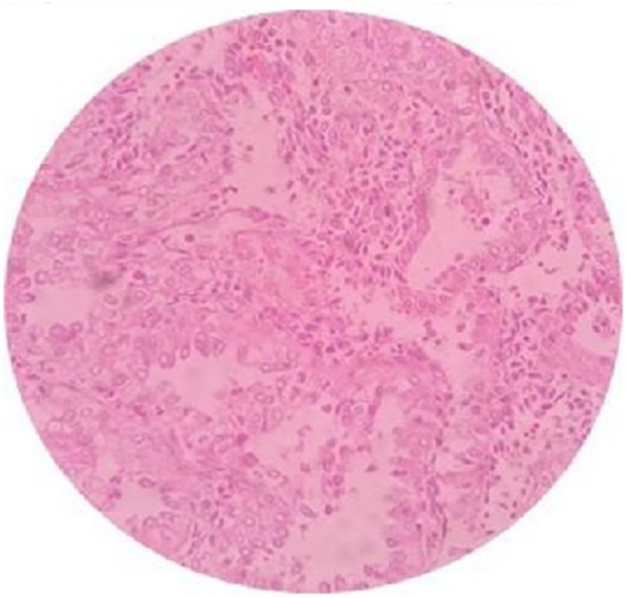

Figure 2: Microscopy: hyperplastic secretory endometrium compatible with decidual remnants (30x magnification).

Case 3: M.C.G.R., 41 years old, secundigravida, active sexual life, with cardiac arrhythmia, mitral prolapse, and glaucoma - taking medication, currently not using contraception, but with previous use of combined oral contraceptives (she could not say for how long she had been taking them or their pharmacological composition). The patient was referred to the emergency gynecology and obstetrics service due to a suspected miscarriage. She reported sudden pain in the supra-pubic region and subsequent elimination of vaginal material interspersed with blood (Figure 3). The transvaginal ultrasound (TV-USG) showed a discreet, thick, liquid-like content on the endometrium, suggesting a hematic component with no other alterations. Quantitative and qualitative BHCG results were negative. The anatomopathological test presented as follows: microscopy - 10x objective, hematoxylin and eosin stained decidualized endometrium (Figure 4).

Figure 3: Elastic material taken from the external orifice of the cervix.

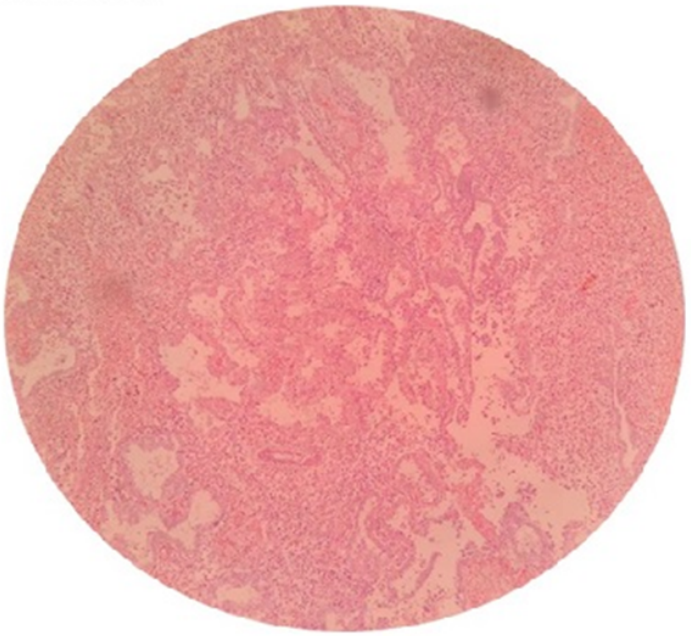

Figure 4: Microscopic examination stained with hematoxylin and eosin corresponding to decidualized endometrium (10x magnification).

Case 4: V. L., 36 years old, G2PC2A0, in menacme, with no comorbidities, taking oral contraceptives (ethinylestradiol 0.035 mg + cyproterone acetate 2mg) for six years, attended the gynecology emergency service carrying a pinkish fibroelastic material (Figure 5), which she had eliminated vaginally hours before, associated with sudden cramp-like pain in the lower abdominal region that ceased soon after the discharge of the content. The material was set to anatomopathological analysis, which resulted in endometrial tissue with decidual stroma - microscopy 10x objective, hematoxylin, and eosin staining (Figure 6).

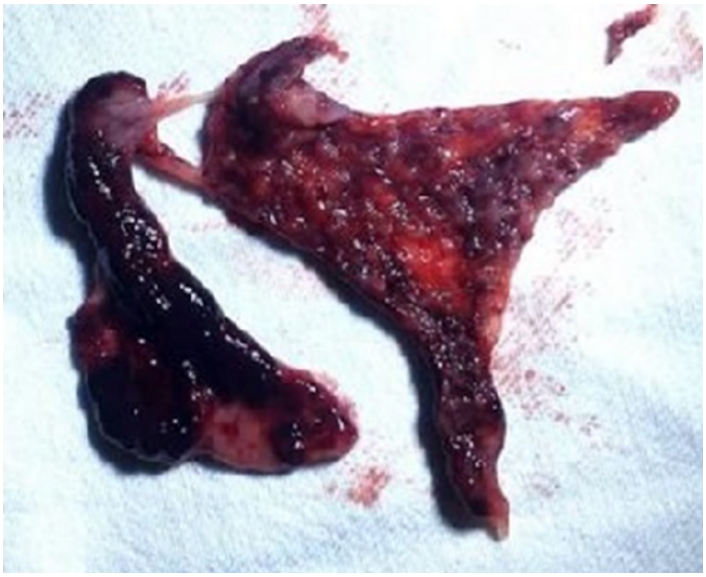

Figure 5: Macroscopic appearance of a mold membrane removed from the uterine cervix.

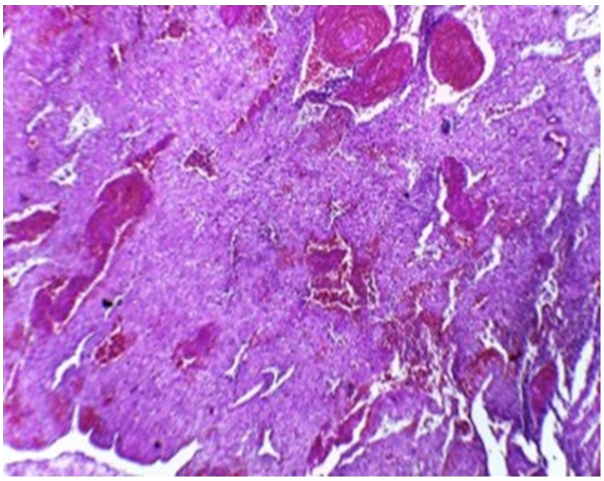

Figure 6: Microscopic examination, 10x magnification, corresponding to endometrial decidua with polymorphonuclear infiltration.

Case 5: R.L.L., 37 years old, with no previous pathologies, using dienogest 2mg for about three years. However, she had previously used combined contraceptives - she could not specify the dosage or formula. Between interruptions and returns, she has taken oral contraceptives for around 20 years. She presented to the gynecological service for moderate intensity, short-lived bleeding associated with dysmenorrhea, and elimination of membranous material (Figure 7), which she brought from her home. She had a TV-USG from the month before, which showed an enlarged uterus (volume 342 cm^3) containing hypoechoic, intramural images, the largest on the anterior uterine body wall, measuring 4.7 cm, suggesting uterine fibroids. Endometrial thickness 2mm, left appendages unchanged, right appendage containing simple ovarian cyst (3.3 cm). On physical examination, the abdomen was painless on palpation and the uterus was palpable 2cm below the umbilical scar. On speculum examination, there was a slight bleeding from the external orifice of the cervix with no other alterations. The anatomopathological analysis indicated fragments of the endometrium with stromal decidualization.

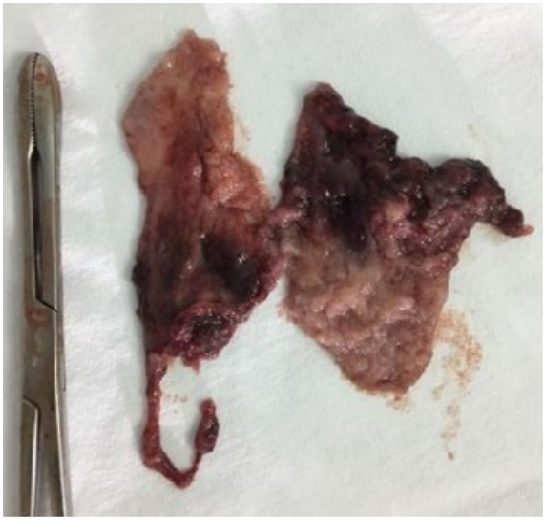

Figure 7: Tissue content expelled spontaneously through the vagina.

Case 6: E.L.B., 28 years old, in menacme, G1P0A1, with a desire for pregnancy, no comorbidities, denies current and prior usage of contraceptive methods. She sought the gynecology emergency room carrying a brownish material, recently eliminated vaginally (Figure 8) after experiencing sudden and intense pelvic pain which ceased entirely after the elimination of the content. The BHCG result was negative, and the pathology corresponded to MD (degenerated decidual remains and endometrial fragments).

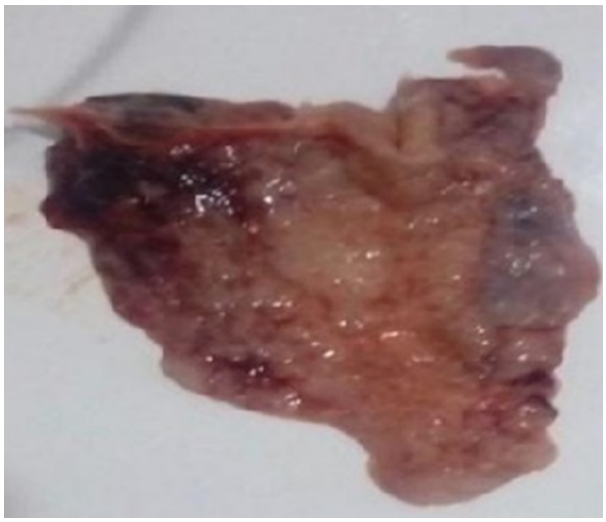

Figure 8: Tissue eliminated via the vagina after uterine cramps.

Case 7: M.D.P., 52 years old, multiparous, with failed menstrual cycles for less than a year, with hot flushes, no comorbidities, denies the use of current contraceptive methods but had previously used combined oral contraceptives, although cannot report the composition measure duration of use. She was admitted to the emergency department following sudden moderate colic-like pain in her lower abdomen, associated with discreet vaginal bleeding that had started three days previously and elimination of membranous material vaginally. She reports that after eliminating the membrane, the abdominopelvic pain improved, although the vaginal bleeding remained mild. The patient continued follow-up at the gynecology outpatient clinic since the incident and has not had other similar symptoms to date. Pathology results: decidualized endometrium, suggestive of MD.

Case 8: L.K.N.L., 32 years old, G6PN3C1A2 - last abortion in February 2023 without the need for curettage, with menstrual irregularity, taking norethisterone enanthate 50mg/ml + estradiol valerate 5mg/ml (Mesigyna ®) - could not specify the duration of use but referred using this formulation since she started using contraceptives, with no comorbidities. Due to a recent miscarriage, she had menstrual irregularity for four months and vaginal bleeding that began six days ago, associated with pelvic pain and elimination of vaginal material (Figures 9 and 10). Hence, she was referred to a gynecological/obstetric emergency department. Physical examination was unremarkable, the BHCG test was negative, the other laboratory tests were unchanged, and the pathology test suggested MD.

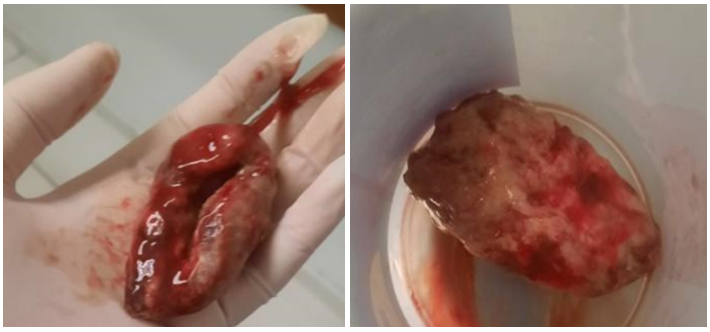

Figure 9: Anatomopathological report of vaginally eliminated product.
Figure 10: Macroscopic images of material spontaneously eliminated by the patient in the form of a uterine mold.

Discussion

The term MD was first described by the Italian anatomist Giovanni Battista Morgagni, also known as Gianbattista Morgagni, in the 18th century [4,5,8]. MD is recognized by the elimination, via the vagina, of elastic material, sometimes similar to the uterine cavity, with a membranous appearance corresponding to the uterine endometrium after the decidualization of the stromal cells [3,5,13,14]. Pain precedes the elimination of the tissue through the undilated uterine cervix [5-7].

To explain the pathophysiology of MD numerous postulates were proposed in the 18th and 19th centuries. Initially, it was hypothesized that the descent of the membrane was due to an association with endometriosis, abortion, first pregnancy, or infection [7]. The latter was due to the visualization of microabscesses in the tissue slides studied [5,12,16]. However, these etiological hypotheses were ruled out because MD has been described as occurring in women who are nulliparous, unmarried, and without endometriotic pathology or previous infections. These factors may be related to an increased risk of MD, but not to the etiology of the disease [6,7].

Scholars in the 18th century hypothesized that the occurrence of MD was due to the fibrin or lymph exudate that emerged from the uterine mucosa. Still, this hypothesis was also overturned when they proved that the membranous tissue that descended through the vaginal canal was microscopically compatible with endometrial tissue by showing the presence of decidual cells in a state of hyperactive hypertrophy and development [6,7]. Rabinerson and partners suggested that the pathogenesis was due to alterations in cell adhesion mechanisms, mediated by activins, inhibins, integrins, follistatins, and relaxins. The abnormality between these proteins, in contrast to the high level of progesterone, would explain the lack of cell-cell adhesion of the endometrial tissue and its subsequent decidualization [6,14,16]. Greenblatt and others in 1954 described the occurrence of MD as being related to the increased secretion of female hormones, both estrogen and progesterone - either endogenous or exogenous - in association with the development of excessive spiral arterioles, as well as hyper-vasodilation and hyper-vasoconstriction [17]. Oliveira and partners in 2009 shared this same hypothesis and added that the pathology correlates with intense vasospasm of the arterioles and subsequent necrosis, which would trigger the detachment of the endometrial membrane [10].

Still, as a way of explaining the physio-etiopathogenesis of dysmenorrhea caused by the descent of membranes, several current and previous articles have addressed the theory of hyperprogesteronism. An excess of progesterone, whether endogenous or not, would be the determining factor for the excessive decidual reaction with lymphocyte infiltration in the tissue and subsequent shedding of the endometrium, which is then expelled in the form of a uterine mold or even membranes [6,7,18]. Omar and Smith reported that in the past MD was related to the use of depot medroxyprogesterone (DMPA), which, as in the hyperprogesteronism hypothesis, caused an intense inflammatory reaction in the endometrial tissue, leading to its descent. However, in the same article, they provide data to refute this theory by reporting that women used DMPA as an alternative to transdermal patches, combined oral contraceptives, and the minipill and did not have MD as an unfavorable outcome [9,19].

It has also been suggested that MD comes from the use of contraceptives, whether combined or progestogen alone - in high dosages or for extended periods. However, some papers describe women with the condition using contraceptives (combined or not) in low dosages, for short periods, and even in people who have never used hormone therapy [3,6]. Morse, in 1907, evokes the possibility that MD is not a sui generis disease but rather stems from a process mediated by multiple etiologies, with various possible events and microscopic presentations [6,7,20].

Regarding the differential diagnosis of MD, physicians should consider pathologies that involve the discharge of material from the vaginal canal, particularly the hypotheses of botryoid sarcoma (an embryogenic polypoid tumor that mainly affects children/young women), polyp extrusion, or abortion, the latter being the most common differential diagnosis [5-7,10,21]. Since miscarriage is a differential diagnosis, one of the first tests that should be ordered is the BHCG to rule out this cause [9].

The diagnostic suspicion of MD emerges from the discharge of a fibroelastic material in the shape of a uterine mold or membrane, preceded by intense pain, which may or may not be associated with bleeding [4,6]. However, despite the anamnesis, physical examination, and laboratory tests suggesting the pathology, the definitive diagnosis of MD can only be made by anatomopathology [6,10,12,13]. Microscopy shows tissue compatible with the endometrium, often described as a decidualized endometrial stroma, with necrotic cells and a mixed inflammatory infiltrate [10,12,13]. Given the cases described and the literature, it can be strongly affirmed that it is not essential for MD to be preceded by infection. Among all the cases presented, no patient had an infectious condition concomitant with MD - infection may be a risk factor for MD, but not a causal factor. Similarly, the literature suggests that miscarriage and the absence of a previous child could be contributing factors to the occurrence of MD - and, in line with the literature, two patients had a previous miscarriage, and one

was nulliparous. As for age, according to reports in the literature, MD occurs mainly in the second and third decades of life, a fact observed in 62.5% of the patients in the study [5].

One of the most widely accepted hypotheses today, considered by most authors, is the endogenous or exogenous use of estrogen and progesterone, or even progesterone alone - hyperprogesteronism, leading to decidualization of the endometrium and its detachment in the form of a uterine mold. Considering that of the eight patients studied, seven were using exogenous female hormones this could be an explanation for the cases. In addition, of the total studied, six had already taken or were currently taking combined contraceptives. Only one of the seven patients was currently using the minipill when she developed MD. However, this same patient had previously used combined contraceptives. These data raise the hypothesis that the use of exogenous estrogen and progesterone may contribute to the etiology of MD. What is not so clear to establish is whether one of the female hormones stands out in the etiopathology of the disease in question.

A fact that opposes this hypothesis in our report and the literature is that patients not using contraceptives can present MD. Out of the eight patients studied, one had never used exogenous hormones. This same patient has a history of miscarriage and is in her second decade of life - facts that cannot be considered the cause of the dysmenorrhea but rather contributors to it. The hypothesis of an endogenous increase in female hormones could be a plausible explanation for this patient, or even a multifactorial association, as stated by Morse in 1907 [20].

The difficulty encountered in this study was in associating the dosage, therapeutic formula, and duration of contraceptive use. Of the seven women surveyed who were using contraceptives, either previously or currently, three were unable to report the dosage, and four did not know for how long they had been used, which limited their knowledge of whether the amount of hormone used and the frequency of use contributed to the pathology in question.

It is also important to note that, contrary to what some studies suggest, high doses of exogenous estrogen and progesterone are not the only cause of MD. In our report, we observed that even patients using low doses of external hormones are likely to present at least one case of MD at some point during their fertile life. Notably, in one of the cases presented, the patient had uterine myomatosis diagnosed by ultrasound, showing that MD can occur not only in functional dysmenorrhea but also, as the literature points out, in organic dysmenorrhea.

Proposing a single pathophysiological and etiological mechanism based on a series of cases is an immeasurable challenge. What can be assessed from the pictures described, which are in line with the findings in the literature, is that most of the cases presented were the result of an increased vascular response of the endometrium when exposed to an exogenous source of estrogen and progesterone. This could be a hypothesis that certainly requires further studies to establish the exact casuistry, but which significantly contributes as a data source for future research.

Conclusion

Although common, MD deserves to be highlighted in the gynecological context as it is an unknown and underestimated condition by many medical professionals.

The etiological causes are still a challenge in the literature and need more descriptions, research, knowledge, and interest to be affirmed. It is not known, for example, why some women have MD and others do not [6,7,10]. As far as the prognosis is concerned, it seems to be favorable and self-limiting [5,9,12]. In particular, in the cases described, this statement is incomparable since the search was done in the medical records of patients seen in the emergency room, and not all the patients studied continued the follow-up at the hospital's gynecological outpatient clinic to monitor their condition.

Concerning the therapy, most agree that anti-inflammatories and analgesics are good options for the acute treatment of the condition [7]. Even contraceptives could be used in the management of MD because, although they are considered a causal agent, the drug is not related to the recurrence of the condition, which is considered to be self-limiting [10]. The fact is that without the casuistry established in the literature, little can be known about treatment. For this reason, it is crucial to disseminate, contribute, and update the subject to enrich the existing data and serve as a basis for future studies.

References

1. Acqua RD, Bendlin T. Dismenorreia. Femina. 2015; 43: 274-276.
2. Gerzson LR, Padilha JF, Braz MM, et al. Fisioterapia na dismenorreia primária revisão de literatura. Revista Dor. 2014; 15: 290-295.
3. Brandão P, Portela-Carvalho AS, Oliveira C. Non-Painful Out of Pill Membranous Dysmenorrhoea. Obstet Gynaecol Cases Rev. 2018; 5: 1-3.
4. Troncon JK, Rosa-e-Silva ACJS, Reis RM. Dismenorreia abordagem diagnóstica e terapêutica. Femina. 2020; 48: 518-523.
5. Araujo LFO. Dismenorréia Membranosa Relato de Caso e Revisão de Literatura. Vitória ES Universidade Federal do Espírito Santo. 2017.
6. Lopes LWP. Dismenorreia Membranosa Membranácea Um Relato de Caso. João Pessoa PB. Centro Universitário de João Pessoa. 2020.
7. Medeiros CRB, Araújo EFG, Lopes LWP. Dismenorreia Membranosa Membranácea Um Relato de Caso. Femina. 2021; 49: 572-576.
8. Passos RBF, Araújo DV, Ribeiro CP, et al. Prevalência de dismenorréia primária e seu impacto sobre a produtividade em mulheres brasileiras: estudo DISAB. RBM rev bras med. 2008; 65: 250-253.

9. Maciel R, Rodrigues S, Inocêncio G, et al. Dismenorreia Membranosa uma rara e desconhecida entidade. Acta Obstétrica e Ginecológica Portuguesa. 2014; 8: 402-404.
10. Oliveira PP, Eyng C, Zin RMA, et al. Dismenorreia membranosa uma doença esquecida. Rev Bras Ginecol Obstet. 2009; 31: 1900-1903.
11. Marin L, Andrisani A, Buzzaccarini G, et al. Dysmenorrhoea in a woman undergoing hormone replacement preparation for embryo transfer a peculiar case. Prz Menopauzalny. 2023; 22: 55-57.
12. Ferreira TB. Dismenorreia Membranosa uma doença pouco falada. Manhuaçu MG Centro Universitário. UNIFACIG. 2022.
13. Jyoti, Kumari S, Kumar D, et al. Recurrent decidual cast with membranous dysmenorrhea. Int J Reprod Contracept Obstet Gynecol. 2019; 8: 738-740.
14. Rabinerson D, Kaplan B, Braslavski D, et al. Membranous dysmenorrhea The forgotten Entity. Obstet Gynecol. 1995; 85: 891-892.
15. Gil AC. Como elaborar projetos de pesquisa. 6th ed. São Paulo SP Atlas. 2017.
16. Silveira DS, Jaenickie A, Hollanda ES, et al. Dismenorréia membranácea ainda existe Relato de caso. Clini & Biomed Res. 2011; 31: 468-470.
17. Greenblatt RB, Hammond DO, Clark SL. Membranous dysmenorrhea studies in etiology and treatment. Am J Obstet Gynecol. 1954; 68: 835-844.
18. Perdomo CB, Jiménez PS, Fleites LA, et al. Dismenorrea membranácea durante la menarquia. Rev Chil Obstet Ginecol. 2016; 81: 135-137.
19. Omar HA, Smith SJ. Membranous Dysmenorrhea a case series. Scientific World Journal. 2007; 26: 1900-1903.
20. Morse E. A report of four cases of Membranous Dysmenorrhea. Johns Hopkins Hospital Bulletin. 1907; 18: 40-45.
21. Brehmer L, Engberg H. Membranous dysmenorrhea or passage of a decidual cast forgotten phenomenon but not rare? Case report and summary of the literature. Lakartidningen. 2022; 119: 22081.