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Case Report

Intact ovarian ectopic pregnancy: a challenging diagnostic case report*

Gravidez ectópica ovariana íntegra: relato de caso de difícil diagnóstico

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ABSTRACT: Introduction: Ectopic Pregnancy (EPGE) is characterized by the implantation of the fertilized egg outside the endometrial cavity, mainly in the uterine tube (95% of cases). When this implantation occurs in the ovary, an Ovarian Pregnancy (OPGO) occurs, representing 0.5% to 1% of all EPsGE. Diagnosis of GOOP diagnosis is challenging, as the accuracy of recognition by clinical exam or imaging is insufficiently documented. Tools such as transvaginal ultrasound and anatomical and histopathological examinations are essential for recognizing GEEP. **Objective:** To describe the case of a patient with a correct diagnosis of complete GOintact OP and discuss, in light of the literature, diagnostic and treatment methods in light of the current literature. **Case Report:** Female patient, 37 years old, primigravida in which the endovaginal ultrasound showed an empty uterus and gestational sac in an intact right ovary. **Discussion:** The patient underwent laparoscopic treatment and the GO OP criteria were met. However, no pathological findings were considered a possibility of tubal GEEP. Some reports in the literature also lacked confirmation of the pathology, reaffirming the diagnostic complexity. **Conclusion:** The difficulty in diagnosing GO OP is clear, as the tools used led to divergent conclusions, highlighting the importance of a careful and multidisciplinary approach in these situations.

KEY WORDS: Ectopic Pregnancy; Ovarian Pregnancy; Case reports; Missed diagnosis, First trimester of pregnancy.

RESUMO: **Introdução:** A Gravidez Ectópica (GE) é caracterizada pela implantação do óvulo fertilizado fora da cavidade endometrial, principalmente na tuba uterina (95% dos casos). Quando essa implantação ocorre no ovário, ocorre uma Gravidez Ovariana (GO), representando de 0,5% a 1% de todas as GE. O diagnóstico de GO é desafiador, pois a precisão do reconhecimento pela clínica ou por imagem é insuficientemente documentada. Ferramentas como a ultrassonografia transvaginal e os exames anátomo e histopatológico são essenciais para o reconhecimento de GE. **Objetivo:** Descrever o caso de uma paciente com diagnóstico incerto de GO íntegra e discutir, à luz da literatura, métodos diagnósticos e de tratamento. **Relato do Caso**: Paciente do sexo feminino, 37 anos, primigesta em que a ultrassonografia endovaginal evidenciou útero vazio e saco gestacional em ovário direito íntegro. **Discussão**: A paciente foi submetida a tratamento videolaparoscópico e os critérios diagnósticos de GO foram preenchidos. Entretanto, no anátomo patológico foi considerada a possibilidade de GE tubária. Alguns relatos na literatura também não tiveram confirmação da patologia, reafirmando a complexidade diagnóstica. **Conclusão**: Fica nítida a dificuldade de diagnóstico de GO, pois as ferramentas usadas levaram a conclusões divergentes, destacando a importância de uma abordagem cuidadosa e multidisciplinar nessas situações.

PALAVRAS-CHAVE: Gravidez Ectópica; Gravidez Ovariana; Relatos de Casos; Diagnóstico Ausente; Primeiro Trimestre da Gravidez.

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INTRODUCTION

Ectopic pregnancy (EP) occurs when implantation of the fertilized egg occurs outside the endometrial cavity. Some of the factors which increase the risk of ectopic pregnancy are: history of pelvic surgery, previous EP, use of Intrauterine Device (IUD), history of pelvic inflammatory disease and infertility. Approximately 95.0% of cases of ectopic pregnancy occur in the fallopian tube, but there are extratubal structures where the embryo can implant, such as in the ovary[1,2]. In Ovarian Pregnancy (OP), the embryo implantation site is the ovary and corresponds to a rare type of EP (0.5% to 1% of all ectopic pregnancies or 1 in 7,000 to 40,000 live births) and this is even rarer when it comes to intact OP, whose estimated occurrence is 1/10,000 uterine pregnancies and 1/1,000 EPs. The overall risk of OP in pregnant women is estimated to be 0.014% to 0.0025%, while this risk in women with suspected ectopic pregnancy due to symptoms or an adnexal mass is 0.5% to 1%. The accuracy of OP imaging diagnosis is not yet sufficiently documented to assess the occurrence of false negatives[3].

The rarity of OP is due to the anatomy of the structure and the well-codified diagnostic procedures. The exact etiological mechanism of both implantation and development of the ectopic blastocyst is still poorly understood, but it is known that the main associated risk factor, in addition to the usual ones, is the use of IUD[4].

There are reports in the literature that OP can progress until the second trimester or full term. However, there is an association with a high risk of maternal morbidity and mortality[4]. OP diagnosis is based on surgical and histopathological observations and the incidence of this type of ectopic pregnancy is increasing, believed to be due to the development of transvaginal ultrasonography and careful histological analysis of ovarian tissue[5].

In view of the above, this article aims to describe the case of a patient with an uncertain diagnosis of intact ovarian ectopic pregnancy and to discuss the diagnostic and treatment methods in light of the current literature.

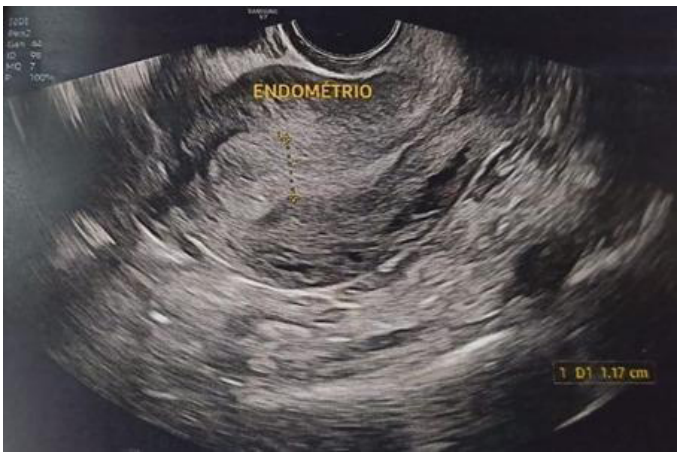
CASE REPORT

A 37-year-old white, married, nulliparous primiparous woman with no relevant personal or family history of pathology. The patient was admitted to the emergency room of a private maternity hospital by self-presentation, presenting an antalgic posture. She complained of lumbosacral pain and discomfort in the left iliac fossa that had persisted for three days. She reported that her Last Menstrual Period (LMP) was 7 weeks and 4 days ago, that her menstrual cycle was regular and that a previous urine pregnancy test had shown a negative result. She reported having self-administered Paracetamol 750 mg on two occasions for pain relief. The patient denied any history of allergies, bleeding, fever, dizziness or abnormalities in physiological functions, highlighting only an isolated episode of nausea, without the occurrence of vomiting.

Upon physical examination, the patient presented palpation tenderness in the right iliac fossa, negative Bloomberg sign, indicating the absence of pain upon sudden decompression of the abdomen and non-palpable appendages. Laboratory evaluation showed: beta-chorionic gonadotropin (BHCG) level at 5718.4 IU/L; hemoglobin 11.6 g/dL; hematocrit 35%; leukocytes 10.090 mm³; and platelets 355,000mm³.

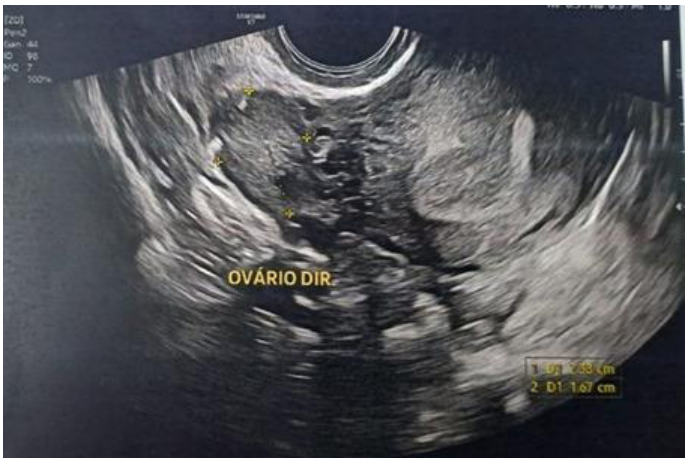
An endovaginal ultrasound revealed an empty uterus of normal size with an endometrium of 11.7 mm; a right ovary with regular contours, heterogeneous stroma measuring 2.8 x 2.1 x 3.5 cm³, a volume of 12.4 cm³, a gestational sac measuring 10.6 mm, a yolk sac measuring 3.3 mm and an embryo measuring 2.4 mm with a fetal heartbeat of 96 beats per minute. There was no free fluid in the cavity. The left ovary, with regular contours and heterogeneous stroma measuring 2.9 x 1.6 x 2.6 cm³ and a volume of 6.2 cm³, was diagnosed by ultrasound as an intact right ovarian ectopic pregnancy (Figure 1, Figure 2, Figure 3, Figure 4).

FIGURE 1 - Ultrasound image of 7 weeks and 4 days of pregnancy, showing an empty uterus, with a volume of 108.8 cm³ (VN: up to 90 cm³) and 11.7 mm endometrium, with a secretory pattern



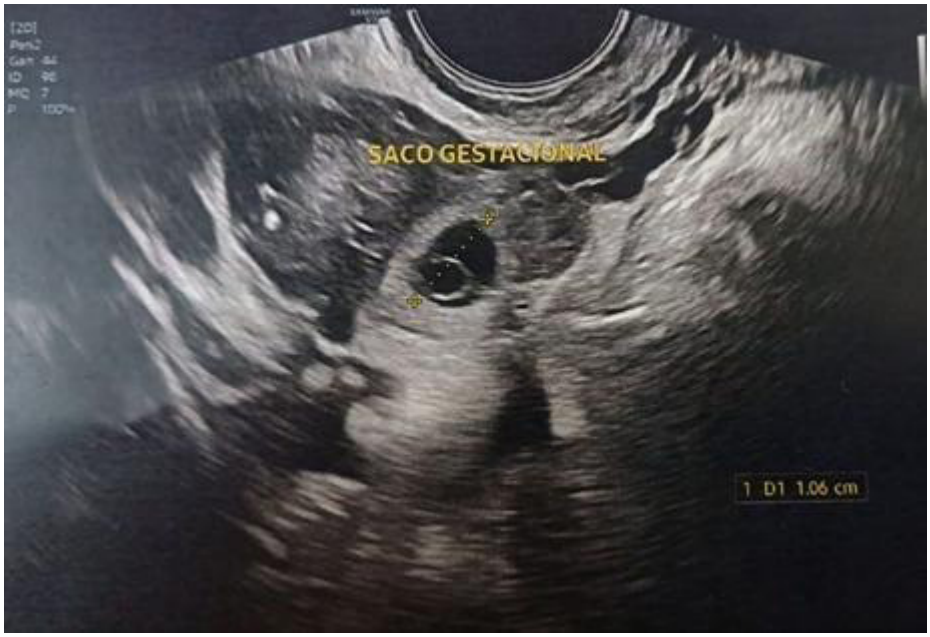
Source: Authors' collection.

FIGURE 2 - Ultrasound image of 7 weeks and 4 days of pregnancy, showing the right ovary with a volume of 12.4 cm³ (VN: up to 9cm³)



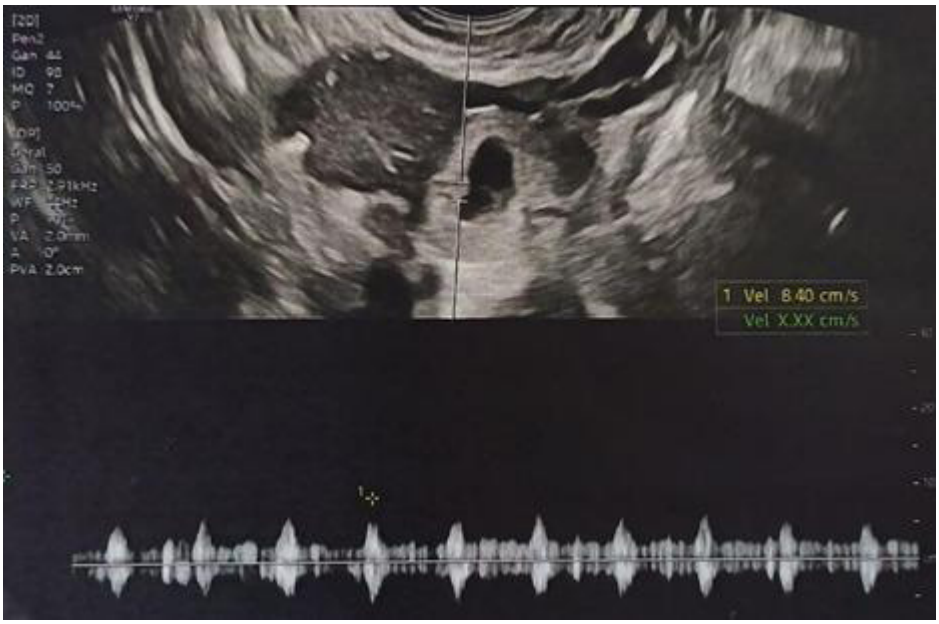
Source: Authors' collection

FIGURE 3 - Ultrasound image of 7 weeks and 4 days of pregnancy, showing right ovary with presence of gestational sac measuring 10.6 mm, yolk sac measuring 3.3 mm, and embryo measuring 2.4 mm



Source: Authors' collection

FIGURE 4 - Ultrasound image of 7 weeks and 4 days of pregnancy, showing cardiac activity present in the embryo, with a heart rate of 96 bpm



Source: Authors' collection

The combination of clinical, laboratory and ultrasound findings led to a diagnosis of ectopic pregnancy, and it was decided to perform surgical treatment using a videolaparoscopic procedure. The patient was duly informed by the surgeon about the possibilities of the proposed surgical treatment, and duly signed the term for the surgery in an informed manner. The patient underwent videolaparoscopy one day after being admitted to the maternity ward, since the team on duty at the admission time did not have the expertise to perform the procedure immediately. The patient was kept under observation in the surgical block while awaiting the surgical procedure as a precaution due to the estimated imminent hemodynamic instability.

A small hemoperitoneum was observed during the surgery, and the right fallopian tube was intact, dilated in its mid-ampullary portion, compatible with an intact ectopic pregnancy in the process of abortion due to the presence of clots in the ampullary portion. The technique used was systematic and atraumatic milking of the right fallopian tube with expulsion of

the remains of the conception product. The left fallopian tube and left ovary were unchanged. The right fallopian tube presented a small amount of bleeding at the end of the procedure, which is normal. The patient subsequently presented good general condition in the immediate postoperative period, abdomen free from complicationsrefere, and only complained of slight pain.

The excised material was sent for anatomopathological analysis. Microscopic examination revealed ovular remains (material consisting of blood clots, chorionic villi with a first-trimester gestational pattern, trophoblastic cells and embryonic/ovular remains), which may correspond to the content of a tubal pregnancy. There were no other relevant histological alterations in the material. Macroscopy revealed several irregular fragments amidst blood clots of soft, light-brown tissue, some with a spongy appearance, measuring 2.0 x 1.0 x 0.6 cm together.

The patient recovered without complications in the immediate postoperative period, and was discharged home the day after the surgical intervention. The following medications were prescribed upon discharge from hospital: Ibuprofen 600 mg every eight hours for a period of three days; Simethicone 125 mg every 6 hours, in case of abdominal distension due to gas; Dipyrone 1 g (every 6 hours), in cases of pain; and Tramadol 50 mg (every 8 hours), in cases of severe pain. Guidance was additionally provided on maintaining a balanced diet and consuming plenty of fluids, with a minimum intake of 2.5 liters per day.

The patient was instructed to avoid vigorous physical activity and sexual intercourse for 60 days. Furthermore, it was emphasized that episodes of menstrual-like bleeding could occur in the first seven days after surgery, with a tendency to gradually decrease. The patient was advised to seek hospital care if the bleeding increased in intensity or persisted after one week, if she had fever, severe pain, vaginal discharge with an unpleasant odor, or signs of infection in the surgical wound. A follow-up medical appointment was scheduled for 30 days after the surgical intervention. A BHCG test was requested during this visit, the result of which was less than 2.0 mIU/mL.

This case report was assessed by the Ethics and Research Committee of the Faculdade Ciências Médicas de Minas Gerais. The study followed the ethical standards for studies involving human beings and was approved by the Ethics and Research Committee (CAAE: 79266324.2.0000.5134). The patient provided informed consent for data publication.

DISCUSSION

Ovarian pregnancy (OP) is a rare form of ectopic pregnancy in which the embryo implants in the ovary, accounting for between 0.5% and 3.0% of all cases of ectopic pregnancy (EP). EP is currently recognized as a public health problem due to its increasing number of cases and the considerable associated morbidity and mortality[4]. The increase in incidence can be attributed to the increasing prevalence of risk factors, as well as to improvements in diagnostic methods[5].

The fallopian tube is the most common site of ectopic pregnancy. Implantation in tubal pregnancies usually occurs in the ampullary region, but it can also occur in the isthmus, in the infundibular region or in the interstitial portion of the tube. Other described sites include the ovary, abdominal cavity, cervix and cesarean scar[6].

Studies indicate that risk factors for ovarian pregnancy (OP) are associated with previous ectopic pregnancy, infertility, genital infections, and use of intrauterine devices (IUDs)[7]. In addition, smoking, sexual activity debut before the age of 18, and multiple partners are also described in the literature as risk factors[8]. However, the use of progestogen-only IUDs and the use of assisted reproductive technologies appear to be more prevalent[4,5]. IUD use was identified in 57.0% to 90.0% of patients with ovarian pregnancy, and its action is related to changes in fallopian tube motility, favoring embryo implantation in the ovary[4,5,9]. On the other hand, OP cases after assisted reproduction methods support the theory of reflux of the fertilized oocyte due to uterine contraction, both due to hormonal stimulation medications used to induce ovulation and due to a reflex contraction resulting from the procedure, being related to up to 50.0% of OP cases[4,10].

In a recent systematic review[2], the authors identified an increase in OP cases which was related to patients undergoing In Vitro Fertilization (IVF), one of the artificial reproduction technologies. Furthermore, when investigating 82 OP case reports, Almahloul (2023) described that 10.0% (n = 8) of the cases were associated with previous ectopic pregnancy, 30.0% (n = 25) with previous abortions, 30.0% (n = 25) with a history of previous surgeries, and 15.0% (n = 12) with IVF[3].

In addition to the aforementioned risk factors, psychiatric disorders appear to favor OP. The pathophysiological mechanism is not fully elucidated, but it is believed that such disorders and associated treatments are related to changes in tubal function, compromising blastocyst transport and favoring extrauterine implantation[8]. However, it is important to note that many patients diagnosed with ectopic pregnancy do not have identifiable risk factors, as illustrated in the case reported. This discrepancy in relation to common risk factors raises questions about the variability of OP cases, highlighting the importance of considering each patient individually, evaluating how particularities interfere in each case.

The scientific literature has not yet defined a predominant age range for OP, nor does it mention ethnicity or countries with the highest incidence. A study in the United Arab Emirates analyzed 82 cases, with an average age of 32 years[3]. We found one case with a patient aged 23 years and another aged 34 years in the national literature[11].

A study conducted in 2019[5] analyzed 12 cases regarding obstetric history, revealing that the women with OP studied had an average of 2.6 pregnancies, 1 birth and 0.4 abortions. According to the literature search undertaken by the authors of the present study, most of the women among the 24 cases of OP identified in several articles had previous pregnancies[1,2,3,5,10]. More specifically, six cases involved primiparous women[2,4,9,11,12,13]. In addition, 12 of these women with previous pregnancies had a history of abortions,[1,5,10] while two cases did not provide details about the patients' obstetric history. These data suggest that the majority of the women with OP studied had previous experience of pregnancies, and in some cases abortions, which contrasts with

the specific case discussed, where the patient was primiparous.

Most OPs are diagnosed in the first eight weeks of pregnancy, as they cause discomfort in patients even before the first amenorrhea, such as pelvic pain (77.3%) resulting from rupture of the ovarian capsule due to pregnancy, hemoperitoneum formation and vaginal bleeding (45.2%), favoring investigation and improving prognosis[3, 10]. However, due to the difficulty of diagnosis[4], it is not uncommon for the gestational sac to rupture in the first weeks, becoming a medical emergency with manifestations of hypovolemic shock, increasing the discovery in the first trimester[10]. Despite factors which favor discovery in the first months, up to 15.0% of pregnancies become full term, and some reported cases reached up to 44 weeks[3].

There is a classic symptomatology of ectopic pregnancy represented by the following triad: amenorrhea, abdominal cramps and vaginal bleeding; however, it is known that the symptoms can be non-specific, discreet and even absent[12]. In the case in question, the patient was asymptomatic and did not present significant findings during the clinical and gynecological examination. This variation of symptoms can make the diagnosis difficult and be associated with an increase in morbidity and mortality.

The serum BHCG level was 5718.4 IU/L, a value which is lower than that expected for a seven-week gestation (6000 to 7000 IU/L), and compatible with the ultrasound diagnosis[11]. The presence of high serum BHCG levels is an indication of pregnancy, and there is a crucial difference in EP from other pregnancies, namely that there is no twofold increase in the levels of this hormone in a 48-hour interval[2].

Transvaginal ultrasound and serial hCG measurement enable early EP identification. The earlier the diagnosis, the faster the therapeutic approach and the lower the risk of complications[12]. However, it is challenging to make a preoperative diagnosis of OP due to the non-specific clinical symptoms and insufficient understanding of the ultrasonographic characteristics of individuals with OP[5].

Although advances in transvaginal ultrasonography have made it easier to diagnose OP[5], it has been reported in the literature that the sonographic manifestations of OP are often atypical. The typical finding would be a double echogenic ring in a hypoechoic mass with or without an embryo and ovarian cortex[2,10]. Furthermore, the manifestations are ambiguous with ovarian corpus luteum, which means that only 11.0% of cases are accurately diagnosed in the preoperative period[2], and many are misdiagnosed as corpus luteum or tubal pregnancy via ultrasound[2,5]. Therefore, care must be taken to ensure that OP is not confused with other ovarian conditions; nevertheless, no specific sonographic criteria have been described, and the sonographic findings reported are individual for each case[5].

Diagnosis is challenging due to its non-specific presentation[3], and the gestational sac is often ruptured when identified, as the ovarian tissue has little elasticity and cannot expand[2]. Diagnosis tends to be difficult, usually requiring an operator-dependent examination, which is transvaginal ultrasound, and the ultrasound signs may vary from case to case.

Surgical diagnosis via exploratory laparotomy can be used for cases in which the OP diagnosis has not been previously established. In 1878, Otto Spiegelberg, a German gynecologist, described four criteria which still remain the standard for intraoperative OP diagnosis: 1) intact ipsilateral tubes and fimbriae separated from the ovary; 2) a gestational sac that occupies the ovary's position; 3) the ovary with the gestational sac must be connected to the uterus by the ovarian ligament; and 4) ovarian tissue in the wall of the gestational sac[4,13]. This diagnosis was only made correctly in 28.0% of the cases reported in the literature, with the remainder relying on histopathological examination[5]. These figures illustrate the complexity of the diagnosis, given that both the preoperative and intraoperative examinations may be insufficient for a correct conclusion in each case.

The ovarian cortex is thin and inelastic, and so ovarian pregnancies almost always rupture. The discovery of intact fallopian tubes and hemorrhagic lesions on the ovarian surface is often used to diagnose ruptured OP during laparoscopies, and gestational tissue may or may not be visible in the pelvic cavity[2]. However, it is still difficult to differentiate this condition from an ovarian corpus luteum and a tubal abortion, reaffirming the complexity of the specific diagnosis[2,5].

A possible treatment for OP is systemic methotrexate (MTX). The treatment form depends on the initial BHCG value. A single dose of MTX 50 mg/m^2 intramuscularly (IM) is used when levels are less than 5,000 mIU/mL. If BHCG values are greater than 5,000 mIU/mL, a protocol with multiple doses of MTX is used. However, if the embryo is alive, local treatment guided by transvaginal ultrasound is performed with injection of MTX into the gestational sac at a dose of 1 mg/kg. Treatment is complemented with the multiple-dose systemic protocol when BHCG levels are greater than 5,000 mIU/mL, starting the day after puncture[14]. Four intravenous injections of MTX 1mg/kg^{-1} and four intramuscular injections are generally indicated for multiple doses[11].

Although drug treatment can be administered to patients with stable vital signs, it should be performed under strict monitoring due to the risk of abdominal bleeding; this risk is due to the increase in the clot formed after necrosis of the embryo sac, which can accelerate rupture of intravascular lesions[2]. It was reported that the success rate in a series of 1,626 conservative laparoscopies without MTX for EP was 93%, showing that definitive resolution does not necessarily include MTX in the treatment[11].

Therefore, there is evidence in the literature that surgical treatment alone in patients without another EP has presented satisfactory results and has been more widely used, as in the case reported herein. In addition, surgical intervention was chosen due to the size of the ectopic pregnancy in the present case, associated with the presence of cardiac activity of the conceptual products. EP management is based on parameters, including the mass size, which should be up to 4 cm in largest diameter for clinical treatment[12].

The patient in this case report underwent videolaparoscopy, which is the treatment of choice for 50% of patients with 7 to 8 weeks of amenorrhea, and the procedure using laparoscopy can be performed in 43.0%, 47.0% and 10.0% for amenorrhea durations < 6, 9 to 10 and > 10 weeks of

gestation, respectively[2]. In addition, the recommended treatment is generally conservative surgery, meaning that it aims to spare the largest portion of ovarian tissue, removing only the ectopic tissue. In doing so, it is possible to remove tissue with precision and avoid damage to the reproductive structures[11], which was the treatment performed in the case described herein. The literature indicates preference for the laparoscopic route due to the shorter hospital stay, lower costs and faster recovery[2].

A small hemoperitoneum and an intact right fallopian tube were seen during the operation, which is compatible with an abortion process due to the presence of clots in the tube's ampullary portion. The systematic and atraumatic milking technique of the right fallopian tube was used, with expulsion of the conception product remains. All of Otto Spiegelberg's criteria were observed during laparoscopy. Although these intraoperative criteria favor OP diagnosis, it is still difficult to differentiate an ovarian pregnancy from a hemorrhagic ovarian cyst at the time of surgery[4]. Therefore, the anatomopathological examination is of utmost importance, as it is the tool which in fact enables confirming the OP diagnosis. The objective of such an examination is to eliminate primary abdominal pregnancies and those grafted onto the ovary, but resulting from tubo-abdominal abortion, and those in which the ovary is not the exclusive implantation site[10].

Although the recommendations are to associate the surgical technique with the use of methotrexate as a treatment, it is clear from the literature that isolated surgical treatment in patients who do not present risks of having another OP has shown good results, and therefore has been the most used, as in this case report[11]. Thus, MTX is only used in cases where the decline in BHCG is not observed with the surgical method alone[14].

The anatomopathological examinations found in the literature reveal ovular tissue infiltrated by foreign tissue compatible with non-ruptured OP[11], while the histopathological examinations show fibrinous hemorrhagic material with trophoblastic cells that overlap the edematous ovarian stroma with a normal follicle[3,15]. The anatomopathological examination in the present case showed ovular remains, with the material being composed of blood clots, chorionic villi with a first trimester gestational pattern, trophoblastic cells and embryonic remains. However, despite the strong evidence of OP, the sample may correspond to the content of a tubal pregnancy, constituting a factor which reinforces how complex the OP diagnosis is, as it is non-specific in the clinical exam, ultrasound and upon laparoscopic visualization[4]. Not all OP reports make it clear that the diagnosis was confirmed by pathology, despite this being expected[3].

The literature reports that there is an increased risk of subsequent episodes after an ectopic pregnancy (EP). Therefore, regular monitoring by a health professional is recommended to ensure appropriate localization of subsequent pregnancies[8]. One study showed that the recurrence rate after the first EP episode is approximately 15.0%, while this rate increases to 25.0% for women with two or more previous EP episodes[14].

Another important point to be raised is the importance of care that is not only individualized, but also humanized. When women go through the abortion process, regardless of the primary cause, their experience is physical, emotional and social, and support and guidance are essential for providing quality and humanized care to women in this situation. This means that the care team must provide dignified and respectful treatment and listen to the patient, in addition to passing on necessary information for the woman to conduct the process and for decision-making and self-care[16].

CONCLUSION

We have reported a case that is difficult to diagnose, which meets all the criteria for ovarian pregnancy, but which may correspond to a tubal ectopic pregnancy according to the pathology report. This highlights the complexity of making an accurate diagnosis of ovarian pregnancy. Correct identification of ectopic pregnancy by transvaginal ultrasound significantly contributes to early management of the condition, resulting in a reduction in complications and more favorable clinical outcomes.

AUTHORS' PARTICIPATION: Valquíria Fernandes Marques Vieira: Conceptualization, Methodology, Validation, Research, Resources, Writing - Review & Editing, Visualization, Supervision, Project Management. Nathália Letícia Borges de Matos: Validation, Research, Resources, Writing - Original Draft, Writing - Review & Editing, Visualization. Rafaela Siqueira Costa Schreck: Validation, Research, Resources, Writing - Review & Editing. Victoria Carolina Barcelos Fonseca: Validation, Research, Resources, Writing - Original Draft, Writing - Review & Editing, Visualization.

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