



UNUSUAL LOCALIZATIONS OF ECTOPIC PREGNANCIES: A SERIES OF EIGHT PATIENTS

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ABSTRACT

The vast majority of ectopic pregnancies are localized within the fallopian tube. Nevertheless, pregnancies have been described to implant in unusual rare sites including: uterine cervix, ovary, abdomen, previous cesarean scar, interstitial/cornual tubal segment and myometrium. Diagnosis and treatment of these unusual implantations presents both diagnostic and therapeutic dilemmas. We present a series of eight cases of unusual localizations of ectopic pregnancies including one intramyometrial, two heterotopic, one abdominal, one ovarian, one cornual, one in the previous cesarean scar and one cervical pregnancy. Diagnosis of these unusual ectopic conceptions is clinically challenging and the treatment options have recently involved major surgical procedures, which affect future fertility.

KEYWORDS: Ectopic pregnancy; Unusual localization; Ultrasound; MRI; Management.

INTRODUCTION

Ectopic pregnancy remains one of the most common causes of mortality among pregnant women. The rates of the disease have dramatically increased over the past several decades due to a combination of increased risk factors as well as early and more effective diagnosis. The majority of these pregnancies are localized in the fallopian tube. Rarely, it can implant in other unusual sites including: uterine cervix, ovary, abdomen, previous cesarean scar, interstitial/cornual tubal segment and myometrium. In addition, an ectopic pregnancy within any of these sites can also occur in the setting of a simultaneous intrauterine pregnancy, a condition known as heterotopic pregnancy. The majority of data regarding these uncommon ectopic pregnancies are rare and limited to small case series. In this article, we present a series of eight cases of unusual localisation of ectopic pregnancies diagnosed and managed in the department of Obstetrics and Gynecology (Military Training Hospital Mohammed V/Morocco) with a literature review to summarize the current data regarding diagnosis and optimal treatment of these unusual locations.

CASES PRESENTATION

Case 1

A 37-year-old woman presented at 5 months of gestation for lower abdominal pain. She had a history of polymyomectomy, vacuum aspiration for incomplete abortion, and cesarean section. She conceived spontaneously and she never had obstetrical ultrasound or antenatal checkups. On admission, patient was with

normal vital signs. Abdominal examination revealed fundal height corresponding to 20 weeks gestation with soft uterus. On vaginal examination, the cervix was closed and posterior. Ultrasound scan showed an empty uterine cavity with a single fetus of 20 weeks gestation, implanted within the myometrium (**Figure 1**). Fetal heart beat was negative with anamnios. An urgent laparotomy was performed, which revealed a preruptured intramyometrial pregnancy, located adjacent to the right cornua. Ovaries and fallopian tubes appeared normal. A circular incision was made in the uterine serosa followed by enucleation of the fetus and placenta. Fistulous tract communicating between endometrial cavity and location of the intramural pregnancy was discovered and repaired with No. 2-0 Monocryl sutures. Visible vessels were coagulated, and the wound was repaired with No. 1 Monocryl sutures.

Case 2

A 32-year-old woman presented to the gynecological emergencies with the chief complaint of lower abdominal pain appeared 48hours before. At this time, the patient was pregnant at 6th week of gestation. She conceived spontaneously and she had no history of pelvic inflammatory disease. Physical examination showed mild tenderness at the right lower abdomen. Transvaginal ultrasonography objectified simultaneous intra and extrauterine gestational sacs according to 6 weeks of gestation with current cardiac activity of both embryos (**Figure 2/A**). Patient was consented for an operative laparotomy few hours later. A total of 200 mL

of hemoperitoneum was aspirated. The left annex and right ovary were normal with a ruptured ectopic pregnancy in the ampullary region of the right fallopian tube. A right salpingectomy was performed and the material was sent for histological examination confirming chorionic villi. Nicardipine (Loxen®) was used for tocolysis. The IUP proceeded well, and the labor was performed at term with a healthy baby.

Case 3

A 25-year-old woman was a case of primary infertility for two years and ultrasound findings of polycystic ovary syndrome. She received ovulation induction by Clomiphene Citrate (CC) 100 mg/day starting on day 2 of the cycle and continued with recombinant FSH on day 7. Transvaginal ultrasound on day 12 showed two good size follicles in the right ovary; endometrium was 12 mm thick. She was given Human Chorionic Gonadotropin (HCG) on day 12 and was advised for natural intercourse on day 13. Her next presentation was at 6 weeks of amenorrhea with lower abdominal pain. On admission, the patient was afebrile with normal vital signs. On physical examination, mild tenderness was found on deep palpation of the right lower abdominal quadrant. Transvaginal ultrasound scan revealed intrauterine gestational sac with fetal pole and visible cardiac activity. A small amount of free fluid was seen in the pouch of Douglas. Given her history of fertility treatment and her physical examination findings, adnexal areas were evaluated with particular detail. A second gestational sac with fetal pole and cardiac activity, adjacent to the right ovary, was visualized, suggestive of heterotopic pregnancy (**Figure 2/B**). An urgent mini-laparotomy was performed; there was a preruptured ectopic pregnancy in the ampullary region of the right fallopian tube. Salpingectomy was performed. Pathological examination confirmed the ectopic pregnancy. Per operatively, intravenous Nicardipine was prescribed for prevention of uterine contractions. The IUP was followed up till 41 weeks and she was induced with vaginal delivery of a healthy baby boy.

Case 4

A 22-year-old woman presented in our department at 4 months of gestation for pelvic pain and vaginal bleeding appeared 3 weeks before, without digestive or urinary disorders. On admission she was afebrile with normal vital signs. In physical examination, the uterus was of a normal size with a perception of a bulging mass in the Douglas. Ultrasonography objectified an empty uterus with a single alive fetus of 15 weeks gestation localized in the Douglas pouch. Abdominopelvic Magnetic Resonance Imaging (MRI) confirmed the abdominal pregnancy; the placenta was inserted in the rectum serosa (**Figure 3**). Under general anesthesia, an exploratory laparotomy has objectified a 400 ml of hemoperitoneum with a single fetus in the Douglas pouch. The placenta was adherent to the posterior surface of uterus and superficial to the anterior surface of rectum. After extraction of the fetus, we proceeded to partial excision

of the placenta located on the rectum. In the second postoperative day, she was received one cure of Methotrexate (1mg/kg) with gradual diminution of plasmatic β HCG level to total negativity after six weeks.

Case 5

A 34-year-old multiparous woman, without surgical history, presented for pelvic pain with 2 months of amenorrhea. Her menstruation cycle was regular. She was hemodynamically stable. Gynecological examination objectified a painful mobile mass in the right lower abdominal quadrant; uterus was of a normal size. Plasmatic β HCG was positive (4950 IU/ml). Transvaginal sonography revealed an empty uterus with a heterogeneous right mass, measuring 40 mm \times 30 mm, associated with free fluid in the pouch of Douglas suggestive of an ectopic tubal pregnancy. Laparotomy was realized. Peroperatively, a total of 400 ml of hemoperitoneum was aspirated and a ruptured ovarian pregnancy was diagnosed in the right side (**Figure 4**). Partial resection of the ovary including the gestational sac was performed. Histopathological examination confirmed an ovarian ectopic pregnancy.

Case 6

A 27-year-old woman, para 1, admitted in our department with the chief complaint of an episode of acute pelvic pain and vaginal bleeding following 11 weeks of amenorrhea. On general examination, her vital signs were within normal limits with mild pallor. Gynecological examination revealed tenderness at the right lower abdomen with bleeding originating from the endocervix. Abdominopelvic ultrasound objectified an empty uterine cavity with a right echogenic mass measuring 30 mm of diameter and moderate peritoneal effusion suggestive of ectopic tubal pregnancy. Plasmatic β HCG level was 2017 IU/ml. An urgent laparotomy was realized, which revealed a ruptured right cornual pregnancy; both ovaries and fallopian tubes appeared normal (**Figure 5**). We performed a right cornual resection with right salpingectomy. The patient's postoperative condition was stable and she was discharged home 72 hours later.

Case 7

A 43-year-old woman, gravid 3, para 2, was admitted for lower abdominal pain and vaginal bleeding at 11 weeks gestation. She had two previous caesarean sections and the last one being 1 year ago. Her vital signs were within normal limits on general examination. Physical examination revealed tenderness at the lower abdomen with bleeding originating from the endocervix. Transabdominal sonography revealed a gestational sac with fetal pole and visible cardiac activity in the anterior wall of lower body of uterus, in the region of the previous cesarean scar, suggestive of a cesarean scar pregnancy (CSP) (**Figure 6**). Myometrial thickness surrounding was less than 10 mm. An exploratory laparotomy was performed. Peroperatively, we found 200 ml of hemoperitoneum with partial ruptured uterine

scar through which amniotic sac was protruding (**Figure 7**). Uterus was evacuated and uterine defect repaired using an interrupted absorbable suture. Total operating time was 45 minutes and the estimated blood loss was less than 150 ml. Her postoperative period was uneventful and she was discharged on the 3th postoperative day.

Case 8

A 26-year-old nulliparous woman presented for vaginal bleeding appeared 2 days before, with 7 weeks of amenorrhea. Her menstrual cycle was regular and there was no history of contraceptive use. Gynecological examination showed a normally sized body of the uterus, dilated cervix with external uterine os closed, and marked tenderness in vaginal fornix. Transabdominal and transvaginal ultrasound revealed an empty uterus

with thickened endometrium. However, in the area of the uterine cervix, 1 cm below the closed internal os, a gestational sac containing structures of a fetus with cardiac activity was identified (**Figure 8**). A presumptive diagnosis of cervical pregnancy (CP) was made. Level of serum β HCG was 70.000 IU/ml. After contraindications had been excluded, single dose intramuscular Methotrexate 70 mg was administered and manual vacuum aspiration was performed on the third day under spinal anesthesia. Cervical tamponade was performed with a Foley catheter. 48 hours later, cessation of vaginal bleeding and a decrease in the plasmatic β HCG level to 1.000 IU/ml was observed. On the third day after surgery, patient was discharged in a good general condition and 2 years later she was diagnosed with another properly situated pregnancy.



Figure 1: Fetal head and femur were distinct from uterus at the right side.



Figure 2: Transvaginal ultrasound showing simultaneous intrauterine and ectopic pregnancy.

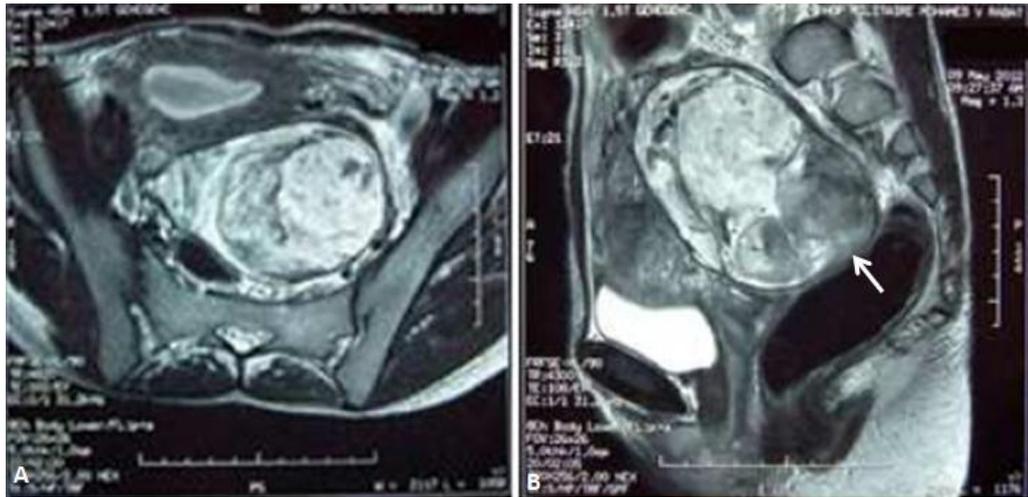


Figure 3: Axial (A) and sagittal section (B) in MRI objectifying an abdominal pregnancy with an empty uterus. Note the insertion of the placenta in the anterior wall of the rectum (white arrow).



Figure 4: Peroperative view of the right ovarian ectopic pregnancy (white arrow).



Figure 5: Ruptured right cornual pregnancy.

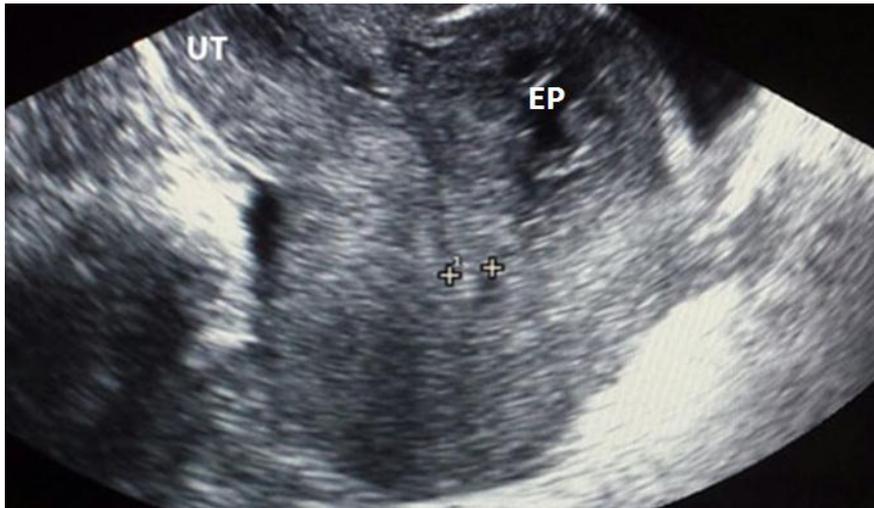


Figure 6: Pelvic ultrasound revealed an ectopic pregnancy (EP) in the region of the previous cesarean scar.

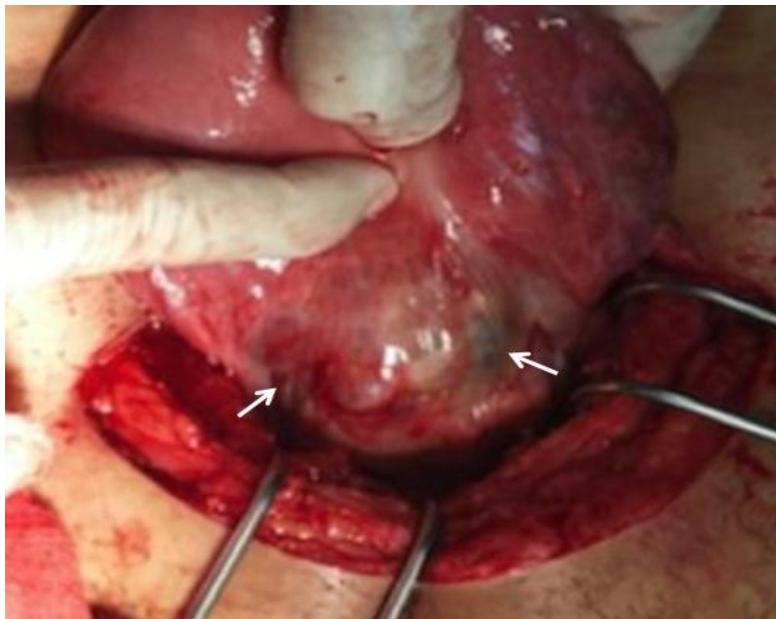


Figure 7: Intact gestational sac with placental tissue seen protruding through the previous cesarean scar (white arrows).

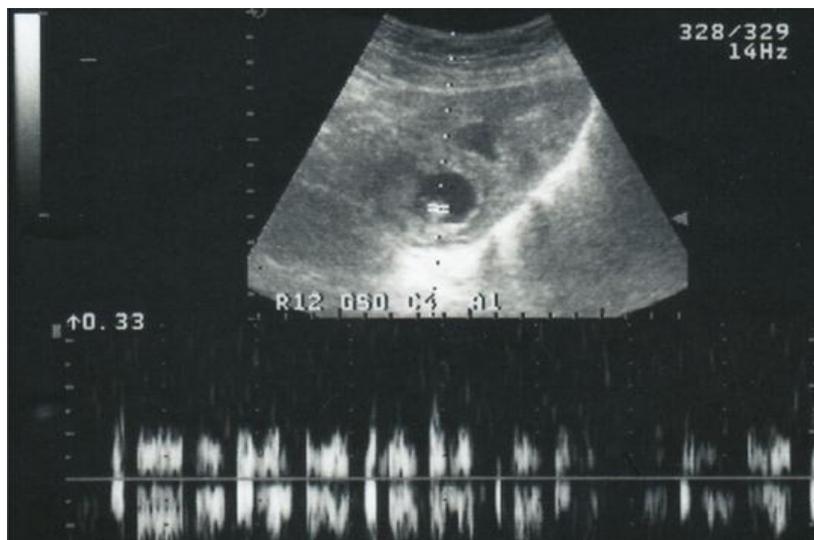


Figure 8: Cervical pregnancy at 7 weeks' gestation.

DISCUSSION

Intramymetrial (Intramural) pregnancy

This localisation accounts for less than 1% of all ectopic pregnancies and defined as a conception entirely surrounded by the myometrium and completely separate from the endometrial cavity. As was in case 1, factors thought to predispose patients that are typically present before the development of intramymetrial pregnancy include prior uterine surgery such as cesarean delivery, myomectomy and curettage.^[1] Prior uterine traumas, such as these surgical procedures, are thought to result in sinus tract formation within the endometrium. Adenomyosis has also been shown to be associated with intramural pregnancy.^[2] In case 1, preoperative diagnosis of intramural pregnancy was easy given the advanced gestational age. However, in early conception, it can mimic a degenerating myoma, missed abortion, gestational trophoblastic tumor or normal pregnancy in a congenitally abnormal uterus and can be difficult to distinguish from an interstitial or cornual pregnancy on 2-dimensional ultrasonography.^[3] The use of color Doppler and 3-dimensional ultrasound may help in the diagnosis of an intramural pregnancy through a more accurate localization of the ectopic gestational sac. MRI has also been reported as a useful imaging modality with the ability to provide the relationship between pregnancy and endometrial cavity.^[3] If not treated, complications resulting from intramymetrial pregnancy include uterine rupture, hysterectomy and subsequent loss of fertility. Treatment modalities described in the literature include expectant management, surgical enucleation, systemic or local Methotrexate injection, hysterectomy, uterine artery embolization and intrafetal injection of potassium chloride.^[4] In the present case, with preruptured intramural pregnancy in advanced gestational age, enucleation of the fetus and placenta with reparation of the fistulous tract was realized, allowing for future fertility to be available in our patient desired childbearing.

Heterotopic pregnancy

Heterotopic pregnancy (HP) is a rare event combining the simultaneous presence of intrauterine (IUP) and EP. It was first described by Duverney in 1708 as an autopsy finding and can follow an assisted or a natural conception cycle.^[5] Its incidence is known to be one in 8000 to 30000 in spontaneous conceptions.^[6] HP mostly happens with known risk factors notably assisted reproductive techniques, ovulation induction, and history of PID or EP. The risk factors we have found were ovulation induction by Clomiphene Citrate (CC) in case 3. CC is used to induce ovulation in selected populations with oligo or anovulation as a strategy to increase follicular number and estrogen concentration and could be associated with HP in up to 1/900 of the cases.^[7] Preoperative diagnosis of HP is difficult and requires a high index of suspicion. Clinical features can vary widely from asymptomatic to abdominal pain, as was in cases 2 and 3, and vaginal bleeding. On ultrasound scan, the identification of a gestational sac outside the uterus is

the gold standard for the diagnosis of EP. According to reviews, in 77 to 85% of cases in whom diagnosis was via ultrasound, diagnosis was made between 5 and 8 weeks of gestation.^[8] Surgical management, via laparoscopy or laparotomy, remains the only viable option for acute presentation of HP. Numerous reported cases are treated by salpingotomy or salpingectomy. The choice between conservative and radical surgery may be difficult. A review demonstrated no difference in survival rates of IUP after conservative and radical treatment for tubal ectopic pregnancy.^[8] In cases 2 and 3, lack of laparoscopic equipment in the operating room, mini-laparotomy was performed with radical treatment for rapid control of active bleeding. In situ administration of potassium chloride can be used in early gestational age. However, since the risks of continued growth and rupture still exist with such non-surgical management, repeated ultrasounds and close clinical monitoring are essential.^[9] Successful expectant management has also been described, but a substantially favorable risk-to-benefit ratio should be demonstrated before adoption of this therapeutic option.^[10]

Abdominal pregnancy

The first case of abdominal pregnancy was described by an Arab surgeon (1000 BC.).^[11] It is an uncommon entity with an estimated incidence of 1 in 2200 to 10200 of all pregnancies and 1% of all ectopic pregnancies.^[12] The risk factors for abdominal pregnancy are similar to risks reported for other ectopic pregnancies with the exception of cocaine use, which is exclusively associated with it.^[13] Abdominal pregnancy can be classified as primary and secondary. In primary pregnancy, the fertilized egg near the ovary will erroneously route into the abdominal cavity and will feed on tissues highly vascularized. Studdiford have described three criteria for diagnosis of primary AP: normal tubes and ovaries, absence of an uteroplacental fistula and peritoneal localization less than 12 weeks.^[14] However, secondary abdominal pregnancy is defined as reimplantation of a ruptured ectopic pregnancy, most commonly tubal, in the peritoneal cavity. Abdominal pregnancy is associated with a wide range of symptoms related to the variable site of implantation, which could be the uterus, bowel, urinary bladder, spleen, liver, or diaphragm. Classical sonographic features of abdominal pregnancy include an empty uterus, absence of a myometrium around the fetus, a poorly visualized placenta, an unusual fetal lie and relative oligohydramnios. Abdominopelvic MRI is a sensitive and specific method for evaluating ectopic pregnancy and can help delineate maternal and fetal anatomy and determine the exact position of the placenta for preoperative planning, as was in case 4. Different therapeutic approaches have been reported for abdominal pregnancy depending on gestational age at diagnosis, site of placental implantation and fertility status. In contrast to tubal ectopic pregnancy, primary Methotrexate administration has a high risk of failure due to the more advanced gestational age at which these pregnancies are discovered.^[15] At an early gestational age, abdominal

pregnancy can be managed by laparoscopy as removal of the small and less vascular placental tissue is easier.^[16] In more advanced pregnancies, laparotomy is the treatment of choice.^[12] Preoperative selective arterial embolization may be done to prevent haemorrhage during removal of placenta. Ligating the umbilical cord and leaving total or partial placental tissue in situ is one option, as was in case 4. The patient can be followed without further intervention, or using arterial embolization or Methotrexate to hasten involution. Expectant management with close maternal and fetal monitoring, to gain fetal maturity, has been described in isolated cases.^[17]

Cesarean scar pregnancy

It has classically been described as one of the rarest forms of EP. CSP is defined as implantation of a pregnancy in the scar from a previous cesarean delivery. The gestational sac is completely surrounded by myometrium and fibrous tissue and is distinctly separate from the endometrial cavity.^[12] CSP rate accounts approximately for 0.15% in women with a previous history of cesarean delivery.^[18] The mechanism of implantation is believed to be migration of the embryo through either the wedge defect in the lower uterine segment or a microscopic fistula within the scar.^[19] Patients with CSP may be completely asymptomatic or present with moderate pelvic pain with or without vaginal bleeding. Severe abdominal pain, profuse bleeding and hypovolemic shock is of concern for uterine rupture. Transvaginal ultrasound with color Doppler can be used for preoperative diagnosis with an estimated sensitivity of 86%.^[12] The first step is to exclude an intrauterine pregnancy with placenta accreta or a CP. An ectopic gestational sac is seen in the anterior wall of lower body of uterus, in the region of the previous cesarean scar. The myometrium between the urinary bladder and the sac is often thinned or absent. Color Doppler typically shows a peritrophoblastic vascularization and is useful for assessing possible invasion of the bladder. As with other ectopic gestations, the goal of treatment is to preserve future fertility while safely terminating the pregnancy. Many types of conservative management have been described in the literature such as local and/or systemic Methotrexate administration, bilateral hypogastric artery ligation associated with dilation and evacuation under laparoscopic guidance, uterine artery embolization, and excision of trophoblastic tissues using laparotomy (as was in case 7) or laparoscopy.^[20,21]

Cornual pregnancy

The term cornual pregnancy is used as a synonym of interstitial pregnancy and accounts for up to 1 to 3% of all ectopic pregnancies.^[22] As the pregnancy grows in the area of the fallopian tube that enters the uterus, surrounding myometrial tissue allows for further development of the pregnancy into the second trimester. Risk factors for development of cornual pregnancy include previous ectopic pregnancy, uterine anomalies,

ipsilateral salpingectomy, IVF, ovulation induction, and PID. Diagnosis can be suspected by transvaginal or transabdominal ultrasonography. 3D ultrasonography has shown to be more accurate.^[23] Diagnostic criteria includes: an empty uterine cavity, gestational sac seen less than 1cm from the lateral edge of the uterine cavity surrounded by a thin layer of myometrium, interstitial line sign (echogenic line extending into the cornual region and abutting the gestational sac).^[24] In advanced gestational age, the cornual pregnancy may be located above the uterine fundus mimicking an eccentric intrauterine pregnancy.^[24] The traditional surgical treatment of cornual pregnancy includes cornual resection, cornuostomy, or hysterectomy. Both laparotomy and laparoscopy may be used. In patients with ruptured cornual pregnancy, laparotomy is preferred, as was in case 6. Hysterectomy is reserved to cases in which hemorrhage is profuse and life threatening. Medical management with Methotrexate can be used if there is hemodynamic stability, no medical contraindications to Methotrexate, and no signs of rupture. The modes for administration include laparoscopy, transvaginal, and through ultrasound guidance.^[24] Uterine artery embolization associated with Methotrexate injection is another effective mode for medical management of cornual pregnancy.^[25]

Ovarian pregnancy

Ovarian pregnancy is a rare localization of EP, accounting for 0.5% to 3% of all ectopic pregnancies.^[12] Risk factors associated with ovarian pregnancy include intrauterine device use, assisted reproductive technology, endometriosis, pelvic inflammatory disease, and history of pelvic surgery. Most commonly, women with ovarian pregnancy present with pelvic pain and vaginal bleeding. In physical examination, as was in patient 5, an adnexal mass can be palpated in up to 60% of cases.^[26] Despite advances in sonographic techniques, the most reported cases of ovarian pregnancy are diagnosed incidentally during surgery for a presumed tubal pregnancy or ruptured corpus luteum associated with early IUP. The anatomic and histologic Spielberg criteria include: normal fallopian tube, gestational sac occupying the ovary and connected to the uterus by the ovarian ligament, and ovarian tissue must be present in the resected specimen connected to the gestational sac.^[12] Surgery with oophorectomy or wedge resection if there is a desire to preserve fertility, like in case 5, is the gold standard for the treatment of ovarian pregnancy. Medical management with systemic or laparoscopic Methotrexate injection have also been described.^[27,28]

Cervical pregnancy

CP results due to implantation of a fertilized ovum in the endocervical canal below the level of internal os with a reported incidence of less than 0.1% of all pregnancies.^[29] Although the exact etiology of CP remains unclear, a few predisposing factors like endometrial damage (after curettage, cesarean deliveries or chronic endometritis), leiomyoma, intrauterine devices

and in vitro fertilization are implicated in its pathogenesis.^[12] Clinically, CP typically present with a period of amenorrhea followed by painless vaginal bleeding. Ultrasound scan plays a crucial role in the diagnosis, as was in case 8. Specific sonographic guidelines have been established and include the following: an empty uterine cavity, decidual transformation of the endometrium, an hourglass uterine shape, a ballooned cervical canal, a gestational sac in the endocervix, a placental tissue in the cervical canal and a closed internal os.^[30] It is crucial to differentiate between a CP and cervical abortion, in which the pregnancy is passing through the cervical canal. In the last one, a residual product of conception is seen in the uterus with open internal os and lack of cardiac activity. Due to the rare incidence of CP, the available literature does not recommend a uniform management protocol and the choice of treatment is still based on reported single cases. According to the available literature, the most effective treatment of cervical pregnancy up to 12 weeks' gestation is conservative treatment by means of Methotrexate.^[31,32] In case 8, spontaneous abortion after administration of Methotrexate was not achieved, and it was necessary to performed a manual vacuum aspiration. Cervical tamponade with Foley catheter was used to prevent hemorrhage.

CONCLUSION

The overall rate of unusual ectopic pregnancies continues to rise. Early diagnosis and appropriate management is critical for reducing morbidity and mortality and preserving the success rate of future pregnancies.

Conflict of interest: the authors declare no conflict of interest.

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