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Rare Location of Extra Uterine Pregnancy about Two Cases: Diagnostic, Clinical and Therapeutic Aspects

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Abstract

Defined as the implantation and development of the egg outside the uterine cavity, ectopic pregnancy is the leading cause of maternal mortality in the first trimester of pregnancy. In Senegal, their frequency varies around 0.6% according to certain hospital data. The tubal location is the most common but other rare and even exceptional locations have been described, often leading to diagnostic error which can lead to heavy female morbidity and mortality. We report two cases through which we will describe the diagnostic, therapeutic and prognostic modalities. It was an observational study of two atypical cases of ectopic pregnancy diagnosed and treated in the gynecology-obstetrics department of the Pikine National Hospital Center. In both cases, a definitive diagnosis was only established after laparotomy. The main challenge lay in performing the surgical procedure in a manner that would preserve future fertility.

Keywords

Ectopic Pregnancy, Ultrasound, Rare Location, Senegal

1. Introduction

Defined as the implantation and development of the egg outside the uterine cavity, ectopic pregnancy is the leading cause of maternal mortality in the first trimester of pregnancy. Its frequency varies between 1.3% and 2.5% of spontaneous pregnancies and can reach 4% to 5% of pregnancies after in vitro fertilization (IVF) [1]. In Senegal, it varies around 0.6% according to certain hospital data. The tubal location is the most common but other rare and even exceptional locations have

been described, often leading to diagnostic error which can lead to heavy female morbidity and mortality. We report two cases through which we will describe the diagnostic, therapeutic and prognostic modalities.

2. Patients and Method

This is an observational study of two atypical cases of ectopic pregnancy diagnosed and treated in the gynecology-obstetrics department of the Pikine National Hospital Center.

2.1. First Case

This is a 32-year-old nulligest patient with a history of a myomectomy a year previously, referred for management of a pregnancy terminated at 17 weeks of gestation and 2 days in retention with failure to induce. On admission, the patient complained of mild and continuous abdominal-pelvic pain. On examination she presented an enlarged uterus and was sensitive to mobilization with a uterine height of 16 cm. The obstetric ultrasound concluded that there was an arrested intrauterine pregnancy with overlapping skull bones and a femoral length corresponding to 17 weeks of amenorrhea and 6 days.

Induction with misoprostol and balloon ended in failure. A second ultrasound with an "ultrasound" Shibangu test was done and showed that the pregnancy was developing outside the uterine cavity but remained in close contact with the uterus.

The Shibangu test (also called the "modified Diadhiou/Shibangu test") method consists of introducing a rigid hysterometer (or uterine cannula) into the uterine cavity, followed by a pelvic radiograph. If the radiograph shows the hysterometer located within an apparently empty uterine cavity (*i.e.*, without a fetal image), this suggests the absence of an intra-uterine pregnancy and supports the diagnosis of an extra-uterine or abdominal gestation. While its diagnostic value is limited compared with modern imaging, the Shibangu test can remain a useful tool for preliminary assessment in contexts where ultrasound or MRI are unavailable or inconclusive.

The diagnosis of abdominal pregnancy stopped at 17 weeks + 6 days was made. On exploration by laparotomy, the peritoneal cavity was free, without abdominal pregnancy with the appearance of a 10 cm corporeal-fundal myoma type 5 of FIGO classification (**Figure 1**). Opening this mass revealed a scar pregnancy unrelated to the uterine cavity (**Figure 2**). Indeed, the pregnancy is located at the site of the previous myomectomy scar.

The pregnancy was extracted (**Figure 2**) without difficulty followed by padding in two layers and the postoperative course was simple with discharge authorized on postoperative day 4. The hysterography performed at M3 came back normal.

2.2. Second Case

This was a 36-year-old patient with 4 live children born vaginally, seen for pelvic

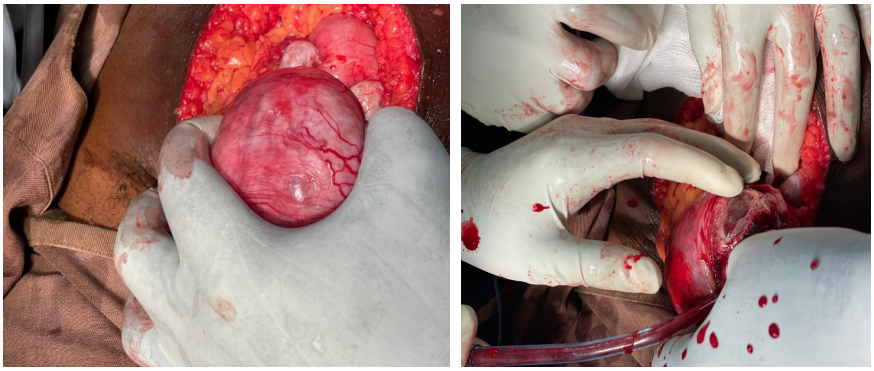

Figure 1. Images of scar pregnancy.

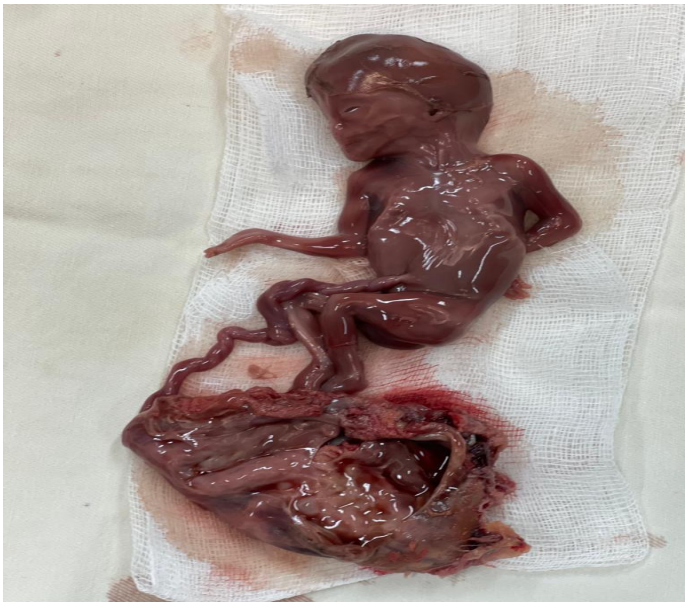

Figure 2. The conceptus.

pain with a notion of late menstruation of 2 and a half months without any particular history. The clinical examination showed an enlarged uterus. The speculum examination showed a purplish Mullerian cervix and the vaginal examination revealed a posterior cervix, long, softened and closed with a uterus increased in volume like three months of pregnancy.

The urine pregnancy test came back positive. The obstetric ultrasound showed a twin, bi-chorionic, intrauterine pregnancy progressing 9 weeks with two bags 18 mm apart (a large "lamda" sign) and one bag located less than 5 mm from the serosa.

The diagnosis of heterotopic pregnancy with cornual location was suspected. Laparoscopic exploration made it possible to visualize a gravid uterus with a tense left cornual pregnancy (pear-shaped uterine horn).

A laparotomy was made allowing the removal of the cornual pregnancy after devascularization of the uterine horn and preservation of the intrauterine one (**Figure 3** and **Figure 4**).

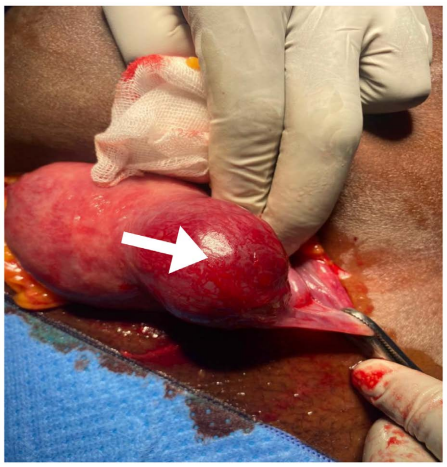

Figure 3. Left cornual ectopic pregnancy (white arrow).

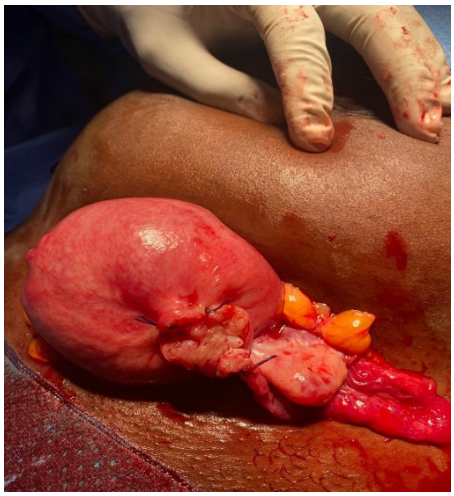

Figure 4. Resection of the left uterine horn.

The patient was put on injectable progesterone and an antispasmodic infusion. The control ultrasound showed a single intrauterine intrauterine pregnancy lasting 9 weeks 4 days. The evolution was favorable with discharge authorized on postoperative day 6. Pregnancy monitoring was ensured in the department with monthly appointments without complications. A prophylactic cesarean section was performed at 36 weeks, allowing the delivery of a healthy newborn female weighing 2900 g.

3. Discussion

3.1. Heterotopic Pregnancy

Heterotopic pregnancy is the association of an GIU and a GEU. The first case was reported by Duvernet in 1708 during an autopsy [2]. Epidemiologically, the frequency of heterotopic pregnancies varies depending on the series: from 1/30,000 in the case of spontaneous pregnancies to 1/100 during ART [3] [4] This frequency is probably underestimated in certain series. The risk factors for hetero-

topic pregnancy are no different from those for classic ectopic pregnancies [5].

But ART techniques have largely modified the epidemiological profile of heterotopic pregnancies [6]. For Sentihes *et al.* [7], certain factors specific to ART would increase the risk of heterotopic pregnancy such as: a high rate of embryos transferred, transfer near a uterine horn, excessive pressure at the syringe, transfer difficulties and the presence of adhesions resulting from endometriotic lesions.

Finally, a history of surgery on the abdomen or pelvis is also mentioned [3] [4].

However, in our case no risk factors were found, leading us to conclude that it was an accidental heterotopic pregnancy.

From a physiopathological point of view, combined pregnancy can result from simultaneous fertilization or delayed fertilization (fertilization of two eggs produced at a short interval during the same cycle by two spermatozoa from two successive coits) [4] [8].

This hypothesis is raised during the induction of ovulation when two injections of HCG are used. As shown in the study by Riadh et al, five/seven patients received ovulation-inducing treatment, four with clomiphene citrate and one with gonadotropins as part of IVF-ICSI [4].

It should be noted that no specific signs of heterotopic pregnancy have been reported, which implies the frequency of late diagnosis at the stage of ruptured ectopic pregnancy, especially in countries with limited resources [3] [4]. In cases with abortion of the intrauterine pregnancy, the persistence of pain and metrorrhagia suggest the diagnosis [2].

The B-HCG dosage has no predictive value for the existence of a heterotopic pregnancy but allows it to be suspected in cases with abortion of the intrauterine pregnancy. [2] [9]

For Parant *et al.* [10], the preoperative diagnosis of heterotopic pregnancy is only made in 10% of cases.

Ultrasound is the main examination for the diagnosis of heterotopic pregnancies, allowing to specify the age of the pregnancy, the quality of the IUGR, the exact site of the ectopic pregnancy and the existence of a possible hemoperitoneum. The diagnosis is certain when an intrauterine gestational sac containing an embryo and a second extrauterine sac containing an embryo with cardiac activity are detected. In our case, the diagnosis of cornual location was suspected on ultrasound in the presence of two gestational sacs 18 mm apart (a large "lambda" sign) and a sac located less than 5 mm from the serosa.

However, ultrasound can be falsely reassuring by only visualizing the ectopic pregnancy. Indeed, for Risk *et al.* [11], the preoperative ultrasound diagnosis of heterotopic pregnancy was only made in 10% to 14% of cases. For Tal *et al.* [12], the combination of clinical and ultrasound data allows for the diagnosis of 41.1% of heterotopic pregnancies. However, the latter should be performed by a knowledgeable and attentive operator. In our case, it allowed the diagnosis to be suggested before the onset of symptoms. The latter is the reference for confirming the diagnosis of heterotopic pregnancy [4] [8]. It allows the size of the uterus to be

assessed, the ectopic pregnancy to be visualized, the condition of the fallopian tube and peritoneum to be assessed, the hemoperitoneum to be quantified, and treatment to be guided. The treatment of heterotopic pregnancy aims to eliminate the ectopic pregnancy while preserving the ectopic pregnancy as much as possible, and to preserve the patient's subsequent fertility. Treatment can be medical or surgical. Laparoscopy is the standard treatment. Uterine cannulation is prohibited. In the case of laparotomy, uterine manipulation should be minimal and prophylactic tocolysis is questionable [4] [13].

In our case, a conversion to laparotomy was performed, allowing the removal of the cornual pregnancy after devascularization of the uterine horn and preservation of the intrauterine one. In case of radical treatment, salpingectomy must be performed without resection of the interstitial portion to avoid weakening the uterus [14]. If a wedge resection of the uterine horn is performed, a prophylactic cesarean section must be considered, as was the case for our patient.

Medical treatment is based on local injection of Kcl under ultrasound guidance and represents a good alternative to surgery [4] [8] [15]. In situ injection of hyperosmolar glucose solution has also been reported [16]. A transient decrease in plasma B-HCG levels after treatment of the ectopic pregnancy is frequently observed and corresponds to the cessation of the ectopic pregnancy.

Methotrexate, whether injected locally or systemically, is not recommended due to its teratogenic and toxic effects on ectopic pregnancy [16] [17].

The prognosis of ectopic pregnancy depends mainly on the early diagnosis [18]. 30% to 75% of ectopic pregnancy cases progress to term after treatment of ectopic pregnancy [2] [6] [11] [16].

A series of 35 heterotopic cornual pregnancies, 11 of which were treated medically, found that five ectopic pregnancy cases progressed to term, three of which were delivered vaginally. While for Sentilhes *et al.* [17], there is a weakening of the uterus even in cases of expectant management, hence the indication of a prophylactic cesarean section at term. For Habana *et al.* [12], the risk of uterine rupture is a theoretical risk and vaginal delivery can be considered.

3.2. Intramural Pregnancy

Intramural ectopic pregnancies are extremely rare and account for less than 1% of all ectopic pregnancies [18].

Theodore Doderlein first described the condition in 1913 in a woman with adenomyosis [19].

The exact etiology and pathogenesis of intramural pregnancies are unclear. Theories include implantation in a focus of adenomyosis, microscopic invasion of the myometrium due to uterine trauma caused by surgical instruments or following difficult in vitro fertilization (IVF) transfers, and external migration and implantation on the serosal surface of the uterus.

Since 2000, for the 22 cases recorded, nine (56%) had undergone prior uterine curettage, three (19%) were known to have adenomyosis, three (19%) were the

result of IVF or IUI, and four (25%) had either a prior myomectomy or cesarean section [20] [21].

In our case, the patient had a prior myomectomy one year earlier.

Historically, the diagnosis of intramural pregnancy was not made until surgery for uterine rupture.

Cornual (interstitial) pregnancy involves implantation within the interstitial portion of the fallopian tube embedded in the myometrium, whereas intramural pregnancy corresponds to a gestational sac implanted directly within the myometrial wall, without communication with either the uterine cavity or the fallopian tube.

On ultrasound, cornual (interstitial) pregnancy appears as a laterally displaced gestational sac located within the interstitial segment of the fallopian tube, surrounded by a thin myometrial mantle and typically associated with a positive interstitial line sign. In contrast, intramural pregnancy is characterized by a gestational sac completely embedded within the myometrial wall, with no communication with either the uterine cavity or the fallopian tube, and absence of the interstitial line sign. The surrounding myometrium is usually thick and homogeneous, allowing clear differentiation from interstitial pregnancy.

Nevertheless, the diagnosis could be made at all stages of pregnancy.

Indeed, there are cases where the diagnosis was made in the third trimester [22] [23]. Fait *et al.* described a case diagnosed at 30 weeks of gestation that resulted in a cesarean section with a live birth and then a hysterectomy. Another case has been described in the literature, a woman with a 26-week gestation who presented with an acute abdomen and hypovolemic shock [24].

An intramural pregnancy can be diagnosed with ultrasound. The gestational sac must be completely surrounded by myometrium and separated from the endometrial cavity. This can be difficult to distinguish from a degenerative fibroid, a pregnancy in a congenitally abnormal uterus, or an interstitial ectopic pregnancy.

Three-dimensional ultrasound and magnetic resonance imaging can be helpful in making a diagnosis [24]-[26].

In our case, a second ultrasound with the "ultrasound" Shibangu test was performed and revealed that the pregnancy was developing outside the uterine cavity but remained in close contact with the uterus. The diagnosis of an abdominal pregnancy with an abortion at 17 weeks + 6 days was made, indicating a laparotomy.

One reason why diagnosis is often delayed may be due to the operator's lack of awareness of the diagnosis.

Historically, these pregnancies were not diagnosed until the time of surgery, so management was often by surgical excision leading to a hysterectomy, as in our case where the diagnosis was also made intraoperatively but did not require a hysterectomy [21]. Some intramural pregnancies are amenable to medical management. Methotrexate is the most commonly used drug and can be administered

locally or systemically. Bouzari *et al.* described successful treatment of a posterior wall intramural pregnancy using a single dose of intramuscular methotrexate (50 mg/m^2) [27]. A multiple-dose regimen using an alternate-day intramuscular route of methotrexate (50 mg/m^2) and leukoviron (0.1 mg/kg) for 8 days has also been described [26]. Methotrexate can also be injected intra-amniotically under ultrasound guidance with or without fetal intracardiac potassium chloride [18] [21]. Endoscopic management is increasingly becoming the reference standard, but it requires a well-trained team [27] [28].

Expectant management has also been described [29]-[31].

4. Conclusion

Ectopic pregnancy (EP) is a public health problem in our environment due to its increasing frequency. Its heterotopic and intramyometrial location poses a real problem due to its rarity, representing 1/30,000 in spontaneous pregnancies, 1/100 during assisted reproductive technology (ART), and less than 1%, respectively. Their diagnosis, often late, is most often made at the stage of rupture, which can quickly lead to death. Careful pelvic ultrasound and laparoscopy at the slightest suspicion allow for their diagnosis before complications occur.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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