About a Case of Failure of Medical Treatment of an Interstitial Pregnancy

Ragmoun Houssem 1, Daadoucha Abdrahmen, Benslima Najeh, Ajili Abir
1 Department of Obstetric Gynecology Ibn El Jazzar Hospital, University hospital assistant in gynecology obstetrics, Ibn El Jazzar street, Kairouan, 3100, Tunisia
2 Department of Radiology Ibn El Jazzar Hospital, University hospital assistant in radiology, Ibn El Jazzar street, Kairouan, 3100, Tunisia
3 Department of Cardiology Ibn El Jazzar Hospital, University hospital assistant in cardiology, Ibn El Jazzar street, Kairouan, 3100, Tunisia

Corresponding author email: houssen.ragm@yahoo.fr

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Abstract Interstitial pregnancy is a rare entity that accounts for nearly 2% of ectopic pregnancies. His diagnosis is almost always based on laparoscopy. The risk of rupture with significant hemorrhage remains high. The treatment is classically surgical by corneal resection, medical treatment is increasingly used. Through an observation of an interstitial pregnancy diagnosed in our department and treated initially medically and then by radical surgery and by means of a review of the literature, we will try to explain the different diagnostic and therapeutic methods used in interstitial pregnancies, we will also learn the importance of patient selection in order to avoid risky changes, especially in the absence of consensus.

Keywords Ectopic pregnancy; Corneal pregnancy; Interstitial pregnancy; Corneal resection; Methotrexate

Background
A diagnosis of ectopic pregnancy is made about 1.5 times per 100. In less than 10% of cases, it is a non-tubular ectopic pregnancy, particularly interstitial or corneal localization, the latter type represent a major challenges since the delay in diagnosis and therefore in the management can be extremely dangerous. The treatment, previously always surgical and radical, becomes mostly minimally invasive, based on treatment with methotrexate according to several schemes.

1 Observation
Mrs. F is 37 years old with an appendectomy in her antecedents. It is a third gesture, second pare, having two live children normally delivered by low way. She has been undergoing micro-progesterone contraception for 6 months. She consulted us for minimal blackish metrorrhagia with a ten day amenorrhea. The clinical examination found a slight lateral hypogastric sensitivity on the right. Ultrasound (Figure 1) objective an ectopic pregnancy in the cornual right seat, fetus with positive cardiac activity of 11 weeks of amenorrhea, low abundance effusion in Douglas. The initial level of ß-hCG was 39,000 mIU / ml. The laparoscopy (Figure 2) showed the presence of a right cornual pregnancy of 8 cm. Given the desire for further fertility evoked by the patient, we was tempted to make a conservative treatment, so we applicate an injection of 40 mg of methotrexate in situ by laparoscopic route in the corneal pregnancy ,followed by an unique injection of 60 mg of methotrexate intramuscularly at the same day.

On the fourth postoperative day, there was an increase in pelvic pain and a rise in ß-hCG levels associated with a drop in the hemoglobin level (7 grams for an initial of 10.5 grams), a decrease in arterial pressure to 8/6 As well as hemoperitoneum accumulation at ultrasound ,so a laparotomy was performed on emergency and demonstrated a right pre break corneal pregnancy with hemorrhage suffusion (Figure 3), in front of low hemoglobin numbers and a rare blood group (O negative), as well as an unstable hemodynamic state, an hysterectomy was performed, corneal resection was considered dangerous, after the transfusion of two Red blood cells.
The examination of the hysterectomy part confirmed the inertial seat of pregnancy (Figure 4; Figure 5).

2 Discussions
The interstitial portion of the fallopian tube corresponds to the proximal segment incorporated into the uterine muscle wall (0.7×1.5 cm). A pregnancy implanted at this site is called an interstitial pregnancy (Tulandi, 2013). When it is located in a rudimentary horn of a bicorn uterus or in the remaining stump of a trunk treated with salpingectomy, it is called corneal pregnancy. Interstitial pregnancy is located outside the round ligament as opposed to the angular pregnancy within (Bouyer et al., 2002). Ectopic pregnancies: interstitial, angular (developed in the tubal ostium at the bottom of the uterine cavity) and corneal localization is often grouped together and represent the same clinical and therapeutic entity (Bouyer et al., 2002).
The macroscopic examination of our hysterectomy part confirms well the interstitial seat of the pregnancy (Figures).

The incidence of interstitial pregnancies is between 2-3% of all ectopic pregnancies and allows relatively late development until 16 weeks of amenorrhea (11 weeks of amenorrhea for our case). Interstitial pregnancies are particularly hemorrhagic due to a rich corneal vascularization and greater myometrial distension, so that the rate of mortality by interstitial pregnancy is logically 2 to 3 times that of tubal pregnancies (Malek-mellouli et al., 2012).

Risk factors are similar to other ectopic pregnancies (history of ectopic pregnancy, pathology and tubal surgery, intra-uterine dystylibene exposure, genital infections, tobacco, in vitro fertilization) except for ipsilateral salpingectomy which is a specific risk factor to interstitial pregnancy (Tulandi and Al-Jaroudi, 2004), in our patient alone contraception by micro progestative was found as risk factor for ectopic pregnancy.

The diagnosis is based on synthesis of clinical examination, plasma HCG and transvaginal ultrasound.

The ultrasound diagnosis of interstitial pregnancies is difficult, and these pregnancies are often symptomatic later, leading to delays in management until the second trimester, but ultrasound criteria have been proposed by Timor-Tritsch for this diagnosis: An empty uterine cavity, an eccentric gestational sac and located at>1 cm from the lateral wall of the uterine cavity and a thin (<5 mm) layer of myometrium around the sac (Timor-Tritsch et al., 1992). 3D ultrasound as well as MRI also allow early accurate diagnosis if interstitial pregnancy is suspected on 2D ultrasound (Filhastre et al., 2005; Júnior et al., 2007).

In our case the diagnosis was delayed to 11 weeks of amenorrhea, the patient did not consult since she attributed its disorders of the cycle to the contraceptive treatment, the ultrasound examination (Figures) confirmed the diagnosis of cornual pregnancy, there is no 3D probe in our department and it was not considered useful to perform an MRI since it was decided to perform a laparoscopy.

By the past, the treatment of interstitial pregnancy consisted of salpingectomy and corneal resection by laparotomy, probably as a result of delayed diagnosis (Moawad et al., 2010) currently interstitial pregnancy is typically diagnosed at an early gestational age and prior to rupture, leaving the opportunity for conservative medical or surgical treatment (Hussein et al., 2014). However, in the presence of signs of severity (hemodynamic failure and presence of abundant hemoperitoneum), the treatment should be surgical by laparoscopic route if possible, but most often by laparotomy. Conservative treatment of the uterus will be preferred whenever possible, but radical treatment (hysterectomy) may be necessary to control hemorrhage (Hussein et al., 2014).
Methotrexate (MTX) is the cornerstone of medical management with different routes of injection (Misme et al., 2015): intramuscular, “in situ” with ultrasound or “in situ” by laparoscopy at a dose of 1 mg / kg. Other molecules are also used, alone or in combination with methotrexate: KCl in situ (5 mmol) (especially in heterotopic pregnancies or in case of contraindication or failure of treatment with methotrexate), mifepristone when initial progesteroneemia is greater than 9 ng / mL (Rozenberg et al., 2003).

The most frequent regimen in the literature is the multi-dose regimen (MTX 1 mg / kg IV / IM on day 1, 3, 5 and 7 with Leucovorin 0.1 mg / kg oral on day 2, 4, 6 and 8 Re-administer therapy 7 days after the last dose) (Jermy et al., 2004) associated with surgical treatment in the event of deterioration of clinical condition. The success rate reported is 66% (Jermy et al., 2004). If, in the case of conventional tubal ectopic pregnancies, a single injection of MTX has become the standard, it appears that repeated interstitial doses are more interesting (Jermy et al., 2004; Moawad et al., 2010) for interstitial pregnancies. There is as yet no consensus on the protocol to be followed for the multidose regimen. There is no consensus regarding the limiting level of HCG or the presence of cardiac activity (Moawad et al., 2010).

Treatment by local injection of methotrexate by endovaginal route under ultrasound control, or especially by laparoscopic route, as well as injection supplements of IM methotrexate in addition to the in situ injection, appears to obtain better results compared to MTX by the general route (Jourdain et al., 2003; Jermy et al., 2004).

It is important to follow the decay of HCG until it is negated. The mean duration of undetectable HCG in serum is 43 +/- 64 days (Jourdain et al., 2003). An interstitial mass or heterogeneous area with persistent vascularization on ultrasound has been reported (Tang et al., 2006). Subject to negativity complete of HCG, they do not constitute a therapeutic failure (Tang et al., 2006).

In our team the management of interstitial pregnancy outside the context of rupture is a celioscopic injected injection of MTX associated on the same day with a single injection of MTX by IM (1 mg / kg), but concerning this patient; The size, the scalability of the pregnancy and the celioscopic observation of signs prelude to rupture, parinaminci, ecchymotic spots (Figures) should have directed us towards surgical treatment in first intention.

3 Conclusions
Interstitial pregnancy is a rare but dangerous localization of ectopic pregnancy, which should be considered during an intra-uterine localization eccentric to more than one centimeter of the lateral wall of the cavity, with a fine myometrial circumferance. The reference treatment is laparoscopic surgery (in the absence of haemodynamic disorder). Medical treatment is more and more used; in the absence of a clear consensus, selection of patients must be discussed on a case-by-case basis to avoid a hazardous evolution.

Authors’ contributions
Ragmoun Houssem: Editing and supervision, read and approved the final manuscript; Daadoucha Abdrahamen: Participated in the drafting of the observation, read and approved the final manuscript; Benhlima Najeh: Participated in the drafting of the discussion, read and approved the final manuscript; Ajili Abir: Checking references. All authors read and approved the final manuscript.

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