

Medical Treatment of Tubar Ectopic Pregnancy with Living Embryo: About Two Cases in Dakar (Senegal)

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ABSTRACT

Objectives: To evaluate the efficacy of treatment with methotrexate, and the possibility of medical treatment of living embryo.

Observation: We report two cases in secondary amenorrhea of 6 weeks received in an algebra table associated with minimal bleeding.

The physical examination had found moderate pain in the left iliac fossa for the first patient and for the second patient in the right iliac fossa with minimal bleeding. The first endo-vaginal ultrasound showed a left lateral uterine mass, the second one a right lateral uterine mass containing a living embryo of six-week amenorrhea. We administered a triple dose of methotrexate to both patients whose improvement could be noticed through a clinical remission and a decrease of the plasmatic β HCG level. Consequently, we decided to release them after 8 days of hospitalization.

Conclusion: The medical treatment of tubal ectopic pregnancy with living embryo is difficult due to the work conditions; furthermore, it is a controversial issue in our country.

Keywords

Ectopic pregnancy, Medical treatment, Methotrexate.

Introduction

The term ectopic pregnancy (EP), is defined as the implantation and development of the fertilized egg outside the uterine cavity. The vast majority of ectopic pregnancies are tubal pregnancies, but can be abdominal, ovarian or cervical. EP remains the leading cause of maternal death in the first trimester of pregnancy in developing countries and accounts for almost 10% of maternal mortality [1]. Knowledge of risk factors makes it possible, on the one hand, to prevent EP upstream and downstream and to avoid recurrence.

In Senegal, EP accounted for 9.3% of emergency laparotomies with an incidence of 0.8 per 1000 pregnancies [2]. The therapeutic strategies of this pathology can range from abstention to radical

surgical treatment, through medical treatment. The criteria of medical treatment are not unanimous.

Most French studies do not recommend a medical treatment for EP on a living embryo [3]. We report two cases of EP with live embryos that have received medical treatment.

Observations

First observation

It was a patient, second gesture, second 30-year-old parish received at Maternity Center Nabil Choucair on 23/12/2014 for iliac fossa pains left spasm type on the backdrop of late menstruation without bleeding evolving for 2 days without vomiting or fever.

In her antecedents, there were 2 vaginal deliveries and a notion of repetitive genital infections treated. The gynecological examination had found pain in the left iliac fossa, a slightly enlarged uterus

with minimal metrorrhagia. An endovaginal ultrasound showed an empty uterus, a left lateral uterine mass corresponding to a gestational sac with a trophoblastic crown and an embryo whose biometry corresponded to 6 weeks of amenorrhea, with a cardiac activity, a uterus empty, a dead-end of free Douglas without effusion and a free interhepato-renal space as shown in Figure 1:



Figure 1: Endovaginal ultrasound showing ectopic pregnancy.

A plasma dosage of the β HCG level performed 4 days previously was found to have a value of 9306.67 IU.

Pre-treatment evaluation with a blood count, liver function and renal status was normal. Explanations concerning the therapeutic options for ectopic pregnancy were given to the hospitalized patient.

We made the patient sign a consent form before administering a methotrexate-based medical treatment. An intramuscular dose of 1 mg / kg was administered; ie 80 mg on the first, the third, and the fifth day. This treatment was associated with taking folic acid at a dose of 0.1 mg / kg orally.

We used ultrasound and biological monitoring to appreciate the effectiveness of the treatment. We performed Ultrasound surveillance on the first, the 12th, the 33rd day, the 40th and the 45th day. At that time, the endovaginal ultrasound found partial lysis of the embryo (Figure 2).



Figure 2: Endovaginal ultrasound showing ectopic pregnancy.

The evolution was favorable and marked by the decrease then the negativation of the β HCG level as shown in Table 1:

Dosing days	date	β HCG (IU / l) Values
1st day	24/12/2014	9306.67
12th day	04/01/2015	4760
33rd day	22/01/2015	70
40th day	29/01/2015	10
45th day	03/02/2015	2

Table 1: Evolution of the kinetics of plasma β HCG during treatment.

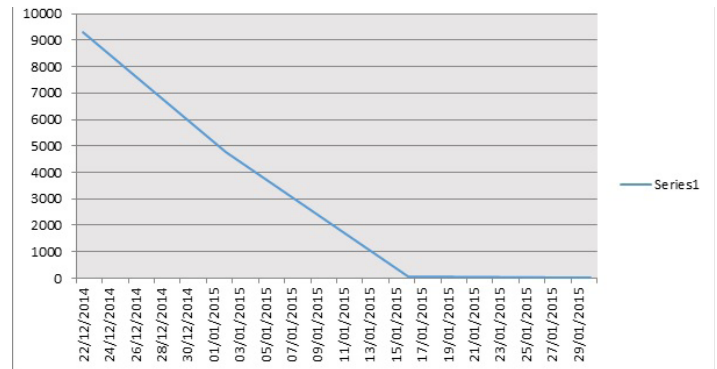


Figure 3: Diagram of β HCG dosage Values.

The patient was put on injectable contraception for a period of 3 months. CBC, renal status, and liver function were normal at control. Exit was allowed one week after hospitalization. HCG monitoring was then performed as an outpatient until recovery

Second observation

It was a 21 year-old second gesture and nulliparous patient received at the maternity department of Aristide Dantec hospital on April 17th 2018 for pelvic pain like spasms following a late six-day menstruation without bleeding, vomiting or fever.

In her antecedents, there was a spontaneous abortion and a notion of repetitive treated genital infections. The gynecological examination revealed pain in the right iliac fossa, a slightly enlarged uterus with minimal metrorrhagia. An endovaginal ultrasound showed an empty uterus, a right lateral-uterine mass corresponding to a gestational sac with a trophoblastic crown and an embryo whose biometry corresponded to 6 weeks of amenorrhea, with a cardiac activity, a uterus empty, a dead-end of free Douglas without effusion and a free interhepato-renal space.

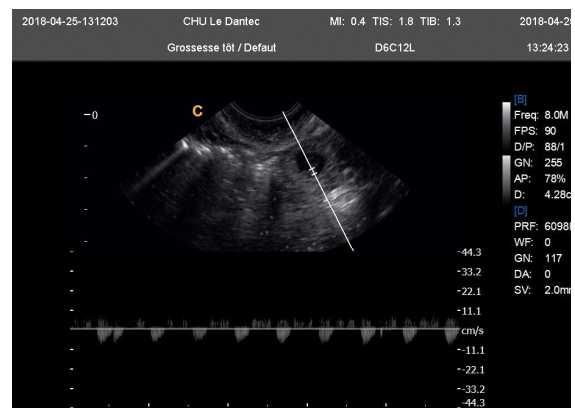


Figure 4: Endovaginal ultrasound showing ectopic pregnancy.

A plasma dosage of the β HCG level achieved was found to be 5607 IU / l. Monitoring the effectiveness of treatment was appreciated by ultrasound and biological monitoring. Ultrasound surveillance was performed on day 1, day 9, and day 16 which revealed partial lysis of the embryo.

The evolution was favorable and marked by the decrease of the β HCG level (Table 2):

Dosing days	date	β HCG (IU / l) Values
1st day	18/04/2018	5607
16th day	03/05/2018	4760
23rd day	10/05/2018	2192.26
45th day	01/06/2018	8.4
60th day	16/06/2018	2

Table 2: Evolution of the kinetics of plasma β HCG during treatment.

The patient was put on injectable contraception for a period of 3 months. CBC, renal status, and liver function were normal at control. The patient was released two weeks after hospitalization.

Discussion

Ectopic pregnancy is a major gynecological emergency. The therapeutic aspects are a subject of controversy, especially for medical treatment with Methotrexate [3-6].

Epidemiological-clinical aspects

The most important risk factor is salpingitis, which is usually secondary to a sexually transmitted disease. The most common is Chlamydia trachomatis infection (the risk is increased up to 7 times) [1,7]. Other sexually transmitted diseases are also incriminated due to Mycoplasma, Neisseria gonorrhoeae [7].

In our observations, we noted antecedents of genital infections with repetition in the two patients and another antecedent of a miscarriage in the second one.

Therapeutic aspects

Treatment indications

In indications and contraindications for the medical treatment of ectopic pregnancy, there is no consensus [3,8]. Currently, the points of discussion lie in the relative contraindications that are the maximum permissible levels of plasma β -HCG and progesterone as well as certain ultrasound criteria such as the presence of a cardiac activity and a hemoperitoneum [1,3,9-11]. In Africa, ectopic pregnancy is most often diagnosed at the stage of tubal rupture with peritoneal flood [2,7].

Our first patient had a plasma β -HCG level of 9306.67 IU / l and our second, a plasma β -HCG level of 5607 IU / L; their endovaginal ultrasound showed a left tubal ectopic pregnancy with a living embryo of 6-week amenorrhea for the first patient, and for the second a right tubal ectopic pregnancy with a living embryo of 6-week amenorrhea. The work conditions in Africa remain difficult although possibilities exist, that's why we have tried with

the patients' consents to treat a symptomatic ectopic tubal pauci pregnancy with cardiac activity.

We referred to the experience of US teams for the medical treatment of EP with cardiac activity whose success rate are 87.5%. Unlike French teams, US teams do not take into account the plasma level of β -HCG, the presence of cardiac activity or hemoperitoneum, [2,12-14]. The presence of cardiac activity is indicative of the activity of the USG. EEGs with cardiac activity have a higher plasma β -HCG level.

However, it is important to note that the failure factors of medical treatment are the presence of cardiac activity, high progesterone levels, and high plasma β -HCG. To minimize the risk of treatment failure, we monitored the pre-therapeutic score of Fernandez et al. which was indicated in both observations [14-16].

Therapeutic protocols

Regarding the medical treatment of ectopic pregnancy, there are currently several protocols:

The multiple-dose regimen, especially in the United States, includes 4 doses of Methotrexate at 1 mg / kg intramuscularly on days 1, 3, 5, and 7 and 0.1 mg / kg of folinic acid [3,15,17].

The limitations of this protocol are hospitalization, financial cost, and side effects such as stomatitis, leukopenia, nausea, abdominal pain, alopecia, and elevated liver enzymes. The single-dose regimen used mainly in Europe and some African countries is administered at the dosage of 1 mg / kg or 50 mg / m² [3,18,19]. The administration schedule includes a dose administered on the first day at a dose of 1 mg / kg. In our two patients, we opted for the multi-dose protocol to minimize the risk of therapeutic failure.

The control of the efficacy of the treatment is done by assaying the plasma level of β -HCG on the 3rd day, the 5th day, the 8th day, the 15th day, the 20th day and the 28th day [19]. With the multiple-dose regimen, we noted the fall in plasma β -HCG levels as shown in Tables 1 and 2.

Treatment monitoring

In both cases, the monitoring of the treatment is based on the determination of the plasma β -HCG fraction [20]. Day 1 is the base rate; on the third day, a physiological rise is observed; between the 4th and the 7th day, we observe a decrease of 15 to 30% which makes it possible to affirm that the treatment is effective; then the plasma dosage of β -HCG is done once a week until negativation. In other words, when the base level becomes less than 20 IU / l. The duration of the negativation varies between 25 and 35 days [21,22].

In our patients, we observed a decrease of almost 50% on the 12th day after methotrexate injections. We obtained the negativation at the 45th day and this could be explained by the presence of a cardiac activity at the beginning of the medical treatment.

Post-treatment surveillance consists not only in evaluating the

effectiveness of medical treatment but also in watching for its side effects, particularly the adverse effects of methotrexate. Side effects are less important after single injection than after multiple injection. Folinic acid supplementation after multiple injection of MTX limits these side effects. In both cases, we did not find any major side effects.

Conclusion

EP is one of the leading causes of maternal mortality, accounting for 4.9% of maternal deaths in developed countries. Thanks to β -HCG dosage and endovaginal ultrasound, the diagnosis of EP became earlier, sometimes before the onset of clinical signs.

The medical treatment of EP is presented as a real alternative to surgical treatment in well-defined indications; but its application to the living embryo is still controversial.

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