

## Angular pregnancy at 6<sup>th</sup> week of gestation treated with minimally invasive surgery preceded by systemic and local medical therapy with methotrexate. Case report

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**SUMMARY:** Angular pregnancy at 6<sup>th</sup> week of gestation treated with minimally invasive surgery preceded by systemic and local medical therapy with methotrexate. Case report.

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**Introduction.** *The angular pregnancy is characterized by the abnormal position of the blastocyst, on the corner of the uterine cavity. It can lead to miscarriage, fetal death or preterm birth, as well as to spontaneous rupture of the uterus due to overdistension. Therefore it requires early diagnosis and careful management.*

**Case report.** *We present a case of a woman in the sixth week of gestation, with a diagnosis of angular pregnancy, treated with methotrexate, first systemically and after locally, and then followed by hysteroscopy with resection of the gestational sac.*

**Discussion.** *Methotrexate promotes the detachment of the trophoblast. The administration of a further dose via intra-amniotic allowed to reduce systemical doses and therefore also the possible side effects. In this way we made hysteroscopic resection of the gestational sac possible and easier, in order to avoid more complicated and invasive interventions.*

**Conclusions.** *This type of approach has therefore proved to be effective, preserving the uterus from surgical stress and maintaining the possibility of future pregnancies, with excellent compliance by the patient. In any case, we focus attention on the need for early diagnosis, as well as the desire of the mother and the specific characteristics of the clinical case to treat.*

**RIASSUNTO:** Gravidanza angolare alla VI settimana trattata con chirurgia minimamente invasiva preceduta da terapia medica sistemica e locale con methotrexate. *Case report.*

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**Introduzione.** *La gravidanza angolare si caratterizza per la posizione anomala della blastocisti, all'angolo laterale della cavità uterina. Può portare ad aborto spontaneo, morte fetale o parto pretermine, come anche a rottura spontanea dell'utero per sovradistensione. Necessita dunque di diagnosi precoce e un attento management.*

**Caso clinico.** *Presentiamo un caso di una donna alla VI settimana di gestazione con diagnosi di gravidanza angolare, trattata con methotrexate per via sistemica prima e locale poi, seguita da isteroscopia con resezione della camera gestazionale.*

**Discussione.** *Il methotrexate favorisce il distacco del trofoblasto. La somministrazione di una dose anche per via intra-amniotica ha permesso di ridurre le dosi per via sistemica e quindi anche i possibili effetti collaterali. È resa così possibile e più semplice la resezione della camera gestazionale per via isteroscopica, al fine di evitare interventi più indaginosi ed invasivi.*

**Conclusioni.** *Questo tipo di approccio si è dunque rivelato efficace, preservando l'utero da ulteriori stress chirurgici e mantenendo la possibilità di gravidanze future, con ottima compliance da parte della paziente. Ad ogni modo poniamo l'attenzione sulla necessità di una diagnosi precoce, oltre che sulle volontà della gestante e sulle caratteristiche specifiche del caso clinico che si valuti.*

**KEY WORDS:** Trans-vaginal ultrasound - Methotrexate - Hysteroscopy - Angular pregnancy.  
Ecografia trans-vaginale - Methotrexate - Isteroscopia - Gravidanza angolare.

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## Introduction

Angular pregnancy is a rare form of ectopic pregnancy, in which the blastocyst nestles in the corner of the uterine cavity, medially to the utero-tubal junction (1).

It accounts for 2% of all ectopic pregnancies (2) and it is often confused, wrongly, with interstitial pregnancy, in which the implantation occurs, instead, in the intramural portion of the tube covered by the myometrium. In angular pregnancies, the gestational sac implants in the endometrium, the placenta strongly develops in thick, contracting tenacious adhesion with the uterine muscle, it is crumpled and his detachment is difficult.

Clinical diagnosis is extremely difficult and it is necessary to use ultrasonography. The role of transvaginal (TV) ultrasound is fundamental, as it will detect, in case of angular pregnancy, the eccentric location of gestational sac, surrounded, unlike the interstitial pregnancy, by a continuous albeit very thin layer of myometrium.

In over 75% of cases, the evolution involves abortion between 12<sup>th</sup> and 20<sup>th</sup> weeks of gestation, fetal death or preterm birth of a child who does not survive. Sometimes it is possible the spontaneous rupture of the uterus even in absence of contractions, as a result of overdistension of the walls of the angular recess, where pregnancy nested, particularly thin at this level; this condition is often catastrophic, sometimes making hysterectomy necessary and endangering the life of the patient (3).

We report a case of angular pregnancy, successfully treated with combination of medical therapy with methotrexate and minimally invasive conservative surgery.

## Case report

A 43 years old woman at 6<sup>th</sup> week of gestation of her 5<sup>th</sup> pregnancy (1 vaginal delivery, 1 miscarriage, 2 cesarean sections) came at the emergency department of Obstetrics and Gynecology of "Federico II"

University Hospital of Naples, with bleeding of dark red color from genitals. She exhibited a TV ultrasound done in another hospital on the same date, which showed presence of pregnancy on left tubal angle. It was therefore performed a physical examination (Table 1) and a TV ultrasound, which revealed an uterus increased in volume, with presence of an inhomogeneous hyperechoic area of 42 x 14 mm, referring to clots; furthermore it was reported, on the left cornual tract, probably in correspondence of the crossing point between uterus and fallopian tube, the presence of a gestational sac containing a single embryo with crown-rump length (CRL) of 4mm, with fetal heart motion seen (Fig. 1), corresponding to 6 weeks of gestation. The picture was compatible with diagnosis of angular pregnancy, during 6<sup>th</sup> week, metrorrhagia; so the patient was hospitalized. Blood tests were applied (blood group and Rh factor; complete blood count, coagulation, and serology) and also dosage of serum  $\beta$ -hCG, in addition to ECG and cardiological examination. All performed tests resulted in the standard, the value of  $\beta$ -hCG was 9078 mIU/ml. In the following days seriated samples of  $\beta$ -hCG were performed.

The woman was adequately informed of her condition and possible risks to the unborn and her own life, associated with angular pregnancy; considering that she had already had two cesarean sections and the concerns about possible complications, she decided for termination of pregnancy according to the law 194/78 article 6.

Treatment with methotrexate started via intramuscular injection (IM) at a dose of 1mg/kg on days 1 and 3, in combination with folic acid IM at a dose of 0.1 mg/kg on days 2 and 4. In this phase, the pregnant was clinically monitored, with blood tests and  $\beta$ -hCG seriated assays.

After first dose of methotrexate,  $\beta$ -hCG serum levels were reduced to 4601 mIU/ml, after the second to 3730 mIU/ml. On the 4<sup>th</sup> day, the patient was subjected to diagnostic hysteroscopy, which confirmed, defining with further precision the exact site of the implantation, the diagnosis of angular pregnancy. During the examination it was also per-

TABLE 1 - MEDICAL EVALUATION AT TIME OF HOSPITALIZATION.

Blood pressure	80/40 mmHg	
Cardiac frequency	70 bpm	
Abdomen	No tenderness	
Gynecological evaluation	Uterus	Increased in volume, movable, not painful
	Cervix	Closed cervical os
	Genitals	Slight bleeding dark red coloured

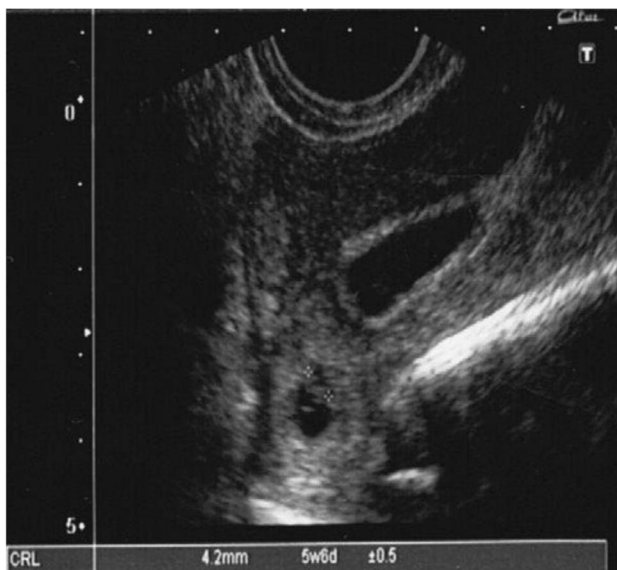


Fig. 1 - CRL at sixth week of gestation.

formed methotrexate administration at a dose of 50 mg, directly inside the gestational sac, which showed absence of evolution and irregular margins. This resulted in sharp drop in the values of serum  $\beta$ -hCG to 1023 mIU/ml.

After two days, it was performed an operative hysteroscopy with resection predominantly cold, to reduce the possibility of thermal damage to the uterine wall, which is very thin at this level, of the gestational sac, which appeared almost completely collapsed confirming the efficacy of systemic and local therapy with methotrexate. The sampled material was then subjected to histological examination. The patient was discharged the day after the hysteroscopic examination, to her will. She was controlled as outpatient with seriated doses of  $\beta$ -hCG until it became negative.

## Discussion

Given the high risk of miscarriage, preterm labor, rupture of the uterine wall with massive hemorrhage, placenta accreta, IUGR (intra-uterine growth retard), post-partum placental retention and post-partum endometritis, and also given the difficulties due to implant site, of executing maneuvers such as curettage and removal of placenta, it is difficult to determine prognosis of angular pregnancy; so the management of this pathology requires attention.

The options to treat angular pregnancy are multiple and vary depending on time of diagnosis, risk factors, choice of patient and the desire for future pregnancies.

A conservative approach is possible when the diagnosis is made early.

Tanaka et al., in 1982, reported the first case of angular pregnancy successfully treated with multiple doses of methotrexate (4).

In our case, the diagnosis of angular pregnancy was made after 6 weeks of gestation, and this allowed the choice of a combined approach, as minimally invasive conservative surgery preceded by medical therapy with methotrexate. The rationale for such therapy was that methotrexate promotes the detachment of trophoblast, considerably making resection of gestational sac easier and less laborious. This is of fundamental importance in a disease as the angular pregnancy in which the sac is implanted in an area where myometrium is very thin and therefore delicate, and wherein the retention of tenaciously adherent chorionic residues is frequent. Drug administration, done as well as via IM, also directly in the gestational sac, allowed to reduce systemic doses and to prevent side effects, such as myelosuppression, hepatotoxicity, pulmonar fibrosis, alopecia, stomatitis and photosensitivity. The diagnostic hysteroscopy has made it possible to establish with certainty the site of the pregnancy, while the subsequent operative hysteroscopy was performed to remove the gestational sac that looked almost completely collapsed, demonstrating the effectiveness of treatment with methotrexate. In this way, we avoided more invasive laparoscopic or laparotomic interventions, such as salpingectomy, cornual resection, or hysterotomy.

The use of a cold blade resection allowed to reduce to minimum the possibility of thermal damage to the uterine wall, which appeared extremely thin in correspondence of the implantation site. There was no abnormal bleeding. Furthermore, any kind of disruption in the myometrium, one of the most frequent complication of procedures like hysterosuction or curettage, was avoided in order to not interfere with the possibility and the outcome of any subsequent pregnancies.

The woman was discharged on the day following the operative hysteroscopy, with considerable reduction of the duration of hospitalization, and followed outpatients with seriated doses of  $\beta$ -hCG until complete negativization.

## Conclusions

The combined approach which we experienced, with medical therapy followed by cavitary revision with hysteroscopy, has proved to be efficient and at the same time harmless to the patient, improving

compliance and, especially, increasing the possibility of future pregnancies and reducing the risk of uterine rupture during subsequent pregnancies.

Early diagnosis, of which we emphasize the importance, was an essential factor in avoiding poten-

tially dangerous consequences associated with this condition. We must always take into account the wishes of the patient, symptoms, risk factors that can differentiate the various cases, directing towards the most appropriate treatment to the situation.

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