CASE REPORT

Spontaneous interstitial pregnancy on a tubal stump after unilateral adenectomy followed by transvaginal colour Doppler ultrasound

Luca Bernardini2,3, Mario Valenzano1 and Giovanni Foglia1

Department of Obstetrics and Gynaecology, 1I and 2II Divisions, S. Martino’s Hospital, University of Genoa, Genoa, Italy
3To whom correspondence should be addressed at: S. Martino’s Hospital-Pad-1, University of Genoa, L.R. Benzi 10, 16138, Genoa, Italy

Transvaginal colour and angio Doppler blood flow analysis combined with serial measurement of human chorionic gonadotrophin (HCG) concentration is reported here for the first time to study the local vascularity of a cornual pregnancy and to monitor the effectiveness of medical therapy. Interestingly, a strong relationship between morphological changes of trophoblastic tissue and the intensity of neovascularization was noted. Systemic single-dose methotrexate (MTX) therapy allowed successful treatment of an interstitial ectopic pregnancy involving part of the proximal portion of a tubal stump. We suggest that, by adding colour Doppler to conventional transvaginal ultrasonography, the outpatient surveillance of ectopic pregnancy evolution following MTX therapy is greatly enhanced. This is of particular value in cornual pregnancies which are highly likely to develop harmful complications during surgical intervention or even during puncture for local MTX injection.

Key words: colour Doppler/ectopic/interstitial pregnancy/systemic methotrexate

Introduction

The incidence of ectopic pregnancies has greatly increased during the past two decades. As such events become more common, so have reports of unusual sites of implantation. Ovarian, cervical, abdominal and cornual pregnancies occur mainly as the consequence of pelvic surgeries or pelvic inflammatory disease and treatment for assisted reproductive technologies (ART) (Balmaceda et al., 1991). However, discounting assisted reproduction, the occurrence of these unusual types of ectopic pregnancies is considered otherwise to be rare. Here we report the case of a nulliparous woman presenting with an interstitial ectopic nidation on the side of a residual tubal stump from previous unilateral adenectomy. In our opinion, the ectopic pregnancy implanted too far away from the internal cavity of the uterus to satisfy the echographic criteria for typical cornual pregnancy definition (Agarwal et al., 1996; Timor-Tritsch et al., 1996). The clinical course of this pregnancy was monitored on an outpatient basis by means of transvaginal colour-angio Doppler ultrasonography and serial measurement of serum human chorionic gonadotrophin (HCG) concentrations. At a gestational age of 61 days, due to the persistence of high hormonal values and the rich local vascularization, a single intramuscular (i.m.) dose of methotrexate (MTX) was administered. A few days later, serum HCG concentrations fell until undetectable at 36 days post-MTX injection. To our knowledge this is the first case report of a spontaneous cornual pregnancy involving a tubal stump in the presence of a contralateral corpus luteum. A comment on the advantages of colour-angio Doppler in the clinical management of this special case of ectopic pregnancy is made in the discussion.

Case report

The patient was a 36-year-old, gravida 4, nulliparous woman, who had had two spontaneous abortions and one pregnancy previously. She had regular menstruation and was suffering from secondary infertility of seven years’ duration. The patient’s medical history included a first laparotomy in 1985 for appendectomy, and a second in 1990 for total left adenectomy. This was done because of a ruptured left tubal pregnancy involving the ipsilateral ovary and a worsening of the patient’s vital signs. Two early abortions occurred in 1994 and 1996. In April 1997, a spontaneous conception again ensued. At a gestational age of 33 days, the initial HCG value was 95 IU/l, and this rose within one week to 3220 IU/l (Immunoenzymatic assay (IEMA), Biochem Immunosystem Company, Biodata, Milan, Italy; IRP # 75/537). At a gestational age of 52 days, an ectopic pregnancy in the left tubal stump was diagnosed during routine transvaginal colour Doppler ultrasonography using a 7 MHz transducer (Toshiba, SAL. 340, Tosbec, Japan). A gestational sac of 28.6 mm with no signs of embryonic viability was seen (Figure 1). Simultaneous colour/angio Doppler studies showed the presence of intense vascularization, a single intramuscular (i.m.) dose of methotrexate (MTX) was administered. A few days later, serum HCG concentrations fell until undetectable at 36 days post-MTX injection. To our knowledge this is the first case report of a spontaneous cornual pregnancy involving a tubal stump in the presence of a contralateral corpus luteum. A comment on the advantages of colour-angio Doppler in the clinical management of this special case of ectopic pregnancy is made in the discussion.
pattern remained basically unchanged. During this period the serum HCG concentrations reached a plateau (12,990–12,470 IU/l). At this time it was decided to administer a single i.m. dose of MTX (100 mg) and hospitalize the patient for one day. On the day of MTX injection the serum HCG concentration was 12,470 IU/l. A complete blood count was carried out and liver and renal functions were monitored before and after the MTX injection. The response to MTX therapy was followed by monitoring serum HCG concentrations on alternate days, and by weekly transvaginal sonographic examination. On a few occasions, a 6 MHz transducer (Esaote, AU-IDEA, Genova, Italy) was also used. On day 4 after the MTX injection, serum HCG concentrations fell to 8400 IU/l, and one week later to 2220 IU/l. By this time (gestational age 73 days) the gestational sac was showing signs of initial resorption concomitantly with a marked reduction of the local vascularization (Figure 3). By day 81 of gestation, the trans-sonic cavity of the sac had disappeared and a mass of variable echodensity with minimal signs of local blood flow remained (Figure 4). Concomitantly, serum HCG concentrations fell to 48.6 IU/l. Finally, on day 97 of gestation, HCG serum concentrations became undetectable (<5 IU/l); this was one day before the patient experienced a full menstrual period. Changes in serum HCG concentrations for the entire duration of this case are shown in Figure 5. The last echographic scan was made at 10 weeks after the MTX injection and showed no indication of any remnants of the ectopic mass; signs of previous vascularization were totally absent. None of the common chemotherapeutic side effects of MTX treatment was ever reported by the patient.

Discussion

Although operative laparoscopy is generally considered as the ‘gold standard’ for treating tubal ectopic pregnancies (Clasen et al., 1997), medical treatment is viewed with increasing interest since it can greatly reduce the morbidity intrinsically related with surgery and anaesthesia. This is particularly important in the case of infertile patients for whom any

Figure 1. Transvaginal sonogram made on day 52 of gestation showing an ectopic pregnancy at the left tubal stump. Note the lateral dislocation of the sac far from the intrauterine mid-line.

Figure 2. Transvaginal colour-angio Doppler images of abundant blood flow at the periphery of the sac and within the placenta. No flow was seen in the embryonic tissue inside the sac.

Figure 3. Day 73 of gestation; transvaginal ultrasonography showed signs of initial resorption. Colour Doppler mapping demonstrated a reduction of local blood flow.

Figure 4. Day 81 of gestation. The internal cavity of the sac had disappeared. Ectopic mass remnants were showing minimal signs of residual vascularization.

Figure 5. Changes in serum HCG concentrations for the entire duration of this case.
avoidance of additional surgical intervention translates into a reduced risk of repeating ectopic pregnancy, in addition to maximal preservation of their future fertility potential. Current evidence suggests that the overall efficacy (tubal patency and pregnancy rate) following conservative laparoscopic surgery does not differ significantly from that observed using systemic MTX therapy (Maymon and Shulman, 1996). Although the latter is considered to be less expensive than operative laparoscopy, and the risk of trophoblastic activity has been shown to persist even after laparoscopy, no final conclusions can be drawn yet to favour one approach over the other, as each has its own benefits and contraindications (Alexander et al., 1996). Outpatient, single-dose intramuscular MTX without leucovorin rescue has long been proposed as a reliable method to treat patients with an unruptured tubal pregnancy <3.5 cm (Slaughter and Grimes, 1995; Stovall et al., 1991).

We agree with the concept that systemic MTX is a valid option when laparoscopy is not required for making diagnosis and the ectopic mass is smaller than 4 cm, when the gestational sac is no longer viable, and when the ectopic pregnancy cannot be safely and easily punctured under echographic guidance (Carson and Buster, 1993). In the present case, all these conditions were satisfied. Medical treatment is particularly emphasized in the case of cornual pregnancy where surgical intervention has intrinsic complications. In fact, surgical intervention for cornual pregnancies requires laparotomy and resection of the uterine horn and is often complicated by diffuse blood loss and inevitable hysterectomy. Treatment of cornual pregnancies with MTX has been attempted either by systemic or local injection or even oral routes of administration, with an overall success rate of 80% (Henderson and Lim, 1994; Hajenius et al., 1996; Timor-Tritsch et al., 1996). It is difficult to attempt strict comparisons since most studies published on cornual pregnancy are heterogeneous with regard to the type of patients described, the diagnostic approach adopted, the MTX dosages and citrovorum rescue used, and the size or viability of the gestational sac reported. In our opinion, there appear to be no clear advantages in using local MTX injections over systemic MTX therapy (Cohen et al., 1996). Moreover, the risk of ectopic rupture and profuse bleeding following needle extraction may always occur, even if potentially safer routes for puncture and injection of cornual pregnancies are used (Timor-Tritsch et al., 1996). Cornual pregnancies occur most frequently subsequent to treatment for assisted reproduction (60%) (Karsdorp et al., 1992; Fernández and Benifla, 1996; Agarwal et al., 1996). In the remaining cases, a history of possible tubal damage is almost universal.

Our patient was definitely at increased risk of another ectopic pregnancy, considering the likelihood of right tubal damage or diffuse pelvic adhesions from previous pelvic and abdominal surgeries. It is well known that after salpingectomy a pathological contralateral tube significantly decreases the chances of intrauterine pregnancy, while increasing the risk of ectopic pregnancy (Dubuisson et al., 1990). This is even more true for nulliparous women (Tuomivaara and Kauppila, 1988).

To speculate upon the mechanisms involved, it is conceivable that following ovulation from the right ovary, an oocyte may have been normally fertilized in the right tube and some days later taken up to the contralateral tubal stump by the intrauterine fluids. Cases of ectopic pregnancies contralateral to unilateral intra-Fallopian gamete and embryo transfers have indeed been reported and may support this speculation (Keeping et al., 1993). Alternatively, it cannot be excluded that an ovum could have transmigrated and passed through a fistula into the tubal stump where successive sperm fertilization and local embryonic nidation occurred. We could find only one study referring to the specific risk of repeating interstitial ectopic pregnancies after salpingectomy (Agarwal et al., 1996). These authors reported seven cornual pregnancies in patients with prior salpingectomy undergoing in-vitro fertilization (IVF) and embryo transfer. Four out of seven cases were treated by MTX, with only one being successful. Interestingly, the other three cases were tubal implantations with one rupture during treatment. We stress that whenever a history of prior salpingectomy is present and at least one normal functioning ovary remains, careful transvaginal ultrasound monitoring should be provided from the early stages. In fact, whether or not ART is scheduled, the chances of an embryo spontaneously implanting at the cornu or at the residual tubal stump are probably higher in such cases. Thickness and blood supply to the myometrium surrounding a cornual sac differ from those to a tubal wall, as well as the risk of rupture and MTX therapy failure in those conditions. In these circumstances the addition of angio and colour Doppler mapping could enhance the prediction about pregnancy development and response to MTX. Notably, we observed a temporal relationship between the degree of vascularization and concomitant serum HCG concentrations. This clinical finding supports experimental evidence of the role played by HCG in vascular function and the neoangiogenesis process (Hill et al., 1997).

It is also known that biologically interdependent processes such as HCG secretion and cytotrophoblast proliferative-cell

Figure 5. Human chorionic gonadotrophin (HCG) concentrations; the gestational sac was visualized by echography on day 52 of gestation. On day 61, a single dose of i.m. methotrexate (MTX) was administered.
activity are inhibited by MTX, which suggests that the process of trophoblast invasion is confined to the mucosal region of the tube (Floridon et al., 1996; Kiss et al., 1997). Altogether, this means that serial serum HCG measurement in conjunction with transvaginal colour Doppler ultrasonography are ideal instruments for simultaneous monitoring of trophoblast cell bioactivity, local spread of implantation, and also the efficacy of MTX therapy. However, this may not always be the case. In fact, when the ectopic pregnancy is located exclusively at the isthmus of the tube, the pattern of trophoblast invasion may differ, and the risk of rupture will be persistently high despite all the criteria for MTX injection being satisfied and HCG concentrations rapidly falling (Kim and de La Vallee, 1997).

Further studies using colour Doppler should address the issue of ectopic pregnancy outcome when the isthmic rather than the interstitial portion of tubal wall is more extensively involved. To this end, additional morphological characterization of these rare ectopic pregnancies could be obtained during laparoscopy and considered in perspective. Unlike the case of tubal pregnancy where endovaginal colour-pulsed Doppler study of blood flow in uterine arteries may improve the accuracy and speed of early diagnosis (Kirchler et al., 1993), in the case of an interstitial pregnancy, early diagnosis is less of a priority since this is usually made by conventional B-mode ultrasound. Adding colour/angio Doppler mapping of local vascularity confers a great advantage when a decision must be made between medical rather than surgical management, as well as for expectant management and/or follow-up of therapy. In the case of a cornual pregnancy, presumably the greater the vascularity, the more effective the MTX, and any drug effect on trophoblasts will be reflected in changes of local vascularization and embryonic biochemistry.

References


Received on October 13, 1997; accepted on March 13, 1998