CASE REPORT

Intrafollicular ovarian pregnancy after ovulation induction/intrauterine insemination: pathophysiological aspects and diagnostic problems

J. Bontis1,2,3, G. Grimbizis1,3, B. C. Tarlatzis1,3, D. Miliaras1,4 and H. Bili1,3

1st and 2nd Departments of Obstetrics and Gynecology, Aristotle University Thessaloniki, 3Infertility and IVF Center and 4Pathology Laboratory, ‘Geniki Kliniki’, Thessaloniki, Greece

Ovarian pregnancy is a rare variant of ectopic implantation. A case of an intrafollicular ovarian pregnancy after ovulation induction/intrauterine insemination is presented. The woman had primary infertility of 4 years. Diagnostic laparoscopy revealed endometriosis and adhesions. After adhesolysis and laser vaporization of endometriotic implants, the patient underwent ovulation induction with artificial insemination by husband/intrauterine insemination; she conceived at her second attempt. The pregnancy proved to be an ovarian intrafollicular one. She was treated by right partial ovariectomy. Three months later she conceived spontaneously with an intrauterine pregnancy which is still ongoing. The diagnostic problems resulting from the coexistence of ovarian hyperstimulation and the intrafollicular development of pregnancy are discussed. A re-evaluation of the criteria for the diagnosis of ovarian pregnancy based on the currently available diagnostic methods is proposed. Moreover, the pathophysiology of ovarian and especially intrafollicular implantation is reviewed.

Key words: ectopic pregnancy/ovarian pregnancy

Introduction

Ovarian pregnancy is a rare variant of ectopic implantation. Its incidence after natural conception ranges from 1 in 7000 to 1 in 60,000 deliveries and accounts for 1–3% of all ectopic gestations (Hallatt, 1982; Crimes et al., 1983). Despite the increased incidence of ectopic pregnancies after assisted conception, ovarian pregnancy is still a rare phenomenon (Marcus and Brinsden, 1993).

Although the early use of quantitative serum β-human chorionic gonadotrophin (HCG) measurements and pelvic ultrasonography increases our diagnostic capabilities in suspected ectopic pregnancies (Raziel et al., 1990), ovarian pregnancy still represents a diagnostic problem (Chelmon et al., 1994). Furthermore, several theories have been suggested in an effort to explain its occurrence either naturally (Tan and Yeo, 1968; Hallatt, 1982; Raziel et al., 1990; Cataldo, 1992) or after in-vitro fertilization (Marcus and Brinsden, 1993).

A case of an intrafollicular primary ovarian pregnancy after ovarian superovulation and artificial insemination by husband/intrauterine insemination (AIH/IUI) is reported. This seems to be a very rare condition, because to our knowledge only one similar case has been reported in the literature (El-Lakany et al., 1985). The diagnostic problems, caused by the intrafollicular development and the coexistence of superovulated ovaries, as well as the pathophysiology of its occurrence, are discussed.

Case report

The patient, aged 31 years, presented in November 1993 with primary infertility of 4 years. Her history was notable for secondary dysmenorrhoea during the last 6 years with increasing severity. The hormonal evaluation was within the normal limits. Hysterosalpingography revealed a normal uterine cavity and patent tubes but with findings suggestive of adhesions. She then underwent a laparoscopy in January 1994 which showed endometriosis (stage II), with superficial endometriotic implants on both ovarian surfaces, uterosacral ligaments, lateral peritoneum and pouch of Douglas. Moreover, filmy adhesions were observed between the ovary and the tubes as well as the lateral peritoneum. Adhesolysis and vaporization of the endometriotic implants with CO2 laser (Sharplan 1060, Laser Industries, Tel-Aviv, Israel) were performed. The woman was then treated with gonadotrophin-releasing hormone analogue for 4 months.

The patient subsequently underwent ovulation induction with AIH/IUI as described previously (Tarlatzis et al., 1991). In the first treatment cycle (January–February 1995) she was administered buserelin (Suprefact; Hoechst AG, Frankfurt Am Main, Germany) and human menopausal gonadotrophin (HMG; Humegon, Organon, Oss, The Netherlands; or Pergonal, Serono, Aubonne, Switzerland) in the long desensitization protocol (Tarlatzis et al., 1993, 1994) and developed three follicles, but no pregnancy ensued. In her second attempt (March 1995) she underwent ovarian stimulation with HMG-FD (Humegon FD; Organon) alone, developing two follicles; after AIH/IUI she conceived. The initial β-HCG serum concentration 14 days after IUI was 11,000 mIU/ml, with a steady increase that reached 32,000 mIU/ml 26 days after IUI. An ultrasound assessment revealed an ‘empty’ uterus, despite the high β-HCG concentrations, whereas the ovaries were found to have large luteal cysts (mild ovarian hyperstimulation). With the possible diagnosis of an ectopic pregnancy, it was...
Figure 1. Chorionic villi (arrowheads) within the cavity of the corpus luteum (arrows). Haematoxylin and eosin stain, original magnification ×25.

Discussion

The histological aspects of ovarian implantation are very interesting and of crucial importance for its pathophysiology. Hallatt (1982) concluded that implantation occurs within the ovary under its capsule but on the corpus luteum. Furthermore, he postulated that it is probably not possible for implantation to occur within an already well developed corpus luteum. On the other hand, Tan and Yeo (1968) proposed that primary ovarian pregnancy could be classified histologically into two distinct forms: intrafollicular and extrafollicular. The intrafollicular type, when large enough, will become partly extrafollicular and even partly extra-ovarian after its rupture. The extrafollicular form includes several histological types such as interstitial, cortical, superficial and juxtafollicular (Tan and Yeo, 1968). Intrafollicular development seems to be extremely rare, and only one of the nine cases reported by Tan and Yeo (1968) was a histologically proven intrafollicular ovarian pregnancy. Our findings, contrary to the suggestions of Hallatt (1982), indicate that implantation can occur within the corpus luteum, in agreement with the histological classification of Tan and Yeo (1968).

Two mechanisms have been proposed to explain ovarian implantation (Cataldo, 1992). One theory suggests that fertilization occurs normally and implantation on the ovary follows reflux of the conceptus from the tube (Crimes et al., 1983). Reverse migration of an embryo towards the Fallopian tube and implantation on the ipsilateral or contralateral ovary are also supported by the occurrence of ovarian pregnancies after in-vitro fertilization and embryo transfer (Marcus and Brinsden, 1993). According to the second theory, various disturbances in ovum release are responsible for ovarian implantation (Tan and Yeo, 1968; Hallatt, 1982). Thus, intrafollicular fertilization may take place following failure of ovum extrusion after follicular rupture (Tan and Yeo, 1968).

Alternatively, fertilization of an extruded ovum which remains adherent to the ovarian stigma may occur, followed by implantation into its own ruptured follicle or into other parts of the ovarian tissue (Tan and Yeo, 1968; Hallatt, 1982). This second mechanism probably better explains the cases of intrafollicular and special categories of extrafollicular pregnancies (interstitial and cortical). Predisposing factors for ovarian implantation are thought to be pelvic inflammatory disease (especially previous oophoritis), as well as the use of an intrauterine device (Tan and Yeo, 1968; Hallatt, 1982; Raziel et al., 1990). Although the endometriosis diagnosed in our patient is not considered to be a predisposing factor (Hallatt, 1982), the possible contribution of defective ovum release due to changes on the ovarian surface cannot be ruled out. In addition, the application of IUI may have pushed some spermatozoa all the way to the tubes or even to the ovarian surface. However, in cases of direct intrafollicular sperm insemination, the injection of sperm cells into the follicle does not seem to increase the risk for ovarian pregnancy, probably because of the unfavourable conditions for fertilization inside the follicle (Nuojua-Huttunen et al., 1995).

Correct pre-operative diagnosis of ovarian pregnancies is quite difficult, and usually they are misdiagnosed as corpus luteum cysts (Tan and Yeo, 1968; Hallatt, 1982; Raziel et al., 1990). The introduction of serum β-HCG measurements as well as the use of early pelvic ultrasonography has increased the diagnostic capabilities in cases of ectopic implantation.
Thus, the ultrasound assessment, especially with a vaginal probe, showing an 'empty' uterus in the presence of β-HCG concentrations above the 'discriminatory zone' (Romero et al., 1985), is highly suggestive of ectopic implantation. Moreover, the existence of a thick-walled cystic mass in the ovary showing internal echoes with or without fetal heart motion during vaginal ultrasound scanning probably indicates an ovarian pregnancy (Marcus and Brinsden, 1993). Marcus and Brinsden (1993) reported that the diagnosis of ectopic pregnancy using transvaginal ultrasound scanning was correctly made in all the described cases, and in five out of seven of them the diagnosis of ovarian gestation was suspected from findings in the ovary. In cases of an unknown site of ectopic implantation, the diagnosis is usually confirmed by laparoscopy. However, in our case there were additional diagnostic problems. The intrafollicular development of the ovarian pregnancy was combined with the existence of luteal cysts in the superovulated ovaries, making the diagnosis extremely difficult.

Whichever approach is used in the treatment of ovarian pregnancy, the conservation of ovarian tissue is essential, given that in most cases these are infertile patients (Marcus and Brinsden, 1993). The preferred therapeutic procedure is partial ovariecotmy (ovarian wedge resection), including the site of the ectopic implantation, or ovarian cystectomy. It seems that despite the increased vascularity of the ovarian tissue, the risk of uncontrollable haemorrhage is minimal and the patients usually exhibit an uneventful recovery (Raziel et al., 1990; Marcus and Brinsden, 1993). In our case, a partial right ovariecotmy was applied, removing the section of the ovarian tissue containing the bruised and haemorrhagic cyst. The patient experienced an uneventful postoperative course.

Therefore, in cases of superovulated ovaries the diagnosis of an ovarian pregnancy, especially of the intrafollicular type, can be based on the following criteria: (i) a positive serum β-HCG test; (ii) an ultrasound assessment revealing an ‘empty’ uterus in the presence of β-HCG concentrations above the ‘discriminatory zone’ or serum β-HCG concentrations not declining after curettage; (ii) intact Fallopian tubes and no indication of pregnancy in the peritoneal cavity after a thorough investigation; (iv) a gestational sac located on the surface of the ovary or indicating intrafollicular implantation by alterations in the appearance of the corpus luteum; (vi) serum β-HCG concentrations declining after surgical excision or medical treatment; and (vii) the histological identification of ovarian tissue in the sac wall after surgical or laparoscopic excision. This diagnostic approach is based on the initial criteria proposed by Spiegelberg (1878), with the addition of the currently available new diagnostic modalities, as has also been suggested by other investigators (Chelhom et al., 1994).

In conclusion, the histological data from this case report support the view that implantation within the corpus luteum can occur. The coexistence of ovarian hyperstimulation with the intrafollicular development of an ovarian pregnancy poses additional diagnostic problems. A re-evaluation of the diagnostic criteria for ovarian gestation is proposed based on the currently available new diagnostic modalities.

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