LETTERS TO THE EDITOR

Delivery of twins following heterotopic grafting of frozen-thawed ovarian tissue

Sir,
We have recently published a case report in your journal (Stern et al., 2013) describing the first reported clinical pregnancy following heterotopic grafting of cryopreserved ovarian tissue in a woman after a bilateral oophorectomy. At the time of writing the article the patient had a 26-week intrauterine twin pregnancy and we would like to provide an update on the outcome of this pregnancy.

As described, the patient had undergone oophorectomy for a granulosa cell tumour 9 years previously followed by prophylactic removal of the remaining ovary and subsequent ovarian tissue cryopreservation. After repeated assessments revealed no tumour recurrence, and no evidence of tumour in the stored tissue, she had frozen-thawed ovarian tissue grafted to the anterior abdominal wall on two occasions. There was no evidence of tumour seen at either laparoscopy. The patient underwent low-dose stimulation and in vitro fertilization resulting in two embryos which were transferred. Her pregnancy proceeded eventfully apart from a brief admission at 26 weeks for threatened preterm labour and a shortened cervix, which remained stable. The patient subsequently had an elective lower segment Caesarean section at 37 weeks and delivered two healthy girls weighing 3320 and 3262 g.

At operation there was macroscopic evidence of tumour involving the diaphragm and a peritoneal deposit at the left pelvic brim. There was no evidence of tumour in the graft sites. All macroscopic tumour was resected and histology confirmed granulosa cell tumour.

Recurrent tumour development could be directly related to grafting of ovarian tissue. It could also be due to a recurrence of peritoneal deposits precipitated by the hormonal environment provided by a pregnancy, in a tumour known to be sensitive to hormonal stimulation. Whilst the absence of tumour extraperitoneally at or near the graft sites might support hormonal reactivation, we cannot exclude the possibility that tumour recurrence resulted from the grafted tissue. The patient will commence hormonal suppression with an aromatase inhibitor once breastfeeding is discontinued and a further laparoscopy is planned.

While the prognosis for this patient remains excellent, this unfortunate outcome serves to remind us of the possibility of tumour cell transmission with grafting despite comprehensive prior histological and biochemical assessment.

The danger of ignoring pregnancy and delivery rates in ART

Sir,
We were primarily attracted to the recent paper by De Neubourg et al. (2013) because its subtitle states: ‘A case study in reducing the incidence of multiple pregnancies’. A simple presentation of the Belgian historical assisted reproductive technology (ART) experience would have been surprising but, likely, would not have initiated this letter. The effort to present the Belgian experience as a successful example of reducing multiple pregnancies, however, mandates a response.

Belgium is probably the first country where colleagues and government made, what we consider a Faustian bargain, by mandating single embryo transfer (SET) for large percentages of infertile women undergoing ART in return for government coverage of ART expenses. Other countries have followed (Bissonnette et al., 2011) and Stillman et al. (2013) recently even suggested that such agreements further validate the wide utilization of SET.

We do not think so, and the various reasons for our opposition to the broad utilization of SET have been noted (Gleicher and Barad, 2006, 2008, 2009, 2013; Gleicher, 2011, 2013a,b). A single quote from the abstract of De Neubourg’s paper makes here our point when the authors state that: ‘Over 20 years of registration, the pregnancy rate has remained constant, despite the reduction in number of embryos transferred, optimization of laboratory procedures and stimulation protocols, introduction of quality systems and implementation of the EU Tissue Directive over the period 2004–2010’.

Viewing this statement from the other side of the Atlantic, one has to ask how Belgian colleagues can accept such a static performance level without comments; indeed, one has to ask how physician and patient communities alike are not up in arms looking at these results?

As this revealing paper demonstrates, delivery rates per retrieval in Belgium between 2004 and 2010 fluctuated for fresh cycles between 17 and 21%. For the same years, data from the national registry maintained by the society for ART demonstrate in the USA live birth rates of 30.9–33.2%. Maybe even more interesting, the Belgian data demonstrate delivery rates of 9.5–12.7% during these years for thawed cycles, while USA rates in the same time period were 27.8–33.9%.

Reference