CASE REPORT

Ovarian hyperstimulation syndrome and benign intracranial hypertension in pregnancy after in-vitro fertilization and embryo transfer

P.Lesny1,3, S.D.Maguiness1,3, D.M.Hay3, J.Robinson2,3, C.E.Clarke4 and S.R.Killick1,3

1Academic Department of Obstetrics and Gynaecology, 2Department of Biological Sciences, The University of Hull, 3The Hull IVF Unit, The Princess Royal Hospital and 4Department of Neurology, Royal Hull Hospitals, Hull, UK

Ovarian hyperstimulation syndrome (OHSS) is a dangerous and sometimes life-threatening complication of ovulation induction with exogenous gonadotrophins. While many complications of severe OHSS are recognized we have only identified one review detailing neurological problems. This report concerns a 32-year-old patient with bilateral tubal blockage who achieved her first pregnancy following in-vitro fertilization (IVF) and embryo transfer. Shortly after embryo transfer she developed clinical signs of moderate OHSS with symptoms which were later diagnosed as benign intracranial hypertension (BIH). The BIH was treated effectively using repeated lumbar puncture and diuretics. Spontaneous labour and delivery occurred at 40 weeks’ gestation. There was no neurological sequel and no recurrence of the BIH 2 years after the pregnancy. The possible link between OHSS and BIH is discussed as well as the risks of further pregnancy.

Key words: benign intracranial hypertension/in-vitro fertilization and embryo transfer/ovarian hyperstimulation syndrome

Introduction

Benign intracranial hypertension (BIH), also known as idiopathic intracranial hypertension or pseudotumor cerebri, has an incidence of 0.8–1.7 per 100 000 in the general population. The incidence is higher in obese women of child bearing age (19–24 per 100 000). It can also be precipitated by normal pregnancy, steroid hormones and certain antibiotics. There is a recurrence risk of 10%, sometimes more than once, and a risk of permanent visual impairment of 10% (Corbett, 1995). It is not possible to predict how the disease will affect individual cases, and considerable debate surrounds its management (Corbett, 1995). We report what we believe is the first case of BIH associated with ovarian hyperstimulation syndrome (OHSS) in a pregnancy conceived after in-vitro fertilization (IVF) and embryo transfer.

Case report

A 32 year old woman with primary subfertility, due to bilateral tubal blockage, was referred for assisted conception treatment. She had no relevant past medical history, her body mass index was 20.6 kg/m2 and all routine endocrine investigations were within normal limits.

Ovulation induction for IVF was achieved using pituitary down-regulation with a gonadotrophin-releasing hormone analogue (goserelin; Zeneca Pharmaceuticals Ltd, Macclesfield, UK) administered in the mid-luteal phase, followed by 150 IU of follicle stimulating hormone (Metrodin High Purity®; Serono Laboratories UK Ltd, Welwyn Garden City, UK) for 11 days. The cycle was monitored by vaginal ultrasound. Human chorionic gonadotrophin (HCG, Profasi®; Serono Laboratories UK) 10 000 IU was administered i.m. when the lead follicle had a diameter of 20 mm. Vaginal oocyte retrieval was carried out 36 h later. Nineteen follicles were aspirated and 16 eggs were collected, of which 13 fertilized. After 2 days three embryos of good quality were transferred and 10 embryos were cryopreserved. Luteal phase support was provided using vaginal micronized progesterone (Utrogestan®; Besins Iscovesco Laboratories, Paris, France) in a dose of 600 mg at night commencing on the day of oocyte retrieval.

A week later the patient developed symptoms of OHSS, based on the ultrasound presence of ascites and more pronounced clinical symptoms, which was categorized as mild (Golan et al., 1989) and was managed on an outpatient basis. She required hospitalization 12 days after embryo transfer because of vomiting, headache, abdominal distension and decreasing urinary output. Examination confirmed that there had been a significant increase in both her weight (from 44 to 47 kg) and abdominal girth measurement (from 79 to 86 cm). Ultrasound assessment revealed a right ovary of 7.6×9.5×9.6 cm and left ovary of 4.6×4.4×6.1 cm with a moderate amount of fluid in the upper abdomen, and around the liver and spleen. Fundoscopy showed minimal blurring of the optic discs. Serum investigations revealed no evidence of haemoconcentration, a normal biochemical profile and clotting screen. The serum βHCG was 51 IU/l. A diagnosis of early pregnancy complicated by moderate OHSS was made.

Management consisted of analgesics, antiemetics and i.v. crystalloids with careful clinical and laboratory monitoring. The headache initially improved but after 6 days it became more intense and was accompanied by diplopia, vomiting and confusion. Fundoscopy revealed papilloedema but there were no other abnormal neurological signs. Serum investigations
revealed low albumin concentrations (30 g/l) and βHCG of 214 IU/l. After an i.v. infusion of 300 ml of 20% human albumin solution (3 × 100 ml over 4 h) the confusion and vomiting quickly settled but the headache persisted. Laboratory investigations were within the normal range, with serum albumin reaching 49 g/l. The patient was therefore transferred to the Department of Neurology, Hull Royal Infirmary, Hull. Computerized tomography (CT) showed no abnormalities. Lumbar puncture revealed an elevated cerebrospinal fluid (CSF) pressure of 34 cm H2O. All other parameters measured in the CSF were normal so a diagnosis of benign intracranial hypertension (BIH) was made. The patient’s symptoms improved dramatically after the lumbar puncture and she was discharged home 4 days later taking an oral diuretic (furosemide, Lasix, Borg Medicare, Hitchin, UK, 40 mg daily).

During the pregnancy, the patient was reviewed regularly by the neurologist and 10 subsequent lumbar punctures were performed to monitor and reduce the CSF pressure which stabilized as the pregnancy progressed (Table I). The papilloedema gradually settled with only blurred medial margins at 34 weeks’ gestation. Visual acuity was not affected throughout pregnancy. The fundi appeared normal 8 weeks post-partum. The pregnancy itself was uneventful and after spontaneous labour at term she delivered a healthy boy weighing 3440 g. During labour analgesia was provided with N2O/O2 and opioids.

Two years later a frozen embryo transfer was carried out in a hormonal replacement cycle. Pituitary down-regulation was the same as described above and was followed by oestradiol valerate (Climaval®, Navartis Pharmaceuticals, Camberley, UK) 8 mg orally from the first day of menstrual bleeding until the endometrial thickness reached 10 mm. Then, oestradiol valerate was continued in a dose of 10 mg daily. Luteal support was provided by vaginal micronized progesterone (Utrogestan®; Besins Iscovesco Laboratories, Paris, France) in a dose of 600 mg at night commencing 2 days before transfer. Sadly, this treatment was unsuccessful. There are no more embryos in storage. This patient’s expectations of her family size are unfulfilled and she may seek further treatment.

Table I. Monitoring of cerebrospinal fluid (CSF) pressure throughout pregnancy

<table>
<thead>
<tr>
<th>Week of pregnancy</th>
<th>CSF pressure (mm H2O)</th>
<th>Volume drained (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>26</td>
<td>10</td>
</tr>
<tr>
<td>9b</td>
<td>18</td>
<td>8</td>
</tr>
<tr>
<td>12</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>15</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>19</td>
<td>23</td>
<td>8</td>
</tr>
<tr>
<td>22</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>26</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>30</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td>34</td>
<td>20</td>
<td>6</td>
</tr>
</tbody>
</table>

As in-patient.

Diuretics discontinued.

Discussion

We report what we believe is the first case of BIH associated with OHSS in a pregnancy conceived after IVF and embryo transfer. Despite its name, this condition is not benign and should be treated seriously.

BIH is diagnosed by exclusion and depends on the finding of papilloedema and a normal neurological examination except for evidence of visual loss or lateral rectus muscle palsy. It is also associated with a raised CSF pressure but a normal CT or magnetic resonance image (Smith, 1985; Wall and George, 1991). This patient fulfilled the above criteria. The major differential diagnosis which we considered was a cerebrovascular accident because of its known association with OHSS (Rizk et al., 1990).

There is agreement that obesity is a predisposing factor especially among pregnant women. However, the body mass index of this patient was only 20.6 kg/m2. Hormone changes in pregnancy, oral contraception and menstrual irregularities are cited among causative factors of BIH (Corbett, 1995) but this opinion is not unanimous (Digre et al., 1984). The onset of BIH in this case occurred very early in the pregnancy and was associated with a clinical picture of OHSS. Increased capillary permeability and new capillary formation, possibly secondary to activation of the pro-renin/renin system, increased prostaglandin synthesis, histamine and serotonin, are the main physiological features of OHSS (Ong et al., 1991; Bergh and Navot, 1992). More recently, interleukin-6 and vascular endothelial growth factor have been implicated as aetiological factors in OHSS (Friedlander et al., 1993; McClure et al., 1994). It is also recognized that the severity of OHSS is positively correlated with plasma renin activity (Navot et al., 1992). It has already been established (Yarali et al., 1993) that ascites is produced in OHSS despite isolation of the ovaries from the peritoneal cavity, supporting the role of factors released into the systemic circulation. Isolated acute unilateral pleural effusion as a presentation of OHSS has been reported twice (Kingsland et al., 1989; Wood et al., 1998), which suggests the possibility of an altered response in the individual organ. In our case these mediators may have affected the production/resorption of CSF. In view of the protective effect of the blood–brain barrier we believe that the BIH in this case may have occurred because of changes in local mediators.

Our patient responded very well to lumbar puncture, which in an acute stage was both diagnostic and therapeutic. If we had expected OHSS in this case we could have considered i.v. human albumin infusion at the time of oocyte retrieval. More recently hydroxyethyl starch solution has been used with good effect (Graf et al., 1997). The use of diuretics, particularly in the second half of pregnancy, is controversial because of the potential to decrease placental blood flow related to a decreased circulating blood flow. Other options for treatment would have been use of carbonic anhydrase inhibitors or steroids (Corbett, 1995; De Swiet, 1995). In this case visual fields and acuity were not affected. If they are then surgical intervention in the form of either a lumboperitoneal shunt (Johnson et al., 1981), optic nerve fenestration or decompression (Brouerman, 1988; Sergott et al., 1988) may be carried out. The possibility of a
request for an epidural in labour had been considered and would have been given if requested by the patient.

It has been suggested that subsequent spontaneous pregnancy does not increase the risk of recurrence of BIH above that in the general population (Digre et al., 1984). The dilemma facing us is that, if this patient were to have a further treatment cycle in which ovarian stimulation was used, would a recurrence of OHSS put her at an increased risk of BIH, exposing her to the dangers of its complications? It is not known whether we should recommend IVF/embryo transfer in a natural cycle if a further treatment cycle is requested.

References


Received on January 13, 1999; accepted on May 13, 1999