Severe ovarian hyperstimulation after follicular aspiration

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Summary

In order to maximise the chances of pregnancy, most successful *in vitro* fertilisation programmes use a combination of ovulation induction agents. This treatment can lead to the hyperstimulation syndrome. Aspiration of the follicles is believed to avoid this syndrome. Despite this approach, hyperstimulation syndrome may still develop. The clinical picture and treatment of a patient with severe hyperstimulation is discussed.

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In order to maximise the chances of pregnancy most successful *in vitro* fertilisation (IVF) programmes use a combination of ovulation induction agents. This modifies the normal spontaneous menstrual cycle enabling recovery of several preovulatory oocytes.[1] Plasma oestradiol, ultrasonography and urinary oestradiol glucoronide are used as predictors of ovarian hyperstimulation during induction of ovulation. Aspiration of the follicles is believed to avoid hyperstimulation syndrome. Only one previous report of severe hyperstimulation syndrome after IVF, in which all visible follicles were aspirated,[2] could be traced.

Case report

Laparoscopy and hysterosalpingography confirmed the diagnosis of bilateral hydrosalpinges caused by previous pelvic infection in a 28-year-old gravida 3, para 1, patient. She was ovulating regularly, with a 30-day menstrual cycle. Screening tests for tuberculosis, mycoplasma, syphilis and gonorrhoea were negative.

The patient's first pregnancy, in a previous marriage, resulted in a normal vertex delivery of a live infant. The second pregnancy occurred after the first attempt at IVF. Superovulation was induced with 100 mg clomiphene citrate. Serum oestradiol reached a peak value of 9 535 pmol/l on the day of human chorionic gonadotrophin (HCG) administration. Eight oocytes were obtained and 3 embryos were transferred. This resulted in an ultrasonographically proven pregnancy, which unfortunately ended in an incomplete abortion at 11 weeks' gestation. An evacuation was performed.

Since the regimen for induction of ovulation at this institution had subsequently been changed, the next attempt at IVF was induced by a combination of clomiphene citrate and human menopausal gonadotrophin (HMG) starting on day 5 of the cycle. HMG 150 IU was administered on days 6, 8 and 10 of the cycle. Thereafter, HMG 150 IU was administered daily for 7 days until the leading follicle had reached an ultrasonographic average diameter of 14 mm. During cycle day 17, the leading follicle had reached an average diameter of 18 mm. HCG 10 000 IU was administered.

At laparoscopy 36 hours after the HCG administration, 19 follicles were aspirated and 14 mature oocytes were obtained. The ova were then inseminated with the husband's semen. Forty-three hours after insemination a 4-cell, 5-cell and two 8-cell embryos were transferred into the uterus. Eleven days after embryo transfer the patient was readmitted to hospital with a 3-day history of epigastric discomfort and abdominal pain. She had been vomiting since the previous day. On examination her abdomen was markedly distended with ascites and there was oedema of the legs. This became worse during the next few days. The blood pressure, however, remained constant at 120/70 mmHg.

Laboratory investigations revealed: haemoglobin concentration 13 g/dl; haematocrit 48%; normal electrolytes with urea 4,6 mmol/l rising to 5,4 mmol/l the morning after admission. The β-subunit of HCG on day 10 after embryo replacement was 27,3 U/l and 30,3 U/l on day 17. Pelvic ultrasonography showed enlarged ovaries 8 cm in diameter and ascites. Blood coagulation studies were within the normal range.

The diagnosis was severe ovarian hyperstimulation grade 6.[3]

Treatment

An intravenous line and a subclavian central venous pressure catheter were inserted. The intake and output were monitored. An iso-oncotic solution of plasma proteins (50 g/l) as stabilised human serum (SHS) was infused at a rate of 1 l/24 h. Intravenous furosemide was given to promote diuresis. The central venous pressure was maintained in the 5 - 10 cm water range. Pethidine was given for pain relief. Naproxen 250 mg 4 times daily was administered. The patient responded very well on this treatment. The ascites, oedema and follicle enlargement subsided over the next 8 days. On the 10th day after readmission the patient was discharged. At term she was delivered of a 3 480 g normal healthy female baby.

Discussion

In a series of 487 cycles, using the same stimulation regimen, this was the only case of severe ovarian hyperstimulation despite markedly elevated oestradiol levels and an abundance of mature follicles in many other cases. This can most probably be ascribed to the fact that follicular aspiration appears to be an effective means of avoiding the ovarian hyperstimulation syndrome.[2] Plasma oestradiol level is used as a predictor of ovarian hyperstimulation by some workers.[4] Although in this patient the oestradiol value in the first IVF cycle was higher at the stage of HCG administration than in the second attempt, the ovarian hyperstimulation syndrome did not develop in the first cycle. In the second IVF attempt the patient also received HMG. This may have been an important factor in the precipitation of the ovarian hyperstimulation syndrome. The fact that the patient had regular ovulation cycles before the administration of clomiphene citrate and HMG perhaps placed her at greater risk for the development of the hyperstimulation syndrome.[5]

The most important clinical signs in cases of ovarian hyperstimulation syndrome are massive ovarian enlargement

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accompanied by varying degrees of acute body fluid shift with ascites formation, pleural effusion and sometimes even anasarca. The reason for increased capillary permeability, which is the cause of the sudden body fluid shifts, is unknown.[6] Prostaglandins cause increased vascular permeability by inducing vascular leakage at the postcapillary and collecting venules.[6] In order to counteract this, an antiprostaglandin, naproxen, was administered. The use of indomethacin for this purpose is recommended by Katz *et al.*[7] The absence of teratogenic effects of these drugs is, however, not proven beyond all doubt.

According to Starling,[8] the plasma proteins maintain the colloid osmotic pressure and promote the absorption of water from the extravascular compartment into the intravascular space. Albumin infusions maintain normal colloid osmotic pressure and thus replace and maintain the plasma volume adequately.[9] In this patient albumin was supplemented in the form of SHS. The administration of SHS resulted in a rise of central venous pressure and lowering of the haematocrit indicating expansion of the intravascular volume. Furosemide can then be administered.

In conclusion, aspirating all visible follicles does not exclude the possibility of the ovarian hyperstimulation syndrome. A high level of oestradiol is not indicative of possible development of the syndrome. Plasma protein infusions and diuretics are useful in the treatment of these patients.

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'n Moderne psigiatriese gemeenskapsdiens in die Oranje-Vrystaat

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Summary

The number of patients with psychiatric syndromes in the community may be as high as 15% at any time. The concept of institutionalisation has gradually changed to the concept of community psychiatry. The main aim of community psychiatric service is to treat the patient in the community. Such a service should be within reach of all the patients in the community.

A psychiatric community service has been developed in the Orange Free State over the past 2 years. This has resulted in a reduction of 48% in the chemotherapy budget. Comparing the results with a similar study in Stockholm the reduction of 19% in neuroclinic admissions in Oranje Hospital compares favourably with the 22% reduction in Stockholm. The increase of 90% in the outpatient numbers for the Orange Free State is below the 170% increase reported for Stockholm. A further increase can be expected within the next few years in the Orange Free State.

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Psigiatriese versteurings kom algemeen voor. Ongeveer 15% van die Amerikaanse bevolking vereis op enige gegewe tydstip behandeling vir psigiatriese probleme.[1] Sekere psigiatriese sindrome soos skisofrenie toon moontlik 'n afname in voorkoms.[2] Ander psigiatriese versteurings, soos depressie, toon egter 'n toename in voorkoms.[3] Sommige skrywers rapporteer dat die voorkoms van psigiatriese versteurings in ontwikkelende lande nie verskil van dié in ontwikkelde lande nie.[2,4-7]

Tendense

Psigiatriese behandeling het die afgelope 15-20 jaar veranderings ondergaan en die pendulum het geswaai van institu-