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SHORT COMMUNICATION

Case report

Central retinal artery occlusion associated with severe ovarian hyperstimulation syndrome

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PURPOSE. *Ovarian hyperstimulation syndrome (OHSS) is a serious iatrogenic complication of ovulation induction. It is a potentially lethal condition, with severe complications which include ovarian enlargement, and massive fluid redistribution from the vascular system into free spaces resulting in ascites, pleural effusion, electrolyte imbalance, hemoconcentration, hypovolemia, oliguria, and adult respiratory distress syndrome. Thromboembolism is a rare but extremely serious complication.*
CASE REPORT. *We report a case of severe OHSS, presenting with central retinal artery occlusion (CRAO).*
DISCUSSION. *This combination has not been reported previously. (Eur J Ophthalmol 2001; 11: 313-5)*

KEY WORDS. *Ovulation induction, Ovarian hyperstimulation syndrome, Retinal artery occlusion*

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INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) is the most serious complication of induction of ovulation. Its incidence has increased with the use of gonadotrophin-releasing hormone analogues. The human chorionic gonadotrophin used to induce ovulation and to support the corpus luteum phase, and the endogenous human chorionic gonadotrophin that results from conception both seem to play a central role in the development of OHSS (1). Severe OHSS is rare (1-2%) (2) but potentially life-threatening, with serious complications that include ovarian enlargement, ascites, pleural effusions, renal insufficiency, adult respiratory distress syndrome, intravascular hypovolemia, hemoconcentration, electrolyte disturbance, liver dysfunction, thromboembolism, and death (3).

The incidence of thromboembolic disease associated with OHSS is extremely low: the syndrome was present in about 80% of the reported cases of thromboembolic complications after ovarian stimulation (1). The majority were on the venous side (75%), 60% in the upper limbs, neck and head veins. The other 25% were arterial, mostly intracerebral (4).

This report describes a case of severe OHSS complicated by central retinal artery occlusion (CRAO), and popliteal artery thrombosis. To the best of our knowledge, CRAO with irreversible visual impairment has not been previously reported in association with OHSS.

Case Report

A 34-year-old woman with a three-year history of anovulatory primary infertility was referred with the diagnosis of severe ovarian hyperstimulation syndrome (OHSS), and acute loss of vision in her left eye. During her last menstrual cycle she had received 150 IU human menopausal gonadotrophin (Pergonal; Serono, Aubonne, Switzerland) daily for ten days starting on the fourth day of her cycle, and 10000 IU of human chorionic gonadotrophin (Pregnyl; Organon, Cambridge, UK) on day 15 (12 days prior to admission). Preovulatory levels of estradiol and the number and size of follicles were not stated in the referral letter. She had no personal or family history of thromboembolism.

At admission, the patient complained of sudden loss

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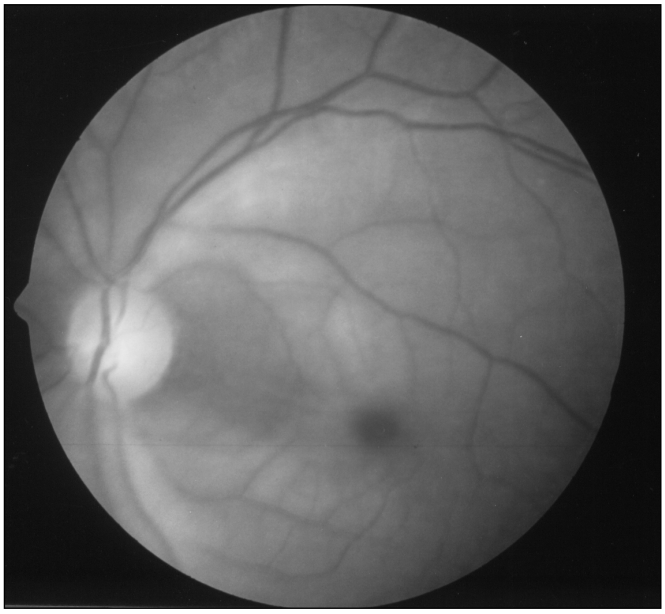

Fig. 1 - *Fundus photograph of the left eye showing ischemic retinal whitening.*

of vision in the left eye, abdominal pain and distension, and pain in the right lower limb. She was dehydrated, with a temperature of 36.8°C, pulse 85 beats per minute, blood pressure 100/60 mmHg, and respiratory rate 22 per minute. Her abdomen was tender, tense and markedly distended, with tense ascites. Chest examination was normal. Examination of both lower limbs revealed no redness or swelling. Abdominal ultrasound showed bilateral multicystic ovaries measuring 23 x 17 cm on the left and 18 x 21 cm on the right, with marked ascites.

The patient underwent bedside ophthalmic examination. Visual acuity was 20/20 in the right eye and hand motions in the left eye. There was a 3+ relative afferent pupillary defect in the left eye. The right fundus appeared normal. Ophthalmoscopy of the left eye revealed diffuse ischemic retinal whitening, and a cherry-red spot consistent with central retinal artery occlusion. No emboli were seen (Fig. 1). A hand-held Kowa fundus camera was used for color photodocumentation. Doppler flow examination of both lower limbs showed no evidence of deep venous thrombosis, but there was marked reduction in the right popliteal artery flow. The ankle brachial index (ABI) was 0.67 in the right leg and 0.98 in the left leg (normal >0.96). These findings were associated with claudication pain in the right leg which suggested recent arterial thrombosis.

Laboratory tests showed an elevated hematocrit and white blood cell count and low serum albumin. Electrolytes, creatinine, urea, cardiac enzymes and arterial blood gases were within the normal range. Chest x-ray and echocardiography gave normal results. Thrombophilia screening (protein C, protein S, antithrombin III, activated protein C resistance, anticardiolipin antibodies, lupus anticoagulants, and homocysteine) was negative.

The patient was treated with intense intravenous fluid management with crystalloid, intravenous heparin 40000 IU every 24 h, and 25% albumin. Serum electrolytes and hematocrit were monitored closely and adjusted. Abdominal ultrasound-guided paracentesis was performed on the third day of admission and 2.8 liters of ascitic fluid were removed. A pregnancy test was positive on the fourth day and pelvic transvaginal ultrasound on day 14 showed two fetal sacs with fetal heart beats. Her general condition improved gradually, and she was maintained on subcutaneous 10000 IU heparin twice daily. Serial ultrasonographic examinations showed a progressive reduction in the size of both ovarian cysts, and normal growth of both fetuses. She had preterm labour at 36 weeks and delivered normal twins weighing 2.1 and 2.4 kg, by cesarean section.

Postnatal Doppler examination of the right leg (eight months after initial presentation) showed improvement in blood flow (ABI 0.87). One year after initial presentation, visual acuity was still hand motions in the left eye. The optic nerve head was pale and the retinal arterioles were attenuated.

DISCUSSION

This report describes a case of severe OHSS complicated by CRAO and popliteal artery thrombosis. Arterial thromboembolism is a rare complication of OHSS. In 1997, Stewart and associates (4) reviewed 15 cases reported in the world literature. Three additional cases have been described (5, 6) since then, bringing the total to 18. Most of these occlusions are characterized by their position in an upper limb or in the cerebral territory. The case reported here was unusual in that the occlusion occurred in the central retinal artery, 12 days after administration of human chorionic gonadotrophin. Arterial and venous thrombosis

may have different pathogeneses as their timing appears to differ. Stewart et al found that arterial thrombosis appears much earlier than venous thrombosis. The mean times of occurrence of arterial and venous thromboses were respectively 14 and 38 days after human chorionic gonadotrophin (4).

The etiology of OHSS-associated thromboembolic complications remains unclear. Hemoconcentration during OHSS changes blood viscosity, promoting stasis, and this, combined with immobility, may put the patient at risk for thrombosis. Hyperestrogenism may induce a hypercoagulable state by increasing the activities of several coagulation factors and lowering antithrombin III, as well as fibrinolysis. The possibility of endothelial damage by activated polymorphonuclear leukocytes as a result of stress-induced leukocytosis in OHSS was also suggested (4). After induction of ovulation with human chorionic gonadotrophin, fibrinogen, factors II, V, VIII, and IX were elevated, even though serum estradiol was halved. There is clinical evidence that estrogens are not directly responsible for the biochemical changes that lead to OHSS and to hypercoagulability (1). Therefore, human chorionic gonadotrophin presumably plays a central role in these two conditions (1). Screening for thrombophilia was done in only the most recent cases. Activated protein C resistance, antithrombin III deficiency, antiphospholipid antibodies, and reduction in protein S concentration were reported in patients with thromboembolic disease after ovarian stimulation (4). In our case, thrombophilia tests were negative.

Based on the pathophysiological changes of OHSS, the goal of therapy is to reinstitute the physiological osmolarity in the vascular system. Substitution with fresh-frozen plasma might seem the most appropriate therapy, because it increases the intravascular oncotic pressure and, by substituting coagulation factors, promotes the restoration of the hemostatic balance. However, human albumin is more suitable: in different concentrations, it is more readily available than fresh-frozen plasma; it raises oncotic pressure more effectively; and there is no danger of transmitting viral diseases. In addition, a crystalloid liquid-like isotonic and NaCl solution should be employed (1). Prophylactic heparin may be proposed in women with associated risk factors such as personal or familial thromboembolic events, obesity, diabetes, smoking and vascular abnormality, and in cases of severe OHSS (4, 6-8).

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