CASE REPORT

Cerebral venous thrombosis secondary to ovarian hyperstimulation syndrome

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We report a case of a woman who underwent in-vitro fertilisation embryo transfer treatment for infertility and developed an acute stroke (left hemiparesis and headache). The stroke was caused by cerebral venous thrombosis due to ovarian hyperstimulation syndrome. We review the current background about this uncommon disorder.

Introduction

Ovarian hyperstimulation syndrome (OHSS) is a rare complication of ovarian stimulation. Overproduction of ovarian hormones and vasoactive substances causes an increase in capillary membrane permeability and acute third-space fluid loss; consequential intravascular volume depletion and haemoconcentration can lead to thromboembolism and death. We describe a woman who developed cerebral venous thrombosis as the presenting feature of OHSS.

Case report

A 42-year-old right-handed woman presented with headache and left-sided weakness of acute onset. She was a non-smoker and had been well before the admission, with no risk factors for stroke and no history of polycystic ovary syndrome. She had been undergoing in-vitro fertilisation (IVF) embryo transfer treatment for secondary infertility. Neurological examination showed intact consciousness with normal vision, sensation and language function, and a left-sided hemiparesis. Plain cranial computed tomography showed an infarct in the right frontal region, and magnetic resonance imaging performed on the next day demonstrated the right frontal infarct as well as thrombosis of the superior sagittal sinus and right cortical veins (Figs 1 and 2). In view of the diagnosis of cerebral venous thrombosis, she was treated with low-molecular-weight heparin, nadroparin, subcutaneously twice daily. By this time we had obtained details of the IVF treatment protocol from the gynaecologist. The patient had been given recombinant follicular stimulating hormone 450 IU daily for 10 days, with gonadotropin-releasing hormone agonist and luteinising hormone added on day 7. The oestradiol level checked on day 9 was 9607 pmol/L (reference level, <10 000 pmol/L) and she was classified as low risk for OHSS. Ten follicles were retrieved, and six mature oocytes and three grade I embryos were transferred back. The luteal phase was supported by per-vaginal progesterone and intramuscular human chorionic gonadotropin (HCG) 1500 IU on days 15 and 18. The patient's neurological symptoms began 1 day after receiving the second dose of HCG. Initial laboratory studies on this admission to our hospital showed no evidence of haemoconcentration with a normal haemoglobin level of 139 g/L (reference range, 115-143 g/L) and haematocrit level of 0.40 (0.32-0.43). Abdominal ultrasound on admission revealed moderately enlarged ovaries (up to 7 cm each in diameter) and a small amount of ascitic fluid. Five days after her admission, she developed marked ascites and oliguria. The haematocrit level had risen to 0.44, and the serum creatinine level rose to 85 g/L (reference range, 44-80 g/L); haemoglobin level was 148 g/L and the pregnancy test was positive. She was treated with intravenous fluid replacement for severe OHSS; her condition improved gradually and 1 week later she was discharged with no residual weakness. Five weeks after her admission, ultrasound showed absence of fetal heartbeat and an evacuation was subsequently performed. After completion of a 3-month course of nadroparin, the prothrombophilia screen (clotting profile, lupus anticoagulant, homocysteine level, proteins C and S) was normal.

Discussion

Ovarian hyperstimulation syndrome is a serious complication of ovulation induction; the incidence of the severe form ranges from 0.5 to 5% of stimulated ovarian cycles.[1] Age of less than 35 years, low body mass index, a history of allergies, and associated polycystic

Key words
Cerebral infarction; Chorionic gonadotropin; Ovarian hyperstimulation syndrome; Ovulation induction

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卵巢過度刺激綜合徵併發腦靜脈栓塞

本文報告一名女子因不育接受體外受精胚胎移植，卻出現左半身癱瘓及頭痛的急性中風罕見病例，而中風的原因為卵巢過度刺激綜合徵導致腦靜脈栓塞。

ovary syndrome are risk factors. Human chorionic gonadotropin is an important contributor, as severe OHSS can be circumvented by withholding HCG or substitution with progesterone for luteal support.[2] Several other factors influence the progression of OHSS, including vascular endothelial growth factor, oestradiol, renin-angiotensin system, interleukin-6, and von Willebrand factor. Vascular endothelial growth factor is the main angiogenic cytokine associated with increased capillary membrane permeability encountered in OHSS.[3,4] Its features include marked ovarian enlargement, ascites, pleural effusion, renal and liver dysfunction, and rarely thromboembolic complications have also been reported.[5] The shift of fluids into the extracellular space leads to intravascular depletion and haemoconcentration, which is associated with increased blood viscosity and coagulation.[3,4] Ovarian stimulation itself causes an increase in fibrinogen and a reduction in antithrombin III concentration as well as a significant increase in clotting time. Lower doses of HCG in high-risk patients, delayed injection of HCG until oestradiol levels drop or stabilise, and the use of exogenous progesterone during the luteal phase can reduce the risk of OHSS.[2] Venous thromboses of the internal jugular, subclavian and inferior vena cava have been reported.[5-8] Arterial thromboses are less common; outside the cerebrovascular circulation, thrombosis of the humeral, femoral, mesenteric, and subclavian arteries, as well as the aorta have been reported.[5-8] In this patient, cerebral venous thrombosis was the presenting feature before she developed the frank features of OHSS. This complication should be considered even in patients at low risk, as IVF is a common procedure.

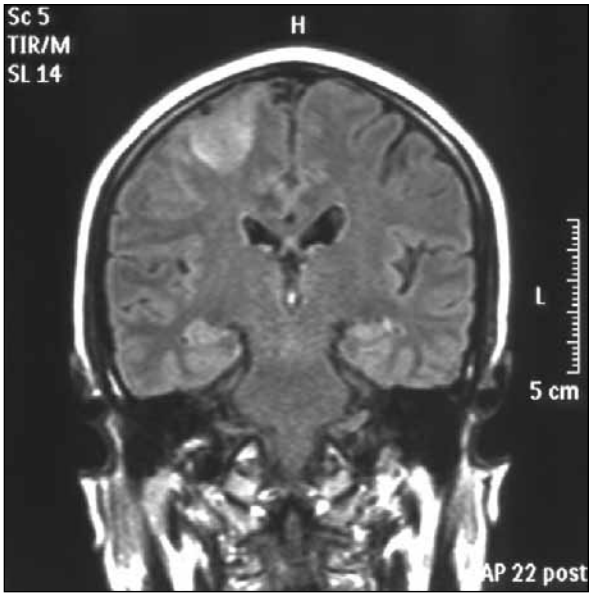

FIG 1. Cranial magnetic resonance imaging sagittal section showing right frontal infarct

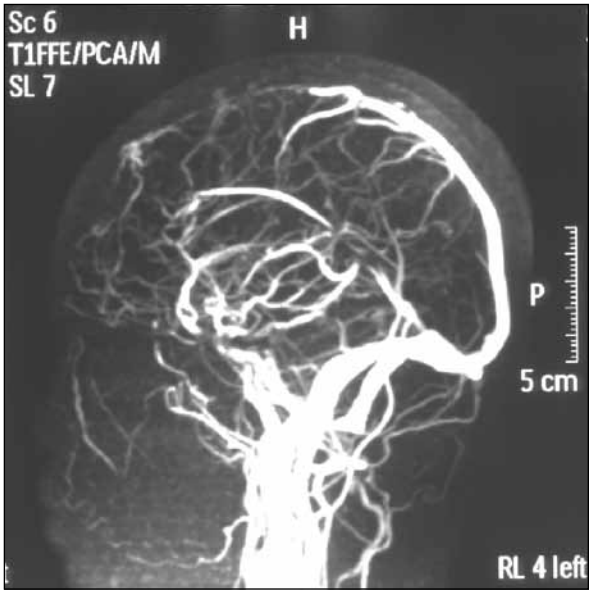

FIG 2. Cranial magnetic resonance venogram demonstrating filling defect as a result of thrombosis of the superior sagittal sinus

References

1. Delvigne A, Rozenberg S. Epidemiology and prevention of ovarian hyperstimulation syndrome (OHSS): a review. Hum Reprod Update 2002;8:559-77.
2. Budev MM, Arroliga CA, Falcone T. Ovarian hyperstimulation syndrome. Crit Care Med 2005;33(10 Suppl):S301-6.
3. Garcia-Velasco JA, Pellicer A. New concepts in the understanding of the ovarian hyperstimulation syndrome. Curr Opin Obstet Gynecol 2003;15:251-6.
4. Abramov Y, Barac V, Nisman B, Schenker JG. Vascular endothelial growth factor plasma levels correlate to the clinical picture in severe ovarian hyperstimulation syndrome. Fertil Steril 1997;67:261-5.
5. El Sadek MM, Amer MK, Fahmy M. Acute cerebrovascular accidents with severe ovarian hyperstimulation syndrome. Hum Reprod 1998;13:1793-5.
6. Alboulghar M, Mansour RT, Serour GI, Amin YM. Moderate ovarian hyperstimulation syndrome complicated by deep cerebrovascular thrombosis. Hum Reprod 1998;13:2088-91.
7. Stewart JA, Hamilton PJ, Murdoch AP. Thromboembolic disease associated with ovarian stimulation and assisted conception techniques. Hum Reprod 1997;12:2167-73.
8. Elford K, Leader A, Wee R, Stys PK. Stroke in ovarian hyperstimulation syndrome in early pregnancy treated with intra-arterial rt-PA. Neurology 2002;59:1270-2.