CASE REPORT

Subclavian and Internal Jugular Vein Thrombosis as a Late Complication of Ovarian Hyperstimulation Syndrome in an ICSI Patient with Heterozygous Factor V Leiden Mutation

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Abstract

Ovarian hyperstimulation syndrome (OHSS) is characterized by ovarian enlargement, weight gain, abdominal distention, generalized edema, ascites and hydrothorax. The optimal management of OHSS is a proper fluid intake together with low dose heparin administration for prevention of thrombosis risk. Thrombophilia may aggravate the risk of thrombosis in OHSS. We report a case of subclavian and internal jugular vein thrombosis as a late complication of OHSS in a patient with heterozygous factor V Leiden mutation in an ICSI cycle.

Keywords: subclavian jugular vein thrombosis, OHSS, ICSI

Özet

Heterozigot Faktör V Leiden Mutasyonlu ICSI Uygulanmış Bir Hastada Ovaryen Hiperstimülasyon Sendromunun Gecikmiş Bir Komplikasyonu Olarak Subklavyen ve İnternal Jügüler Ven Trombozu

Ovaryan hiperstimülasyon sendromu (OHSS) overlerin büyümesi, kilo artşı, batında distansiyon, ödem, asit ve hidrotoraksla karakterize bir durumdur. OHSS'nin optimal yönetimi, tromboz riskini önleyen düşük doz heparin verilmesiyle birlikte uygun sıvı alımıdır. Trombofili, OHSS'deki tromboz riskini artırabilir. Bu olguda heterozigot faktör V Leiden mutasyonu olan bir ICSI hastasında OHSS'nin geç komplikasyonuna bağlı gelişen subklavyen ve internal jügüler ven trombozu vakasını sunduk.

Anahtar sözcükler: subklavyen jügüler ven trombozu, OHSS, ICSI

Introduction

Ovaryen hyperstimulation syndrome (OHSS) is characterized by ovarian enlargement, weigth gain, abdominal distention, generalized edema, ascites and hydrothorax. In OHSS cases, a hypercoagulable state is created due to hemaconcentration resulting from the escape of intravascular fluid into the third space together with pregnancy induced hypercoagulopathy. Hormonal therapies, such as combined oral contraceptive pills, hormone treatment, controlled ovarian hyperstimulation, as well as hereditary hypercoagulopathy increase the risk of thromboembolic events. We report here, a case of subclavian and internal jugular vein thrombosis as a late complication of OHSS in a patient in ICSI cycle with heterozygous factor V Leiden mutation.

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Case Report

A 32 year-old female with 4 years primary infertility was referred to our clinic for IVF and ICSI. Her body weight was 45 kg and her height was 160 cm. The patient's menstrual cycle was regular. Her hysterosalpingogram showed a normal uterine cavity and patent bilateral tubes. Her partner's spermiogram showed 140×10^6 sperm/ml and 70% motility. She did not conceive with clomiphene citrate and intrauterine insemination (IUI) cycles performed 3 times and with gonadotropin and IUI cycles performed 3 times. Her hormonal work-up was normal;

day 3 baseline transvaginal ultrasonography showed bilateral ovaries containing 9 antral follicles.

Ovarian down regulation was initiated with daily leuprolide acetate 1 mg (Lucrin, Abbott, France), beginning on the 21st day of preceding menstruation without taking oral contraceptive pills. After ovarian suppression was achieved, the dose was reduced to 0.5 mg and ovarian stimulation was started with 150 IU of recombinant FSH (Gonal-F, Serono, Randolph, MA, USA), which was reduced on the 5th day of stimulation to 112.5 IU, and on the 8th day of stimulation to 50 IU of recombinant FSH due to high levels of estradiol (2305 pg/L). On the 9th day of stimulation she received 10 000 IU of hCG. E2 level was 2915 pg/L at the time of hCG injection day. At that point, there were 19 follicles between 14 and 20 mm in diameter and 8 additional follicles ≤12 mm. She had transvaginal retrieval of 27 oocytes of which 19 were mature and underwent ICSI resulting in 14 cleaving embryos. Seventy-two hours after oocyte retrieval, 3 grade 1/8-cell embryos were transferred to the uterine cavity. Luteal phase was supported by daily 90 mg progesterone intravaginally (Crinone 8% gel, Serono).

Five days after embryo transfer (ET) she was admitted to our clinic with nausea, vomiting and abdominal discomfort. Patient was hospitalized due to OHSS with enlarged ovaries together with 43% hematocrit level. She was treated with intravenous fluid and albumin replacement with close observation of fluid intake and output. Low molecular weight heparin (LMWH) Clexane (40 mg bid) was started at the day of hospitalization. Her abdominal distention gradually increased and ultrasonography showed ascites. On the 4th day of her hospitalization, a transabdominal catheter was placed for intermittent paracentesis. Nine days after ET, β-HCG was measured to be 50.2 mIU/ml. After repeated paracentesis and proper fluid intake, her hematocrit dropped from 46.5% to 32% and thereafter her abdominal discomfort was relieved. Patient was discharged after 17 days of treatment. On the sixth weeks of her gestation, transvaginal ultrasonography showed twin gestation with normal fetal cardiac activities.

She was readmitted to our clinic on the seventh weeks of her gestation with the complaint of swelling of right upper extremity and severe neck pain on the right side. She was a non-smoker and had no family history of arterial and/or venous thromboembolic diseases. Physical examination revealed a tender swollen right arm, shoulder and neck. The remainder of her examination was unremarkable. Doppler ultrasound of her right arm and neck revealed a large subclavian and internal jugular vein thrombosis. A transvaginal ultrasonography showed twin gestation of 6 weeks 4 days duration appropriate for CRL of each fetus without cardiac activity. Full-dose heparinization (20 000 unit/day) was started and she underwent thrombosis aspiration by radiology support. After successful management of thrombosis aspiration, her neck pain was relieved and swelling of the neck and the arm gradually regressed in 10 days. Suction curretage was performed for missed abortion under heparin treatment. Oral anticoagulant therapy with coumadin 5 mg tablet daily replaced heparinization. She was discharged after 16 days of intensive treatment.

Thrombophilia profile consisting of protien S-C, activated protein-C resistance, antithrombin III, homocysteine, anti-nuclear antibody, anticardiolipin IgG, lupus anticoagulant, and genetic screening for MTHFR, prothrombin gene mutation and factor V Leiden mutation were estimated. All were in normal range, except for factor V Leiden which showed heterozygous gene mutation. The patient is still under medication with oral anticoagulant.

Discussion

Thromboembolic disease associated with ovarian stimulation is an uncommon but potentially fatal complication of the assisted reproductive technology. Hemaconcentration and hyperviscous state and hypercoagulopathy due to estrogenic stimulation of increased coagulation factors may play a facilitatory role in the thromboembolic events of OHSS. In our case, twin pregnancy and OHSS induced hypercoagulable state together with factor V Leiden mutation might explain this thromboembolic event which may be seen in patients even in the mild form or the absence of OHSS (1-2).

The optimal management of OHSS is proper fluid intake together with low dose heparin administration for prevention of the thrombosis risk. However, the duration of anticoagulant therapy after OHSS and the pregnancy outcome is still obscure. In the literature, most cases of thrombosis due to severe OHSS involve the internal jugular vein or the subclavian vein solely. Our case showed a combined form of subclavian and jugular vein thrombosis. Another different aspect of this case was the aspiration of the thrombosis from the subclavian and internal jugular veins without complication. This thrombosis aspiration procedure was easy to perform under X-ray assistance because of the intrauterine ex fetuses.

Thrombophilia may aggravate the risk of thrombosis in OHSS (3). Particularly, resistance of activated protein C with factor V Leiden mutation has been described in patients with recurrent thromboembolic events (4). Schanzer et al. in a review of case reports in the literature involving internal jugular vein thrombosis and OHSS have referred to a patient with protein S deficiency and another patient with antiphospholipid syndrome (5). Arya et al. published 5 cases of internal jugular vein thrombosis following OHSS, two of which had evidence of inherited thrombophilia (6).

In conclusion, considering the thromboembolic events in OHSS, anticoagulant therapies such as LMWH should not be discontinued after discharging patients. However, the duration of these treatments should be individualized after evaluations of the patient status.

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