SPONTANEOUS SEVERE OVARIAN HYPERSTIMULATION SYNDROME COMPLICATED WITH DEEP VENOUS THROMBOSIS

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SUMMARY

Ovarian hyperstimulation syndrome (OHSS) usually occurs up to %10 of women who use especially gonadotropins for artificial fertilization methods, becomes more intense with embryonic implantation, and is associated with high miscarriage rate. Severe forms complicate ~1% of IVF cycles and in the most marked cases, thromboembolic phenomena may occur as a result of hemoconcentration and coagulation disturbances. Severe OHSS is rare in case of spontaneous ovulation and always reported during pregnancy. We present a severe OHSS complicated with femoral and popliteal deep and superficial venous thrombosis in woman with spontaneous pregnancy.

Key words: deep venous thrombosis, hypercoagulability, ovarian hyperstimulation, spontaneous


SPONTAN OVERYEN HİPERSTİMULASYON SENDROMUNA SEKONDER GELİŞEN DERİN VEN TROMBOZU

ÖZET

Overyen hiperstimulasyon sendromu (OHSS) yardımcı üreme metodları için gonadotropin kullanan hastaların yaklaşık %10’da izlenen, özellikle implantasyon olmasyla yoğunlaştı ve artış dışık oranları ile ilişkilendirilen bir durumdur. Ciddi formu IVF sikluslarının % 1’de görürlü; belirgin olan vakalarda hemokonsantrasyon ve koagulasyon bozukluğu nedeni ile tromboembolik hadiseler gelişebilir. Spontan ovulasyon sırasında OHSS çok nadirdir ve genellikle gebelik ile beraberdir.

Bu makalede spontan gebelik sonrasında ciddi OHSS gelişen, femoral, popliteal derin ve yüzeyel venöz tromboz ile komplike olan bir 11 haftalık gebelik olgusu sunulmuştur.

Anahtar kelimeler: derin ven trombozu, hiperkoagulabilite, spontan overyen hiperstimulasyon

Türk Jinekoloji ve Obstetrik Derneği Dergisi, (J Turk Soc Obstet Gynecol), 2012; Cilt: 9, Sayı: Ek 1, Sayfa: 10-3
INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) usually occurs up to %10 of women who use especially gonadotropins for artificial fertilization methods, becomes more intense with embryonic implantation, and is associated with high miscarriage rate(1). Severe forms complicate ~1% of IVF cycles and in the most marked cases, thromboembolic phenomena may occur as a result of haemoconcentration and coagulation disturbances. Severe OHSS is very rare in case of spontaneous ovulation and always reported during pregnancy. Elevated serum hCG (as observed in molar pregnancy, multipl gestation) and TSH levels were accused of spontaneous OHSS (sOHSS). Recently, some FSH receptor (FSHr) mutations were described in patients presenting with sOHSS of the first trimester of pregnancy with normal levels of human chorionic gonadotropin (hCG)(2).

We present a severe sOHSS complicated with femoral and popliteal deep and superficial venous thrombosis in woman with spontaneous pregnancy.

CASE

A 25-year-old, gravida 3, para 1, presented at 11 weeks in her pregnancy with complaints of fullness, pain in abdomen and pain, change of color and swelling in her left leg. Her past medical and surgical history were unremarkable and she denies any medication prior and during to the conception. The pelvic examination was limited because of severe ascites. Her left calf and femur were edematous, erythematous and approximately 7 centimeter wider than right one. Homan's sign was positive on the left. On ultrasound evaluation confirmed 11 weeks healthy fetus, bilaterally enlarged (15x12 mm left and 13x12 mm right) multicystic ovaries and gross ascites (figure 1,2). Doppler flow study showed thrombosis which completely occluded of her left external iliac vein, common iliac vein, deep and superficial popliteal and femoral veins and trifurcation veins. Quantitative -hCG was 109 524 IU/ml, TSH was 0.02 µIU/ml (0.35-4.94 µIU/ml), FT3 and FT4 were normal, complete blood count showed a white blood cell count of 12 600, hemoglobin at 13.2 g/dL, platelet count of 240 000, estradiol >5000 pg/mL, normal prothrombin time and international normalized ratio, normal complete metabolic panel, with albumin 2.9 g/dl, creatinine 0.74mg/dL and blood urea nitrogen 23.

Figure 1,2: Bilaterally enlarged (15x12 mm left and 13x12 mm right) multicystic ovaries and gross ascites.

Her thrombophilia screens for antithrombin III, lupus anticoagulant, protein c and s activity were within the normal limits. Antiphospholipid antibodies (IgM and IgG), anticardiolipin antibodies (IgM and IgG) were negative. The patient was not a carrier of factor V leiden mutation.

She was admitted for management and treatment of severe sOHSS and DVT. Unfractionated heparine 25 000 iu/day I.V. treatment was started. Fluid balance was assessed closely. Her urine output was satisfactory and her laboratory evaluations were stable. After the admission, patient began to have progressive abdominal pain and distention. At the 4th days of the admission, she was developed a shortness of breath and fullness. Chest radiography showed mild pleural effusion. Abdominal ultrasound examination showed large amount ascides and paracentesis was done with a spinal needle and 2 liters of ascitic fluid removed and 25 cc of Albumin I.V. (%25) solution was given at that time. Her clinic condition and DVT improved.
gradually and laboratory testing were stable during the following weeks. The patient was discharged after 17 days of hospitalization with 10 000 IU/day S.C. heparin treatment and appropriate clinic follow up. The patient was otherwise uncomplicated and she delivered a healthy, 3050 gr. female infant at term by vaginal delivery and the postpartum period was uncomplicated.

**DISCUSSION**

Spontaneous OHSS is very rare clinical entity and the etiology of the disease has not been sufficiently explained. The cause of spontaneous ovarian hyperstimulation syndrome is thought to be secondary to mutations of the FSHr gene ovarian hyperresponsiveness to FSH or cross-responsiveness of the FSHr to hCG and/or TSH, which results in ovarian hyperstimulation\(^3\). In addition to this, spontaneous OHSS was defined in women who had previously uncomplicated pregnancy\(^4\). The pathogenesis of OHSS can be explained with overproduction of vascular endothelial growth factor (VEGF), eventually increased vascular permeability, ascites, hemoconcentration, and increased risk of thrombosis\(^5\).

Due to the normal physiologic changes that affect coagulation, pregnancy is considered a hypercoagulable state. The pathogenesis of thromboembolism in OHSS is thought to be increased capillary permeability with resultant hypovolemia and hemoconcentration, and also activation of the coagulation cascade, rise of thrombin-antithrombin III, rise in plasmin-antiplasmin complexes, and in platelets. Hereditary hypercoagulable states also increase the risk for thrombosis. Internal jugular vein thrombosis associated with OHSS has been described in association with factor V Leiden mutation, heterozygosity for both factor V Leiden mutation and prothrombin III UTR mutation, activated protein C resistance, antithrombin III deficiency\(^6\). The risk factors of presenting patients for DVT were pregnancy and OHSS but she had no hereditary hypercoagulable state. The symptoms of OHSS usually have resolved spontaneously, many authors recommend the continuation of pregnancy. In almost all cases, the disease regresses spontaneously with time or delivery. On the other hand, deaths due to hypovolemia, hemorrhage and thromboembolic phenomena have been reported\(^7\). Hospitalization is required in most cases. Monitoring of hemodynamic status, intravenous crystalloid and albumin infusion and prophylaxis of thrombosis are the main principles of management\(^8\). Termination of pregnancy can be considered when conservative management fails, but surgery should be reserved for cases of ovarian rupture, torsion and intraperitoneal hemorrhage. In our case was classified as severe OHSS because of abdominal distension, ascites and enlarged ovaries. Our case needed paracentesis for severe abdominal distension and breath shortness but most of OHSS cases can be managed without paracentesis. We were able to manage the case successfully with expectant management.

**REFERENCES**