CASE REPORT

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Ovarian Hyperstimulation Syndrome Continuing with Very High C Reactivity Protein Level without Infection: A Case Report and Review of the Literature

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ABSTRACT Ovarian hyperstimulation syndrome is an iatrogenic complication of supraphysiologic ovarian stimulation. The syndrome is almost exclusively associated with exogenous gonadotropin stimulation and is only rarely observed after clomiphene citrate treatment or spontaneous ovulation. C-reactive protein, an acute phase protein produced by the hepatocytes, is a marker of systemic inflammation, tissue damage, and/or infection. While the increased C-reactive protein level in the ovarian hyperstimulation syndrome made us think that there is an infection, for making this diagnosis, other infection indicators must be researched on these patients. Although the use of C-reactive protein for infection in ovarian hyperstimulation syndrome is recommended, the level of C-reactive protein may increase without infection. We aimed to identify ovarian hyperstimulation syndrome with very high C-reactive protein level without infection.

Keywords: Ovarian hyperstimulation syndrome; C-reactive protein; infection

Ovarian hyperstimulation syndrome (OHSS) is the most severe complication of controlled ovarian hyperstimulation (COH) for assisted reproduction. The syndrome is almost exclusively associated with exogenous gonadotropin stimulation and is only rarely observed after clomiphene citrate treatment or spontaneous ovulation.[1] The pathophysiological processes caused by the syndrome are not completely clear, and endothelial activation and increase in capillary permeability are the mainstays of many theories.[2] The liquid passes into third spaces in the vascular compartment due to increased permeability of the capillaries. This may cause hypoalbuminaemia, haemoconcentration, electrolyte imbalance, reduced renal perfusion and oliguria, ascites, pleural/pericardial effusions, which may importantly increase significant morbidity and mortality from thrombosis, renal, liver and respiratory failure. According to clinical symptoms and laboratory findings, OHSS is classified as mild, moderate, severe or critical.[3]

C-reactive protein (CRP), an acute phase protein made by the hepatocytes, is a marker of systemic inflammation, tissue damage or infection.[4] Although CRP usage is suggested to ostracize infection in OHSS, CRP level increases without infection causes confusion.[5,6] In this case presentation, we aimed to discuss OHSS case in which no infection is determined, CRP level increased, with plato and can't be found in literature.

CASE REPORT

A 34 year old female patient, gravida 2, parity 0, two ectopic pregnancies which were treated with MXT has given ovulation induction treatment with go-

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nadotrophine at a dose of 75 IU/day FSH (Gonal-f 75 IU, SERONO, Rockland, U.S.A.). Choriogonadotr opin Alfa 250 mcg (OVITRELLE 250 mcg/0.5 ml, Merck Serono, London, United Kingdom) injection applied for follicle maturation and 36 hours later, intrauterine insemination was performed. She applied to our emergency department because of headache, nausea and vomiting. Her medical history revealed that she had not been able to conceive with treatment during the last three years since her last ectopic pregnancy. We found minimal tenderness on lower part of abdomen during abdominal examination. In the laboratory evaluation white blood cells (WBC): 28.900/µL, hematocrit (HTC): 38.5%, platelet (PLT): 246.000/µL, liver function tests, electrolytes, urea and creatinine values were normal. In the transvaginal ultrasonography (TVUSG) examination; it was found that the ovary size had been increased (right ovary 87x95 mm, left ovary 65 x 60 mm). Parenchymal features of both ovaries were still present and there were many cystic lesions of which the biggest ones were 45x39 mm at right and 25 x 43 mm at left, these displays were evaluated as follicle cyst (Figure 1, Figure 2).

Under the light of these findings, the patient was hospitalized with moderate OHSS diagnosis. Daily blood pressure, pulse, temperature, weight, fluid balance, abdominal circumference, WBC, HTC, electrolyte and liver and kidney function tests were monitored. At the first day of the hospitalization, 2000 cc lactate ringer and 1000 cc isotonic were given to the patient whose oral intake was limited due to nausea and vomiting. At the second day of her hospitalization, daily 2500-3000 cc oral intake and 1000

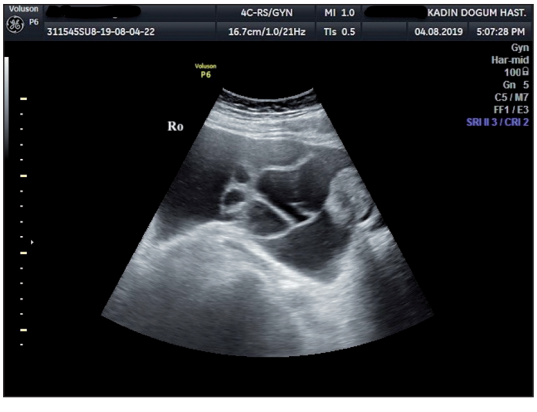

FIGURE 1: Right ovary with free liquid in the abdomen.

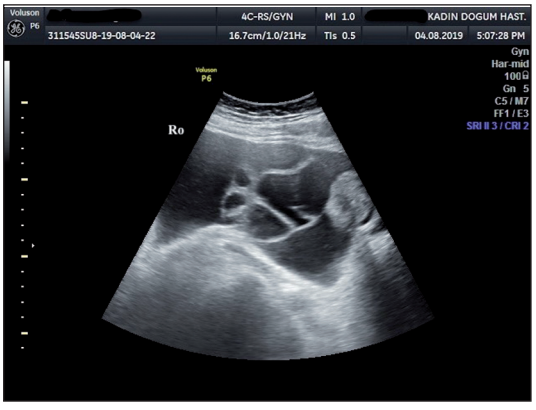

FIGURE 2: Left ovary with free liquid in the abdomen.

cc lactate ringer was given to the patient whose vomiting got better. At the third day of the hospitalization, in the clinical treatment made with regards to infection focus due to 38.1°C temperature just for once, no infection focus was determined, and also in the laboratory evaluation, WBC: 27.170/µL, HTC: 36.5%, PLT: 266.000/µL, liver and kidney function testes and urea control were normal but because of CRP: 317 mg/L blood, urea and cervical culture were taken. Antibiotheraphy was not started since the patient did not have fever, no infection focus was found clinically and no microbial growth was seen in the taken cultures. The patient was started to be monitored by adding CRP to the daily routine laboratory tests. At the 10th day of the hospitalization hCG value was measured 4.03 mIU/mL and pregnancy not detected. At the 14th day of her hospitalization, in her laboratory evaluation, upon seeing that WBC: 11.400/µL, HTC: 37%, PLT: 564.000/µL, CRP: 47 mg/L, liver and kidney functions test results were normal, she was discharged to be checked ambulatory once in every three days and then weekly. After the discharge, ambulatory monitoring were finished upon seeing that laboratory findings were WBC: 8.930/µL, HTC: 34%, PLT: 373.000/µL, CRP<2 mg/L and right ovary size 35x32 and left ovary size were 30x22 in TVUSG at the end of the second week.

DISCUSSION

OHSS is a clinical syndrome manifested by haemoconcentration, electrolyte imbalances, ascites and thrombotic events due to endothelial activation lead-

ing to increased vascular permeability. Management should be conservative and directed at symptoms; many women can be managed as outpatients. However, women with severe or critical OHSS require hospitalization.[2] CRP, an acute phase protein produced by the hepatocytes, is a marker of systemic inflammation, tissue damage or infection.[4] Levin et al. specified that CRP level was increased by 2-3 times in comparison to control group during early OHSS.[6] At the same time, observation of fever (>38 °C) in the nearly half of the early OHSS cases makes it hard to diagnose infection in these cases.[7] Although there are not many studies in the literature regarding this matter, to diagnose infection in early OHSS, Korhonen et al. made receiver operating characteristic (ROC) analysis to determine which cut-off value is to be used and specified this value as 12 mg/L (sensivity 69% and specifity 71%) and at the same time specified that the peak CRP level is 166 mg/L in these cases without infection.[8] In the early OHSS case in our study, although CRP level was increased to 317 mg/L no infection was determined and this value is above cut-off peak and CRP value specified by Korhonen et al. to diagnose infection in early OHSS. No study was found in the literature in this regard.

As a result, even if increasing CRP level in early OHSS makes us think about infection, other infection indications must be examined in such patients to make a diagnosis.

Informed Consent

The patient whose story is told in this case report signed permission for its publication.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Bekir Kahveci, Mehmet Şükrü Budak;* ***Design:*** *Bekir Kahveci, Mehmet Şükrü Budak;* ***Control/Supervision:*** *Bekir Kahveci;* ***Data Collection and/or Processing:*** *Mehmet Şükrü Budak;* ***Analysis and/or Interpretation:*** *Mehmet Ali Vardar;* ***Literature Review:*** *Bekir Kahveci, Mehmet Şükrü Budak;* ***Writing the Article:*** *Bekir Kahveci, Mehmet Şükrü Budak.*

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