

# Causes of Massive Vulvar Edema in Patients with Severe Ovarian Hyperstimulation Syndrome: A Case Report and Literature Review

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Conflict of interest:** None declared

**Patient:** Female, 31  
**Final Diagnosis:** Severe ovarian hyperstimulation syndrome  
**Symptoms:** Ascites • chest discomfort • vulvar edema  
**Medication:** —  
**Clinical Procedure:** Expectant with local treatment • paracentesis  
**Specialty:** Obstetrics and Gynecology





**Objective:** Unusual clinical course  
**Background:** Ovarian hyperstimulation syndrome (OHSS) is a potentially serious complication of ovulation stimulation. Modest vulvar edema is frequently seen in a severe form of OHSS; however, cases of massive bilateral vulvar edema are rare and pathogenesis is uncertain.

**Case Report:** We report a 31-year-old patient with massive vulvar edema and severe OHSS after IVF treatment with GnRH antagonist and gonadotropins. Five days after embryo transfer, she was hospitalized because of severe clinical manifestation of OHSS and on the fifth day after admission she developed a massive bilateral vulvar edema. After conventional medical therapy of OHSS, vulvar edema spontaneously resolved.

**Conclusions:** Hypoproteinemia with low oncotic pressure and certain personal tissue characteristics may play the main role in the pathogenesis of massive vulvar edema in OHSS.

**MeSH Keywords:** Ovarian Hyperstimulation Syndrome • Pregnancy Complications • Vulva

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/913149>

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## Background

OHSS is a potentially serious iatrogenic complication of the early luteal phase or/and early pregnancy after ovulation induction or ovarian stimulation. It is characterized by enlargement of the ovaries and a fluid shift from the intravascular to the third space due to increased vascular permeability and ovarian neoangiogenesis. The incidence of clinically significant OHSS is 2–3% of all *in vitro* fertilization (IVF) patients [1]. Primary prevention of OHSS is identifying the patient's risk factors and choosing an appropriate ovarian stimulation protocol [2]. In severe form of OHSS with ascites and abdominal distension, modest vulvar edema is frequently seen; however, cases of massive bilateral vulvar edema are rare and represent a distressing condition for the patient and gynecologist [3].

## Case Report

We report a 31-years-old patient with clinically fully-expressed OHSS and a massive bilateral vulvar edema. The patient signed a written informed consent form agreeing to the use of her medical records for research purposes.

After unsuccessful intrauterine inseminations, the patient underwent treatment with IVF for idiopathic infertility. This was her second attempt. She was treated with standardized gonadotrophin-releasing hormone (GnRH) antagonist protocol and triggered with choriogonadotropin (hCG). Twelve oocytes were collected, and 1 blastocyst was transferred on the fifth day after retrieval.

The patient was admitted 5 days after the embryo transfer because of abdominal distension and pain. At admission, gynecological examination of vulva and vagina did not reveal any abnormalities. With transvaginal ultrasound examination, we found enlarged and cystic ovaries and ascites. Laboratory tests showed leukocytosis ( $15.86 \times 10^9/l$ ), hemoconcentration, and hypoproteinemia. Measurement of fluid balance revealed a deficit in output of fluid. The treatment of OHSS consisted of low molecular weight heparin, intravenous human albumin, analgesics, and maintenance of electrolyte balance. Because of elevated inflammatory markers and pathological urine tests, antibiotic therapy with amoxicillin was induced. Due to abdominal distension and oliguria, abdominal paracentesis was performed by inserting an intra-abdominal catheter through the left lower abdominal quadrant on the second day after admission.

Because of the chest pain located on the left side with expansion in the left scapula and left hip, a cardiac ultrasound was performed which showed no pericardial effusion and small pleural effusion not requiring puncture.



Figure 1. Modest, mainly unilateral vulvar edema.



Figure 2. Fully expressed massive bilateral vulvar edema in patient with severe OHSS.

Three days later, she had massive bilateral vulvar edema accompanied by vulvar discomfort and difficulty passing urine (Figure 1). Levels of serum albumins and proteins dropped, and the lowest recorded level of proteins was 42 g/L. Gradually, edema of the left lower extremity developed, accompanied with pain in the inguinal region that expanding distally. The patient was transferred to the intensive care unit. Because of very tanned skin of the vulva and burning sensation, a dermatologist was consulted. After excluding other causes of vulvar edema such as trauma, infections, allergy, and obstruction, local treatment of the vulva with ice packs and betamethasone plus gentamicin sulfate cream (Diprogenta, Merck Sharp & Dohme) twice daily were proposed. Due to difficult urinating, a Foley catheter was inserted. Vulvar edema was fully expressed on the 7<sup>th</sup> and 8<sup>th</sup> days of hospitalization and lasted 12 days (Figure 2). On the 14<sup>th</sup> day after embryo transfer, serum  $\beta$  hCG value became positive. The edema did not decrease much after releasing of greater amount of ascites, but it became slightly worsened when the abdominal catheter was removed on the 11<sup>th</sup> day and intra-abdominal pressure slightly increased. The abdominal distension deteriorated once again; an abdominal puncture was performed and 2600 ml of abdominal fluid was removed.

**Table 1.** Causes of vulvar edema in OHSS.

| Authors               | Unilateral or bilateral | Cause   | Outcome and complications                     |
|-----------------------|-------------------------|---|---|
| Coccia et al., 1995   | Bilateral               | Decreased oncotic pressure and increased hydrostatic pressure                                       | Resolved completely                           |
| Cline et al., 1996    | Bilateral               | patent canal of Nuck  | Resolved completely                           |
| Luxman et al., 1996   | Unilateral              | Fistulous tract created (iatrogenically) between the peritoneal cavity and the subcutaneous tissues | Resolved completely                           |
| Vavilis et al., 2002  | Bilateral               | Fistulous tract created (iatrogenically) between the peritoneal cavity and the subcutaneous tissues | Resolved completely                           |
| Kalafat E, 2016       | Unilateral              | Occult inguinal hernia  | Resolved after surgical repair – outcome good |
| Bhairavi et al., 2016 | Bilateral               | Fistulous tract created (iatrogenically) between the peritoneal cavity and the subcutaneous tissues | Resolved completely                           |

After treatment, laboratory test results improved significantly: hemoglobin was 126 g/l, total protein level was 68 g/l, and albumin level was 40 g/l. Vulvar edema resolved almost completely and there was progressive abatement of abdominal distension. The patient was discharged home 17 days after admission. An ultrasound scan showed 1 intrauterine gestational sac with an embryo with heart beat and a yolk sac.

## Discussion

Severe vulvar edema in pregnancy is uncommon. Labial edema can result from local trauma, infection (e.g., genital herpes or other sexually transmitted infections, candidiasis), inflammation, or allergic reaction [2]. Most cases of vulvar edema appear in late gestation and may be associated with other systemic diseases such as malnutrition, renal or hepatic disease, preeclampsia, diabetes, or congestive heart failure [4]. A recent article describes a rare case of unilateral vulvar edema in an OHSS patient due to occult inguinal hernia [5].

The hypothesis of bilateral vulvar edema associated with severe ovarian hyperstimulation syndrome was first proposed by Coccia et al. in 1995 [6], stating that vulvar edema could be the result of decreased oncotic pressure and increased hydrostatic pressure, which occurs during OHSS. There are more suggestions regarding the mechanism of vulvar edema associated with severe ovarian hyperstimulation.

Grossman et al. suggested a hypothesis of the abdominal compartment syndrome. OHSS involves a rapid accumulation of volume in the peritoneal cavity that can lead to organ dysfunction, including respiratory impairment and oliguria.

The increased intra-abdominal pressure indicates that OHSS may be considered a compartment syndrome and meets the criteria for abdominal compartment syndrome in advanced cases [7].

Vavilis et al. described a case in which they suggested the cause of vulvar edema to be a fistulous tract created between the peritoneal cavity and subcutaneous tissues at the puncture site, through which the fluid is forced to the most dependent area [8]. This hypothesis was based on a paper published in 1996: 7 of 9 cases with severe OHSS that required abdominal paracentesis developed a unilateral edema within 10–24 h after paracentesis, corresponding to the puncture site [9]. The authors postulated that the fistula was caused by a large-bore needle between the peritoneum and abdominal subcutaneous tissues, along with the increased intra-abdominal pressure due to ascites, which may facilitate the passage of fluid and the development of ipsilateral edema in the labia.

A different hypothesis regarding the pathogenesis of vulvar edema was suggested: the condition occurs because the patients have a patent canal of Nuck [10].

Table 1 shows the causes of vulvar edema listed by author and year of publication.

In our case, the edema was not directly dependent on intra-abdominal pressure, as it did not decrease after the release of a large volume of ascites. It only slightly worsened when the abdominal catheter was removed and the intra-abdominal pressure increased, thus rejecting the theory of patent canal of Nuck in the pathogenesis. The development of bilateral edema 3 days after left-sided paracentesis also discounted the

theory of a fistula between the peritoneum and subcutaneous tissue developing after the puncture. According to this theory, the edema should be unilateral and must appear earlier [7,8]. In our patient, the volume of edema was mainly parallel with the degree of hypoproteinemia and lower oncotic pressure. Slow improvement of hypoproteinemia led to a gradual cessation of edema and discomfort. The patient was discharged on the 17<sup>th</sup> day after admission, when the vulvar edema had resolved almost completely.

## References:

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## Conclusions

Severe vulvar edema in association with OHSS was first described in 1995; however, it rarely occurs during pregnancies complicated by preeclampsia or after tocolysis for preterm birth [7,8]. According to the literature and our experience, the prognosis of massive vulvar edema in OHSS is favorable, as it is spontaneously resolved by symptomatic treatment. In our case, we did not confirm that the canal of Nuck or paracentesis were involved in the formation of massive vulvar edema in OHSS, which is a rare condition and the pathogenesis is still uncertain. In our opinion the most likely cause of the formation of the vulvar edema is the decreased oncotic pressure and increased hydrostatic pressure, which cause the pathogenesis of OHSS.

## Conflict of interests

None.