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Ovarian torsion and spontaneous ovarian hyperstimulation syndrome in a twin pregnancy: A case report



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ABSTRACT

INTRODUCTION: Ovarian hyperstimulation syndrome (OHSS) is extremely rare in spontaneous pregnancies. Spontaneous OHSS can result from glycoprotein hormones stimulating follicle-stimulating hormone receptors (FSHR).

PRESENTATION OF CASE: We report a twin pregnancy in which ovarian torsion and hemoperitoneum complicating OHSS were treated with left adnexectomy and aspiration. The only trigger for spontaneous OHSS in this case was high levels of chorionic gonadotropin hormone.

DISCUSSION: Multiple pregnancy, gestational trophoblastic disease, primary hypothyroidism, thyroid-stimulating hormone/gonadotropin-secreting adenomas, and mutations of the *FSHR* gene may trigger spontaneous OHSS.

CONCLUSION: Spontaneous OHSS should be included in the differential diagnosis of acute abdomen in pregnant women; if spontaneous OHSS is diagnosed, the etiology should be determined in order to focus the treatment and avoid future complications.

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1. Introduction

Ovarian hyperstimulation syndrome (OHSS) is characterized by enlargement of the ovaries and the formation of multiple cysts. Normally iatrogenic, OHSS mainly occurs in the context of infertility treatments and is extremely rare in spontaneous pregnancies [1–5]. In contrast with iatrogenic forms, which typically appear earlier [2,4,6,7], spontaneous OHSS usually develops between the 8th and 14th weeks of gestation; it is sometimes familial and recurrent [6], and it can occur in non-pregnant women [5,7,8].

Explanations of the mechanisms that could trigger spontaneous OHSS focus on the follicle-stimulating hormone (FSH) receptor, which could be stimulated by high levels of FSH or other glycoprotein hormones with identical beta subunit [8], such as thyroid-stimulating hormone (TSH) [1,5,7], luteinizing hormone (LH), and chorionic gonadotrophin hormone (hCG). Mutations of the FSH receptor (*FSHR*) gene that make the receptors more sensitive are probably also involved [1,3,7,8].

Common risk factors for developing spontaneous OHSS include age <35 years, low body weight, polycystic ovarian syndrome, and previous episodes of spontaneous OHSS [1,4].

Complications are rare, but should always be considered [1,6]. Ovarian torsion occurs in 12%–20% of women with spontaneous OHSS [1,2]; right adnexal torsion is more common than left [2]. It is

crucial to assess the extent of the ischemia and whether gangrene is present to determine whether it is possible to unwind the adnexa or whether adnexectomy is needed [2].

2. Presentation of case

A 30-year-old woman (gravida 1 para 0) was admitted at 11 weeks' gestation for severe abdominal pain. She had no relevant medical or surgical history. Physical examination revealed mild abdominal distention and acute abdomen. Ultrasonography showed normal dichorionic-diamniotic gestation and enlarged ovaries (Fig. 1) with absent blood flow in the left ovary and free fluid in the abdominal cavity suggestive of hemoperitoneum. Laboratory findings were: hemoglobin 8.9 g/dL, hematocrit 26%, white blood cell count 9800/mL, and platelets 185,000/mL. Biochemistry and thyroid function were normal. Laparoscopy for suspicion of spontaneous OHSS complicated by ovarian torsion confirmed bilateral ovarian enlargement and hemoperitoneum. The ovaries measured 10 cm and 9 cm, and the left adnexa was twisted around the pedicle and ischemic (Fig. 2); adnexectomy was performed and two liters of blood were aspirated. Later, the anatomopathologic exam confirmed the ovarian ischemia.

The postoperative period was uneventful, and the patient was discharged on the third day. To perform the genetic test, DNA was extracted from peripheral-blood leukocytes, and the sequences of all exons of the gene for the follicle-stimulating hormone receptor together with intron–exon junctions were determined. In our patient, there was no mutation identified. During follow-up, ultra-

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Fig. 1. Ultrasound: ultrasonography showed dichorionic-diamniotic gestation and an enlarged ovary.

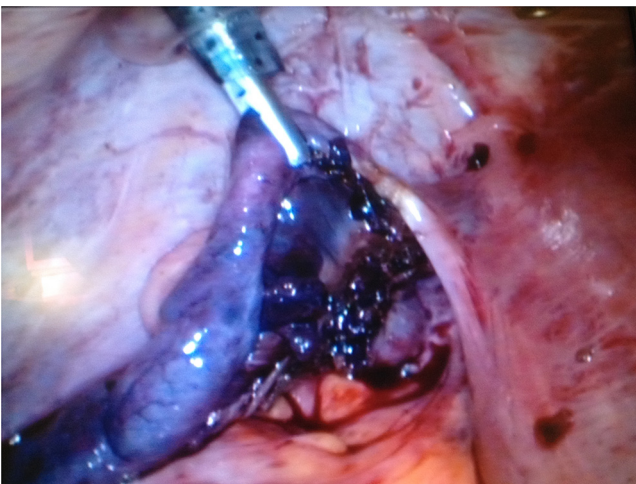


Fig. 2. Surgery: laparoscopic surgery showed the ischemic appearance of the adnexa just after being untwisted.

sonography showed progression of the intrauterine pregnancy, and the right ovary had returned to normal size at 31 gestational weeks. The pregnancy proceeded normally until spontaneous amniorrhexis with spontaneous labor at 34.5 gestational weeks. Two healthy girls weighing 1700 g and 1730 g were delivered vaginally.

3. Discussion

The pathogenesis of spontaneous OHSS involves hyperstimulation of *FSHR* by FSH or other glycoproteins with similar structures. Recently, mutations of the *FSHR* gene leading to an increased sensitivity of the receptor to normal levels of hormones have been also described [1,2,4,8], although a standard genetic test has yet to be developed. Several circumstances may increase the levels or biological activity of these glycoproteins:

- Elevated endogenous levels of hCG can be seen in multiple pregnancies and gestational trophoblastic disease [2]. A variant of β -hCG with higher biological activity could also cause hyperstimulation of the *FSHR* [1,8].
- High TSH levels are seen in primary hypothyroidism [4,8] and more rarely in TSH-secreting adenomas [1,3,5,8]. Patients with spontaneous OHSS related to TSH can be treated with thyroid hormone replacement therapy, so they have a better prognosis

[5,8]. The cysts normally regress 3–6 months after they develop [6].

- Most gonadotropin-secreting adenomas (mostly FSH-secreting tumors) secrete inactive hormones, but some can secrete high or normal levels of FSH with higher biological activity. High estradiol levels with non-suppressed or even normal FSH or LH should raise suspicion of autonomous activity.

The clinical repercussions of OHSS result from an acute fluid shift into the extravascular space, which usually manifests as ovarian cysts, ascites, and pleural and/or pericardial effusion. The onset of the symptoms usually occurs around 8 weeks of amenorrhea and culminate when the level of β -hCG drops, at the end of the first trimester [8]. Some patients do not develop ascites or pleural/pericardial effusion [8].

A search of PubMed for articles published through January 2017 with the terms “Spontaneous ovarian hyperstimulation syndrome” and “case” and “ovarian torsion” found 54 articles reporting a total of 57 cases of spontaneous OHSS (a list of these references is available from the authors): *FSHR* mutations (n = 11), hypothyroidism (n = 11), gonadotropin-secreting tumors (n = 8), and trophoblastic disease (n = 4); no cause was identified in the remaining 23 cases:

The 11 cases in which *FSHR* mutations were identified were mostly familial and recurrent. One article describes a patient with a familial *FSHR* gene mutation who had thyroiditis with increased thyroglobulin and suppressed TSH levels, raising the possibilities that high levels of thyroglobulin may stimulate the mutated FSH receptors or that thyroglobulin receptors may be present in the ovarian parenchyma. An inactive *FSHR* mutation was recently reported, although the mechanism underlying spontaneous OHSS remains to be clarified.

The 11 cases due to hypothyroidism included 5 in pregnant women between 8 and 12 weeks' gestation. The symptoms resolved within a few weeks of starting levothyroxine treatment, and the ovaries had returned to normal size between 21 and 24 weeks' gestation and within 3–4 months in non-pregnant women.

The 8 cases involving gonadotropin-secreting tumors included one patient with a FSH-secreting neuroendocrine tumor, and 7 patients with pituitary adenomas, two of whom had normal FSH levels. All underwent transsphenoidal surgery.

The 4 cases of trophoblastic disease included two patients with partial molar pregnancies, one patient with placental mesenchymal dysplasia mimicking a molar pregnancy in which spontaneous OHSS occurred after miscarriage, and one 12-year-old girl with elevated β -hCG due to a histologically confirmed mediastinal choriocarcinoma.

Of the total 57 cases, 9 had complications. Six patients had ovarian torsion, which was unilateral in five and bilateral in one. Of them, laparoscopic unwinding sufficed in five, but one required adnexectomy. Unilateral laparotomic adnexectomy was also reported in two patients with large ovaries and spontaneous OHSS. Another patient pregnant with triplets underwent laparotomy to drain a pyoperitoneum.

4. Conclusion

Our case reinforces the importance of a prompt and accurate differential diagnosis in all pregnant patients presenting with acute abdomen and ovarian masses, because spontaneous OHSS can be associated with life-threatening complications that require early diagnosis for successful management. The etiology should be determined in order to focus the treatment and avoid future complications.

Conflicts of interest

The authors have no potential conflicts of interest.

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We did not receive any funds from any organization.

Ethical approval

We did not need ethical approval for our case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Authors contribution

All authors were responsible for the diagnosis, data collection and the design of the work. The author conducted the study, including data analysis and interpretation, and the preparation of the manuscript draft, this last one, with important input with the scientific English from John Giba. All authors approved the final manuscript.

Registration of research studies

It doesn't apply.

Guarantor

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