

# Spontaneous Ovarian Hyperstimulation Syndrome in Association with Pituitary Macro-adenoma in a Non-pregnant Female: A Case Report

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## ***Abstract***

Spontaneous hyperstimulation syndrome (sOHSS) is a rare occurrence in females of child bearing age. It could be gestational or non-gestational. The majority of reported cases are in association with multiple pregnancies and co-occurring hypothyroidism. Here, we report a case of sOHSS in a patient with pituitary macroadenoma which regresses on post treatment of pituitary adenoma and recurs with recurrence of the pituitary adenoma.

**Keywords:** Pituitary Macro-adenoma; Spontaneous Ovarian Hyperstimulation Syndrome.

## **Introduction**

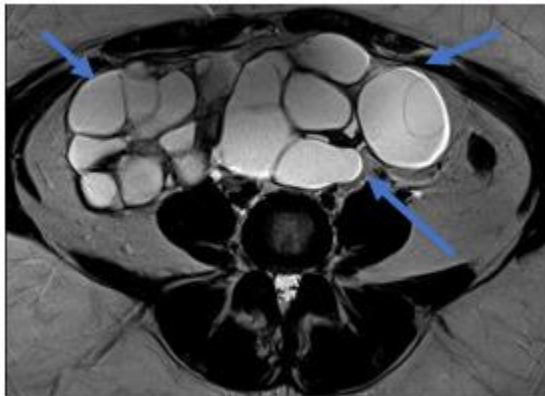
Ovarian hyper-stimulation syndrome (OHSS), is defined as an iatrogenic complication of assisted reproduction technology (ART). The pathogenesis has been described as an exaggerated ovulation process in response to exogenous gonadotrophins. This exaggeration manifests in excessive production of Corpa Lutea, which are proangiogenic structures, promoting neovascularisation of the highly permeable perifollicular vessels. This ultimately results in a massive fluid shift from intravascular to the third space compartment leading to intravascular hypovolemia, overt with clinical fluid overload, resulting in cardiac, renal and liver impairment in severe forms, expediting death in severe cases.<sup>1</sup> Spontaneous ovarian hyper-stimulation syndrome (sOHSS), although rare, has been reported in association with multiple pregnancy, hypothyroidism and polycystic ovarian syndrome (PCOS). The pathogenesis is not fully understood, but two main theories have been suggested to explain it; hypersecretion of glycoprotein hormone, and/or genetic mutation of FSH receptor.<sup>2</sup> Identified clinical manifestations of the disease include enlarged ovaries with multiple follicular cysts, manifesting in abdominal discomfort and pain, and increased vascular permeability and hence fluid accumulation in dependent areas, resulting in ascites, pedal and pulmonary oedema and pleural effusion.<sup>3</sup> The diagnosis is dependent on signs and symptoms identified by clinical assessment, and aided by radiological investigations. The history of exogenous gonadotropin administration is crucial to make a conclusive diagnosis of OHSS.<sup>3</sup> This paper reports a peculiar case of sOHSS in a young non-pregnant female, which has been extensively managed by a multidisciplinary team in two tertiary institutes; The Royal Hospital and Khoula Hospital, with a focus on the imaging findings at each follow-up.

## Case Report

A 28 years old non-pregnant obese lady with no history of ART, presented to our institution with headaches, visual disturbances, galactorrhoea and secondary amenorrhea for 6 months. Her medical background includes obesity and PCOS. Clinical examination revealed a soft non-distended abdomen. Neurologic examination was remarkable for right lower quadrant hemianopia. Biochemical investigations showed negative bHCG levels. Hormonal assessment showed normal thyroid screen and FSH level, elevated prolactin levels of 405 (Iu/L) and Estradiol level of 1095, depressed LH levels of 0.5 Iu/L. Other routine laboratory investigations were unremarkable.

Abdominal imaging with ultrasound then Magnetic Resonance Imaging (MRI) of the pelvis revealed hugely enlarged bilateral ovaries; 48 mL right ovary volume and 28 mL left ovary volume, occupied by multiple variable sized follicular cysts. Further characterisation by MRI shows hypertrophied central stroma bilaterally with features suggestive of ovarian hyperstimulation syndrome [Figure 1]. Concordant brain MRI [Figure 2] showed a 1.3x1.1x1.0 cm lesion occupying the pituitary gland fossa with progressive enhancement on dynamic contrast study leading to pituitary macroadenoma diagnosis.

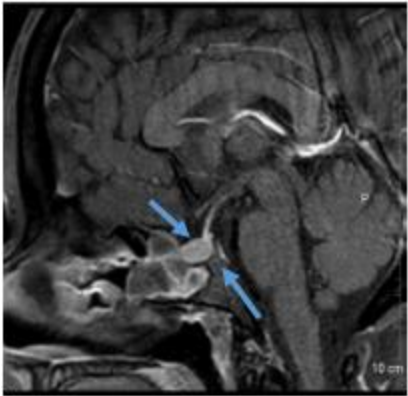
Initial medical management with dopamine agonist resulted in minimal improvement in her symptoms and, therefore, she underwent trans-sphenoidal resection of the pituitary macro-adenoma. Unfortunately, a follow up MRI [Figure 3] done 4 months after the surgery showed a residual lesion measuring 1x0.7x0.6 cm, although there was clinical improvement of the patient's symptoms. A follow up pelvis MRI [Figure 4] was performed as well and showed resolution of ovarian hyper-stimulation features. Four years later, her symptoms recurred. At this time, the laboratory investigations showed similar findings as the initial presentation with negative hCG and thyroid screening, but notably elevated prolactin levels of 21364 Iu/L, normal FSH levels of 6.2 Iu/L and suppressed LH levels of 0.5 Iu/L. A follow up MRI brain [Figure 5] showed interval increase in the size of pituitary macro-adenoma measuring 1.4x1.2x1.2 cm and a follow up pelvis MRI [Figure 1c] showed recurrence of bilateral ovarian hyper-stimulation features. Due to persistent symptoms, the patient underwent another surgery for the pituitary adenoma.



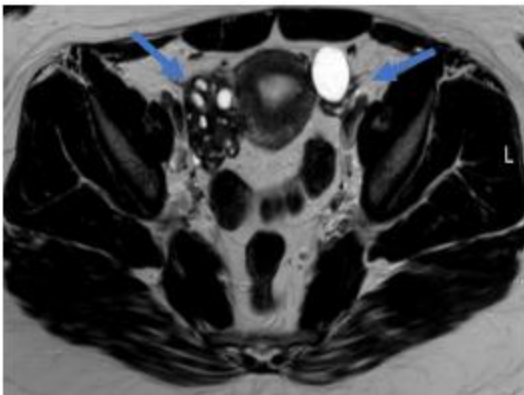
**Figure 1:** Serial Pelvis MRI examinations on axial plane T2-weighted-images at the time of initial presentation demonstrating hugely enlarged ovaries with stromal hypertrophy (arrows).



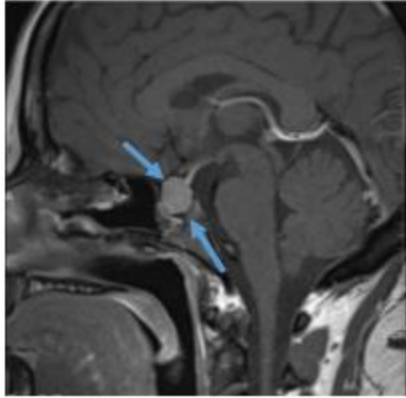
**Figure 2:** Serial Pituitary MRI examinations. Initial pituitary MRI sagittal T1-weighted-image demonstrating a 1.3 cm pituitary macro-adenoma (arrows).



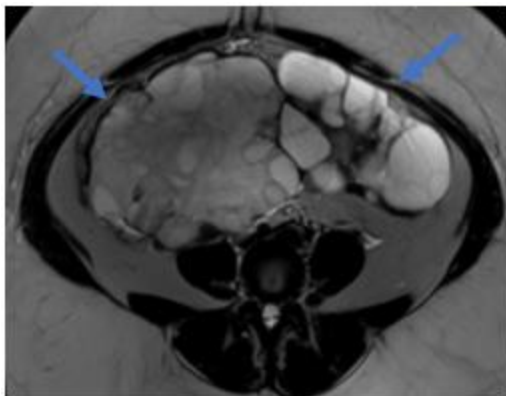
**Figure 3:** A 4-months follow up post-surgical resection sagittal T1 post-contrast image demonstrating a small residual lesion measuring up to 1.0 cm (arrows) and



**Figure 4:** Follow up 4 months after pituitary macroadenoma resection demonstrating interval resolution of the enlarged multicystic ovaries with normal appearance of the ovaries (arrows).



**Figure 5:** A 4-year follow up demonstrating interval increase in size of the pituitary macroadenoma measuring up to 1.4 cm at the time of symptoms recurrence.



**Figure 6:** Follow up at 4 years of surgery at the time of recurrence of the patient's symptoms demonstrating recurrence of the marked enlargement of the ovaries with multiple follicles and prominent stroma in keeping with recurrence of ovarian hyperstimulation syndrome (arrows).

## Discussion

sOHSS is a rare disease that is seen in females of childbearing age. Its pathogenesis is not well studied nor understood. However, several risk factors have been identified, including multiple pregnancies, hypothyroidism, PCOS, young age, low body weight and previous sOHSS. Our subject in this study is a young female, who had previous history of sOHSS and PCOS. She was however, not pregnant, did not have hypothyroidism, and had a high body mass index. sHOSS is associated with high levels of bHCG levels, hence, a strong association with pregnancy, which causes an abnormally high level of neovascularisation, causing a fluid shift to the extravascular compartments. Our case had bHCG levels of  $<1$  at each visit, and have not been pregnant since the onset of her symptoms. However, she was diagnosed with FSH secreting pituitary macroadenoma, which was the attributed cause of sOHSS in her case. Though FSH levels were within the normal ranges at each analysis (16.3 and 6.2 Iu/L). The clinical manifestations of the disease include abdominal pain and distension and ascites, of which, our patient have had none. Rather, she presented with headaches, nausea, amenorrhoea, and visual disturbances, on a background of a history of PCOS.

Radiological investigations using ultrasound, Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) usually yield the same findings in sOHSS cases. These findings typically are symmetrically enlarged ovaries, usually more than 12 cm in size, multiple non-uniform cysts, giving a 'spoke-wheel' appearance, in addition to associated free fluid in the abdomen.

Our patient had symmetrical enlargement of her ovaries, with multilobulated cysts of varying sizes, with the characteristic spoke-wheel appearance.

Similar cases of FSH secreting macroadenomas causing sOHSS, in non-pregnant patients with normal thyroid function have been reported<sup>5,6,7</sup>. All of which have suggested surgical resection of the macroadenoma as the standard treatment of choice. Further suggestions of treatments include radiotherapy and medical therapy with dopamine agonists and somatostatin analogues also reported, though these are case dependent. Our patient have undergone medical treatment with dopamine agonist (cabergoline), for which she did not respond well, then progressed to surgical excision of pituitary macroadenoma.

## Conclusion

We report a rare cause of spontaneous ovarian hyperstimulation syndrome secondary to FSH secreting pituitary macroadenoma in a young non-pregnant female with no history of ART or thyroid disease with emphasis on interesting serial pelvic MRI and pituitary MRI examinations at the time of initial presentation, follow up after first surgical pituitary macroadenoma resection and at the time of pituitary macroadenoma recurrence with recurrence of the sOHSS.

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