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CASE REPORT

Spontaneous Ovarian Hyperstimulation Syndrome in a Young Nonpregnant Female: A Diagnostic Dilemma

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Introduction

Ovarian hyperstimulation syndrome (OHSS) is usually an iatrogenic disorder and associated with ovulation induction therapy with exogenous gonadotropins administration for in-vitro fertilization [1]. Only few cases have been reported of spontaneous OHSS development without conception or without any therapy for ovulation induction [2–4]. This case report describes association of spontaneous ovarian hyperstimulation with primary hypothyroidism in a young female. Informed consent has been taken from the patient before describing the case here.

Case Report

A 15-year-old, unmarried female presented to the emergency with complain of heavy menstrual bleeding, abdominal distension and pain since two weeks. Abdominal pain was dull aching, non-radiating and mild in intensity. Physical examination revealed pallor and pedal edema. Her skin was dry and had hoarseness of voice. Abdominal examination showed mild distension. Local examination revealed mild bleeding PV. Urine pregnancy test was negative.

Investigations revealed severe anemia with hemoglobin – 2 g/dL and International normalized ratio (INR) – 1.14. She was transfused 2 units of packed RBCs. Ultrasonography (USG) of pelvis showed grossly enlarged multicystic bilateral ovaries. Right ovary measured 8 cm*11 cm*5.3 cm (AP*TRANS*CC; volume 240 cc), and largest cyst has diameter of 35*27 mm. Left ovary measured 8.6 cm*4.6 cm*7.6 cm (AP*TRANS*CC; volume 160 cc), and largest cyst has diameter of 46*31 mm (Fig. 1). Uterus was normal in shape and size. Mild ascites was present. Serum CA-125 value was within normal limits. Hormonal evaluation revealed T3—0.38 ng/ml (normal 0.7–2.0 ng/ml), T4 1.7 µg/dl (normal 5.5–13.5 µg/dl), TSH (thyroid hormone stimulating hormone)—413.2 µIU/ml (raised) (normal 0.3–4.25.0mIu/ml), anti TPO (thyroid peroxidase antibody)—804.0 U/ml, βhCG < 2mIU/ml (normal), serum prolactin—47.17 ng/ml (raised), serum luteinizing hormone (LH)—0.02 mIU/ml (mildly reduced), serum follicle stimulating hormone (FSH)—9.55 mIU/ml (normal), and serum estradiol—200 pg/ml (raised).

Based on all the investigations and imaging studies along with clinical findings, diagnosis of spontaneous ovarian hyperstimulation was made. Endocrinologist opinion was taken, and patient was started on tablet levothyroxine 100 µg/day.

She was followed up after 3 months. Her symptoms were resolved and repeat thyroid profile was- T3- 1.20/T4-9.40/TSH—50 µIU/ml. Repeat USG pelvis showed markedly decrease in size of ovaries. Right ovary measured 6.39 cm*3.81 cm*5.31 cm (AP*TRANS*CC, volume 67.74 cc). Left ovary measured 6.51 cm*2.64 cm*5.28 cm (AP*TRANS*CC, volume 47.49 cc), (Fig. 2). She was symptomatically better, her periods became normal, abdominal distension decreased and size of both ovaries significantly reduced.

Discussion

OHSS is most often iatrogenic and sometimes life-threatening complication of controlled ovarian hyperstimulation. Rarely, high levels of human chorionic gonadotropin (HCG) in normal pregnancy, hypothyroidism, or FSH receptor mutation leads to spontaneous OHSS. There are

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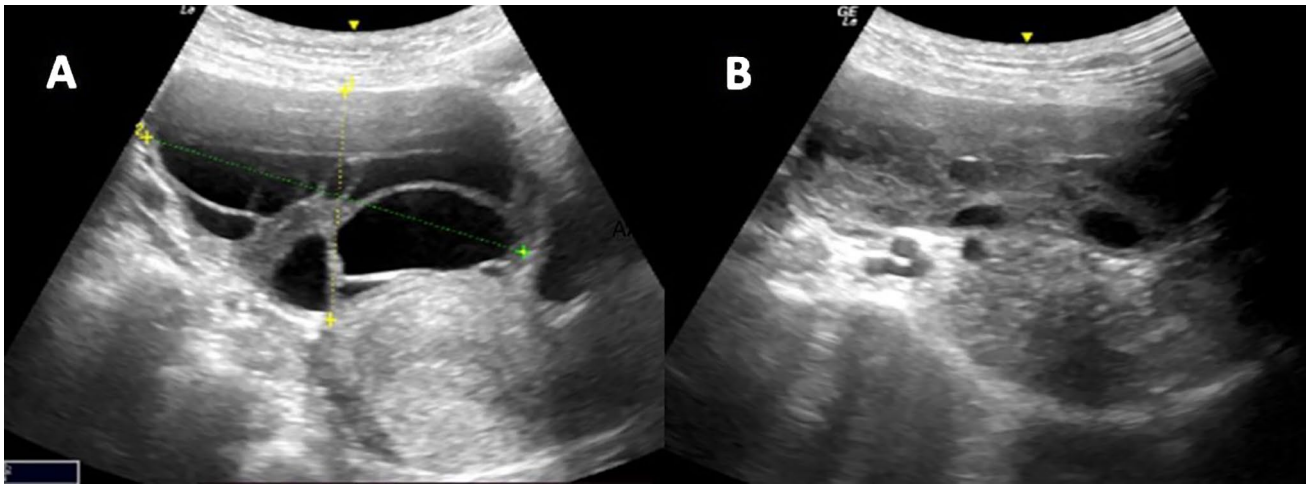

Fig. 1 Right (**A**) and left (**B**) ovaries: grossly enlarged with multiple cysts with spoke wheel appearance

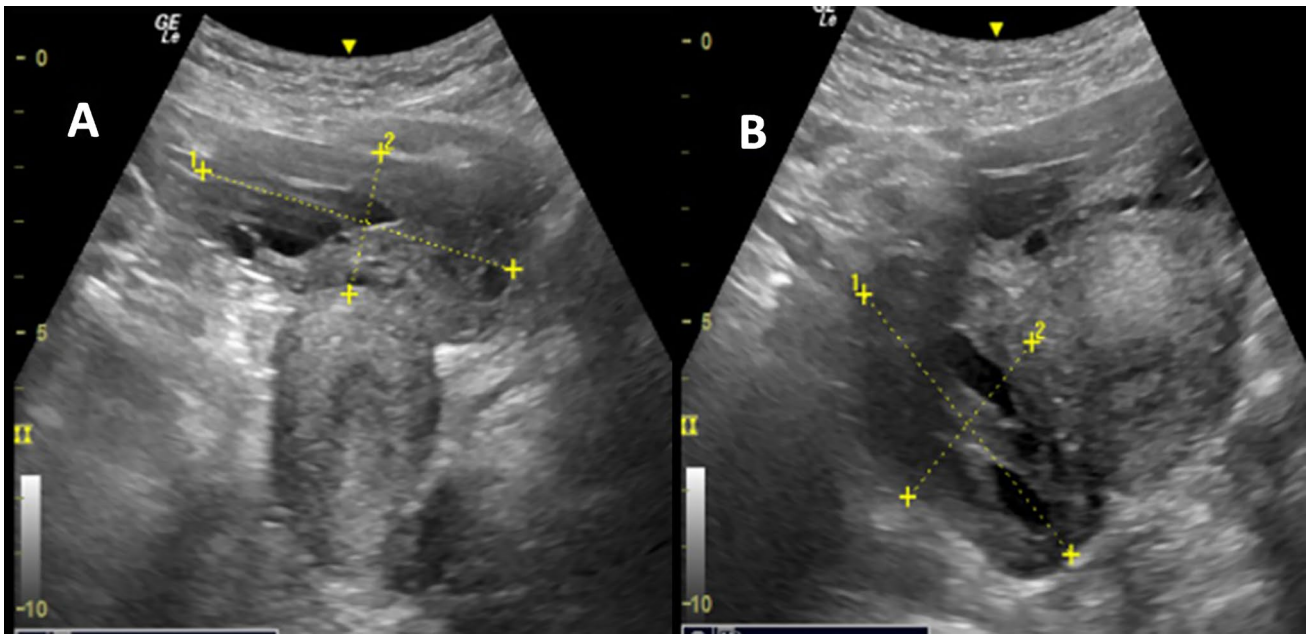

Fig. 2 Right (**A**) and left (**B**) ovaries: post treatment

very few cases of spontaneous OHSS in non-pregnant adolescent girls [2, 4].

The pathophysiology of spontaneous OHSS and its association with hypothyroidism is still not clear. The postulated mechanisms are: (a)excessive production of less potent estriol, leads to decreased feedback regulation resulting in excessive gonadotropin release, which would result in spontaneous OHSS in those subjects [4]; (b) in females with hypothyroidism high levels of thyroid-stimulating hormone can directly stimulate ovaries and can lead to ovarian hyper stimulation; and (c) mutations of the FSHR gene can cause ovarian hyper-responsiveness to circulating FSH or even cross-responsiveness of FSHR to hormones having a structure similar to FSH, such as HCG or TSH. The clinical manifestations of OHSS are usually due to an increase in capillary permeability of mesothelial surfaces. Gonadotrophins leads to activation of certain vasoactive substances such as vascular endothelial growth factor (VEGF), cytokines (IL-2, IL-6, and IL-8), tumor necrosis factor-alpha (TNFα) resulting in increased vascular permeability and extravascular fluid accumulation in OHSS. The patients of OHSS usually have varied presentation depending upon the severity of the disease. The clinical manifestations are abdominal pain, abdominal

distension, discomfort, nausea, vomiting, diarrhea, ascites, pleural and pericardial effusion, hypovolemia, oliguria, hemoconcentration, electrolyte imbalance, etc. Radiological findings of both spontaneous and iatrogenic OHSS include enlarged multicystic ovaries with typical finding of spoke wheel appearance. This ovarian morphology can be demonstrated on transabdominal ultrasonography as shown in our case (Fig. 1). Only few cases of spontaneous OHSS with hypothyroidism have demonstrated this typical radiological finding. However, ovarian malignancy is important differential diagnosis and needs to be excluded. There are few case reports where laparotomy has been done before excluding diagnosis of ovarian tumor and spontaneous OHSS was later confirmed on histopathological report [2, 4]. In another report, the patient underwent unilateral oophorectomy and contralateral ovarian cystectomy before the diagnosis of spontaneous OHSS was made leading to compromise of future fertility.

Timely diagnosis and management of spontaneous OHSS is very important to prevent the occurrence of severe complications. Mild and moderate cases often require only monitoring and symptomatic treatment. Severe cases require critical care including correction of hypovolemia, acid–base disorders, and electrolyte imbalance, diuretics, paracentesis and thrombolytic therapy. Surgery may be required in cases of ruptured cyst, haemorrhage or torsion [2].

Unlike other cases, our case presented with complain of heavy bleeding. The other cases of sOHSS in adolescent girls presented with abdominal distension and pain. In our case patient had menstrual complain along with abdominal distension. Our case was managed conservatively as reported previously. There was resolution of the cystic ovarian enlargement with appropriate treatment of the underlying cause, as shown in our case within three months after initiation of thyroid hormone replacement therapy.

Conclusion

Spontaneous OHSS due to hypothyroidism in non-pregnant women is a rare clinical entity and it may present as abdomen distension or menorrhagia. High index of suspicion and thorough investigations are required for definitive diagnosis of OHSS and to avoid unnecessary surgical interventions in these patients. This subject requires further study and knowledge of this rare condition among treating physicians is very essential.

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Declarations

Conflict of interest The authors report no financial or other conflict of interest relevant to this study.

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