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Original Research Paper

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UNCOMMON PRESENTATION OF SPONTANEOUS OVARIAN HYPERSTIMULATION SYNDROME TRIGGERED BY PRIMARY HYPOTHYROIDISM : CLINICAL INSIGHTS AND CASE SERIES ANALYSIS

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ABSTRACT Ovarian hyperstimulation syndrome (OHSS) is completely iatrogenic and unique to stimulatory infertility treatment. OHSS secondary to treatment with exogenous gonadotropins, clomiphene citrate, gonadotropin releasing hormones has been described extensively in the literature. However, OHSS has been rarely reported in women with hypothyroidism during naturally conceived pregnancy. Very few cases have been reported in a women who is neither pregnant nor undergoing ovulation therapy suggesting uncommon presentation of hypothyroidism.

KEYWORDS : Primary hypothyroidism, spontaneous Ovarian hyperstimulation syndrome, Thyroid stimulating hormone, thyroxine.

INTRODUCTION:

Ovarian hyperstimulation syndrome (OHSS) is a complication commonly associated with women undergoing ovulation induction therapy for in vitro fertilization, with an incidence of 0.2-1%. Spontaneous OHSS is extremely rare in naturally conceived pregnancies. OHSS in the absence of exogenous gonadotropin is very rare and only a few cases have been reported in the literature.[1,2,3,4,5,6,7,8] The condition was first reported by Van Wyk and Grumbach in 1960[9] as a combination of polycystic ovaries, primary hypothyroidism and precocious puberty. Since then, there have been sporadic reports of OHSS[10,11,12,13]. Spontaneous OHSS in pregnancy typically occurs between 8-14 weeks of gestation, while iatrogenic OHSS generally occurs between 3-8weeks of gestation[14,15].

Case report:1

A 23 year old female presented to the casualty with a history of amenorrhoea for 2 months and complaints of abdominal distension and breathlessness for the past week. On examination, her vitals were stable, but her oxygen saturation on room air was 92%. Abdominal examination revealed a grossly distended abdomen with a fluid thrill++. She was admitted for further management.

Initial investigations revealed a low hemoglobin level (7.5gm/dl) with normal serum total protein and albumin levels. An ultrasonography of the abdomen and pelvis revealed bilaterally enlarged ovaries with multiple enlarged follicles; the largest measuring 4.5*4.2cms in the right ovary and 7.0* 4.3cms in the left ovary, with few follicles showing internal hemorrhagic changes with septations, suggestive of ovarian hyper-stimulation syndrome. There was also an early live intrauterine pregnancy of approximately 10weeks and 6days gestation, along with gross ascites containing echoes. There was no history of primary infertility or intake of ovulation induction drugs.

Based on the radiological findings, the patient was evaluated for ovarian malignancy. Elevated levels of serum alpha fetoprotein and CA 125 detected, while serum Beta HCG and serum ADA levels were normal. Ascitic fluid tapping revealed a serum ascites albumin gradient (SAAG) ratio of <1.1. Ascitic fluid culture sensitivity showed no bacterial growth and ascitic fluid cytology was normal.

To evaluate the cause further, thyroid profile was done, which revealed a significantly elevated serum thyroid stimulating hormone (TSH) level of >100 microIU/ml and a low free thyroxine (T4) level of 1.10mcg/dl.

Based on the clinical, laboratory and radiological findings, a diagnosis of spontaneous ovarian hyperstimulation syndrome was made and the patient was started on Tab Thyroxine 75 microgram OD for one and half months and discharged with advise to follow up after one and half months.

Upon follow up, thyroid function tests were repeated,which showed a mild increase in serum T4 level (4.60microgram/dl) with TSH levels remaining high. A subsequent ultrasound showed a mild reduction in the size of the largest follicle in the right ovary to 2.4*2.8cm and 7*3.6 cms in the left ovary, with complete resolution of ascites. The dose of Tab Thyroxine was increased to 100microgram OD and advised to follow up in another month and a half.

At this follow up, serum TSH levels had decreased to 15.11 microIU/ml and T4 levels were within the normal range at 10.03mcg/dl. Pelvic Ultrasonography showed normal bilateral ovaries and a single live intrauterine pregnancy of 29 weeks 4 days gestation.

Patient was followed up until term, delivering a healthy female baby weighing 2.5kgs via vaginal delivery. A post delivery ultrasound revealed bilateral normal ovaries.

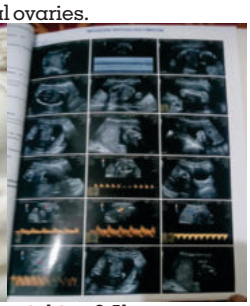

Fig 1. Image of healthy female baby weighing 2.5kgs
Fig 2. Ultrasound image with B/L normal ovaries after starting

levothyroxine

Case report 2:

A 24 year old female presented to the out patient department with a history of one and half months of amenorrhea, intermittent pain abdomen for the past 8 days, difficulty and increased frequency of micturition. She has had regular menstrual cycles in the past with a married life of 1 year.

Her initial blood tests were normal, and urine for Beta HCG was negative. Pelvic ultrasonography revealed well defined anechoic lesions with thin septations in the bilateral adnexal region, with no evidence of internal vascularity. The lesions measured 9.51*5.88cms on the left side and 11.06*6.38cms on the right side, suggestive of bilateral benign ovarian neoplasm (serous cystadenomas).

Based on these radiological findings CA125 levels were assesed and found to be raised (95.87 U/ml). Thyroid evaluation revealed a TSH level of >100 microIU/ml and a slighttly low T4 level of 4.18mcg/dl. The patient was started on Tab Thyroxine 100mcg OD and was advised to follow up in out patient department after 6weeks.

Upon follow up, the repeat TSH level decreased to 28.593microIU/ml and the T4 value of normalised to 7.980mcg/dl. A repeat ultrasound of the pelvis showed bilateral normal ovaries with no evidence of cysts. The dose of Tab Thyroxine was increased to 125mcg OD for the next 6weeks.

On further follow up, the repeat TSH level normalised to 1.2microIU/ml.

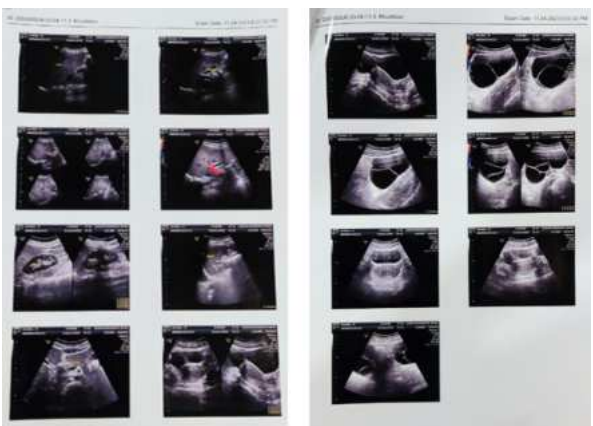

Fig 1&2: Pelvic ultrasonography images showing well defined anechoic lesions with thin septations in the bilateral adnexal region, with no evidence of internal vascularity

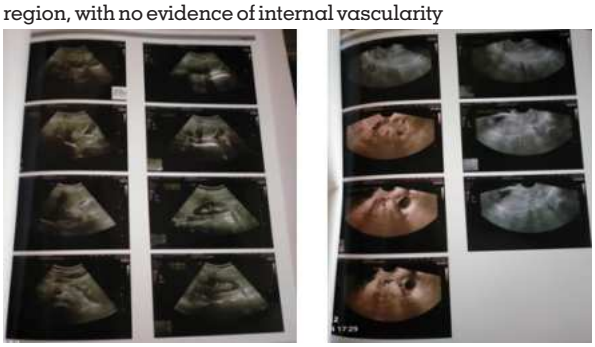

Fig 3 &4 : Pelvic ultrasonography images post treatment with Tab Thyroxine

DISCUSSION:

Spontaneous OHSS can occur both in pregnant and non-pregnant women. De Leener[16] classified spontaneous OHSS syndrome into three types based on clinical presentation and FSH receptor mutation.

- Type I is associated with the mutated FSH receptor and this type may cause recurrent spontaneous OHSS.
- Type II is secondary to high levels of human chorionic gonadotropin (hCG) as in hydatiform mole and multiple gestation and is the most frequent one.
- Type III is related to hypothyroidism.

Golan and Weissman[17] classified OHSS (both spontaneous and iatrogenic) into three categories with five grades based on the clinical manifestation and imaging findings:

Mild OHSS: presence of bilateral multicystic enlarged ovaries; Grade 1 shows abdominal distention and discomfort, while Grade 2 presents with additional nausea, vomiting, and/or diarrhea and enlarged ovaries measuring 5–12 cm.

Moderate OHSS: represents Grade 3 and presents with features of mild OHSS plus evidence of ascites on ultrasound.

Severe OHSS: presents as Grade 4 with clinical evidence of ascites and/or hydrothorax and dyspnea and Grade 5 with change in blood volume, hemoconcentration, coagulation abnormalities, and diminished kidney perfusion and function.

The pathophysiology of spontaneous Ovarian Hyperstimulation Syndrome (OHSS) associated with hypothyroidism is not well studied. Some explanations include: (a) In hypothyroid patients, there is an excessive production of estriol via the 16-hydroxylation pathway, instead of the normal 2-hydroxylation pathway. This may lead to excessive gonadotropin release due to reduced feedback regulation, as estriol is less potent than estradiol. This could potentially result in spontaneous OHSS in affected individuals. (b) Elevated levels of thyroid-stimulating hormone (TSH) in women with hypothyroidism may directly stimulate the ovaries, leading to ovarian hyperstimulation.[6]

Activating mutations of the FSHR gene can cause ovarian hyper-responsiveness to circulating FSH or cross-responsiveness to hormones with structures similar to FSH, such as human chorionic gonadotropin (hCG) or TSH. A mutation in the hCG/LH receptor gene has been linked to an increased ovarian response to normal hCG levels, leading to ovarian hyper-responsiveness.

It is imperative that all health care providers, including gynecologists, surgeons and physicians should consider hypothyroidism and other endocrine disorders in the differential diagnosis of adult females presenting with multicystic ovarian tumors to avoid unnecessary and catastrophic ovarian resection.[9]

In non-pregnant subjects, the clinical presentation of spontaneous OHSS ascites, ovarian enlargement and pleural effusion may misdiagnose this condition as advanced ovarian malignancy and may end up in exploratory laparotomy. Hence, proper evaluation and correct diagnosis are important for the prevention of mismanagement.

Rarity of this condition may also be due to misdiagnosis and by missing the diagnosis that can result in mismanagement or severe complications of this condition

CONCLUSION:

Spontaneous ovarian hyperstimulation syndrome secondary to hypothyroidism may be the cause of ovarian enlargement and Levothyroxine replacement seems an appropriate primary therapeutic option. Proper endocrinological assesment of patients is recommended as it may avoid unfavourable outcomes.

This case series describes a rare clinical course of a pregnant women with severe hypothyroidism who presented with OHSS , in whom oophorectomy was considered and a non pregnant female with features of OHSS.

Primary hypothyroidism is an endocrine pathology highly

prevalent globally, and the failure to recognise it as a possible etiology of ovarian cysts can lead to inadvertant oophorectomy.

REFERENCES.

1. Ahmed Kamel RM. Spontaneous ovarian hyperstimuation syndrome in a naturally conceived singleton pregnancy. Fertil Steril. 2010;94:351. e.1-4.
2. Cardoso CG, Graça LM, Dias T, Clode N, Soares L. Spontaneous ovarian hyperstimulation and primary hypothyroidism with a naturally conceived pregnancy. Obstet Gynecol. 1999;93:809–11.
3. Edwards-Silva RN, Han CS, Hoang Y, Kao LC. Spontaneous ovarian hyperstimulation in a naturally conceived pregnancy with uncontrolled hypothyroidism. Obstet Gynecol. 2008;111:498–501.
4. Yamashita Y, Kawamura T, Fujikawa R, Mochizuki H, Okubo M, Arita K. Regression of both pituitary and ovarian cysts after administration of thyroid hormone in a case of primary hypothyroidism. Intern Med. 2001;40:751–5.
5. Taher BM, Ghariabeh RA, Jarrah NS, Hadidy AM, Radaideh AM, Ajlouni KM. Spontaneous ovarian hyperstimulation syndrome caused by hypothyroidism in an adult. Eur J Obstet Gynecol Reprod Biol. 2004;112:107–9.
6. Bassam T, Ajlouni K. A case of ovarian enlargement in severe primary hypothyroidism and review of the literature. Ann Saudi Med. 2006;26:66–8.
7. Kubota K, Itho M, Kishi H, Igarashi S, Minegishi T. Primary hypothyroidism presenting as multiple ovarian cysts in an adult woman: A case report. Gynecol Endocrinol. 2008;24:586–9.
8. Shu J, Xing L, Zhang L, Fang S, Huang H. Ignored adult primary hypothyroidism presenting chiefly with persistent ovarian cysts: A need for increased awareness. Reprod Biol Endocrinol. 2011;9:119.
9. Van Wyk JJ, Grumbach MM. Syndrome of precocious menstruation and galactorrhea in juvenile hypothyroidism: an example of hormonal overlap in pituitary feedback. J Paediatr. 1960;57(3):416•435.
10. Panico A, Lupoli GA, Fonderico F, Colarusso S, Marciello F, Poggiano MR, et al. Multiple ovarian cysts in a young girl with severe hypothyroidism. Thyroid. 2007;17:1289–93.
11. Gordon CM, Austin DJ, Radovick S, Laufer MR. Primary hypothyroidism presenting as severe vaginal bleeding in a prepubertal girl. J Pediatr Adolesc Gynecol. 1997;10:35–8.
12. Ryan GL, Feng X, d'Alva CB, Zhang M, Van Voorhis BJ, Pinto EM, et al. Evaluating the roles of follicle-stimulating hormone receptor polymorphisms in gonadal hyperstimulation associated with severe juvenile primary hypothyroidism. J Clin Endocrinol Metab. 2007;92:2312–7.
13. Browne LP, Boswell HB, Crotty EJ, O'Hara SM, Birkemeier KL, Guillerman RP. Van Wyk and Grumbach syndrome revisited: Imaging and clinical findings in pre- and postpubertal girls. Pediatr Radiol. 2008;38:538–42.
14. Smits G, Olatunbosun O, Delbaere A, Pierson R, Vassart G, Costagliola S. Ovarian hyperstimulation syndrome due to a mutation in the follicle-stimulating hormone receptor. N Engl J Med. 2003;349:760–6.
15. Zalel Y, Katz Z, Caspi B, Ben-Hur H, Dgani R, Insler V. Spontaneous ovarian hyperstimulation syndrome concomitant with spontaneous pregnancy in a woman with polycystic ovary disease. Am J Obstet Gynecol. 1992;167:122–4.
16. De Leener A, Montanelli L, Van Durme J, Chae H, Smits G, Vassart G, et al. Presence and absence of follicle-stimulating hormone receptor mutations provide some insights into spontaneous ovarian hyperstimulation syndrome physiopathology. J Clin Endocrinol Metab. 2006;91:555–62.
17. Golan A, Weissman A. Symposium: Update on prediction and management of OHSS. A modern classification of OHSS. Reprod Biomed Online. 2009;19:28–32