Brief Communication

Huge bilateral ovarian cysts in adulthood as the presenting feature of Van Wyk Grumbach syndrome due to chronic uncontrolled juvenile hypothyroidism

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ABSTRACT

Juvenile primary hypothyroidism causing cystic ovaries and pseudoprecocious puberty (Van-Wyk Grumbach syndrome (VWGS)) is well documented in literature. There are only a few reports of primary hypothyroidism presenting as ovarian cysts in adults. Here we present a case of huge bilateral ovarian cysts in adulthood as the presenting feature of VWGS due to chronic uncontrolled juvenile hypothyroidism. Large uniloculor right ovarian cyst (119 × 81 × 90 mm) and a multicystic left ovary (55 × 45 × 49 mm) were detected in a 24 year lady with secondary amenorrhea, galactorrhea, and palpable abdominal mass with history of neonatal jaundice, delayed milestones, short stature, and precocious menarche at age of 7.5 years age. She had elevated levels of cancer antigen (CA)-125 which normalized post levothyroxine supplementation. Elevated CA-125 may lead to misdiagnosis of ovarian carcinoma and inadvertent treatment. Bilateral ovarian cysts in adults are a rare presentation of juvenile hypothyroidism. It is necessary to screen for primary hypothyroidism in patients presenting with bilateral ovarian cysts to prevent unnecessary evaluation and treatment.

Key words: Juvenile hypothyroidism, ovarian cysts, von grumbach syndrome

Introduction

Cases of multicystic ovaries with primary hypothyroidism have been reported in girls as a cause of pseudoprecocious puberty,[1,2] and in adult females with abdominal pain.[3] The ovarian cysts are thought to be due to increased ovarian sensitivity to gonadotropins[4] or more likely an action of increased circulatory levels of thyroid stimulating hormone (TSH) (secondary to chronic untreated primary hypothyroidism) on follicle stimulating hormone (FSH) receptor (FSHR) causing gonadal stimulation.[5,6] Here we report a case of juvenile primary hypothyroidism presenting in adulthood as abdominal mass due to huge bilateral ovarian cysts.

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Case Report

A 24-year-old woman presented to us with history of secondary amenorrhea, galactorrhea, abdominal pain, and distension of 6 months duration. Detailed inquiry revealed history of prolonged neonatal jaundice, delayed developmental milestones, short stature, and poor scholastic performance since childhood. She attained menarche at age of 7.5 years. She had irregular cycles with duration varying from 30 to 45 days with 4-6 days flow till 6 months back when she developed secondary

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amenorrhea. Examination was significant for short stature (height: 114.2 cm; <3rd percentile, standard deviation score (SDS)), weight 25.3 kg (<3rd percentile; SDS), subnormal intelligence, facial puffiness, pallor, pedal edema, dry coarse skin, and cold extremities. Thyroid was not palpable. She had spontaneous galoctorrhea from her left breast. Heart sounds were muffled. Abdominal examination revealed a painless palpable cystic mass sized 11 cm × 10 cm involving the whole abdomen [Figure 1]. She had delayed relaxation of deep tendon reflexes.

Investigations revealed microcytic hypochromic anemia, elevated serum TSH (>75 μIU/ml), elevated prolactin (>150 ng/ml) with low free thyroxine (T4) and luteinizing hormone (LH). FSH levels were normal. Serum for tumor markers revealed elevated CA-125 levels, normal beta human chorionic gonadotropin (HCG), and alpha fetoprotein [Table 1]. Blood glucose, liver function tests, renal function tests, and electrolytes were normal. Abdominal ultrasonography and computed tomography showed a large uniloculor cystic SOL in right adnexa measuring 119 × 81 × 90 mm and a multicystic SOL in left adnexa measuring 55 × 45 × 49 mm suggestive of ovarian cysts [Figure 2]. The uterus was bulky with thickened heterogeneous cervix. Moderate pericardial effusion was noted on echocardiography. Levothyroxine was started at 50 μg per day which was gradually increased to 100 μg per day over 4 weeks. Last evaluated 12 weeks after the initial diagnosis, there was resolution of pericardial effusion, reduction in size of bilateral ovarian cysts along with normalization of CA-125 levels.

Discussion

Hypothyroidism presenting during childhood with pseudoprecocious puberty and ovarian cysts is a well-defined condition, but rare in today's world. Widespread use of neonatal screening program has led to diagnosis of most of the patients of congenital hypothyroidism in the neonatal period. Van Wyk and Grumbach first reported multicystic ovaries with precocious puberty in patients with hypothyroidism in 1960.[1] There are a few reports of adult hypothyroid patients presenting with ovarian cysts.[3] These patients usually present with abdominal pain, menorrhagia, and hypothyroid symptoms. Our patient in contrast presented with an abdominal mass secondary to huge ovarian cysts and secondary amenorrhea. Precocious menarche at 7.5 years age likely due to pseudoprecocious puberty was missed during her childhood, so were the neonatal and overt clinical features of primary hypothyroidism.

Several hypotheses about the mechanism of ovarian cyst formation associated with hypothyroidism have been proposed. Firstly; structural similarities between TSH, FSH, and their receptors may have some role. Extremely high levels of TSH can bind to FSHR and lead to activation of follicular cells. In bioassays, human recombinant TSH has been noted to bind to FSHR and cause a dose dependent cyclic adenosine monophosphate (c-AMP) elevation.[5] A second explanation is changes in the gonadotropin levels seen in severe hypothyroid patients. They may have relatively high FSH levels and low LH levels. This is proposed to be due to the overlap effect of increased thyroid-releasing

Table 1: Biochemical investigations

Parameter	Value
Free T4 (0.80-1.90)	0.56 ng/dl
TSH (0.40-4.0)	>75 μIU/ml
FSH	9.60 IU/l
LH	<0.10 IU/l
Prolactin (1.9-25)	>150 ng/dl
CA-125 (<35)	66.7 IU/ml
Beta hCG (<8)	0.26 mIU/ml
Alpha fetoprotein (0.1-10)	7.10 ng/ml

T4: Thyroxine, TSH: Thyroid stimulating hormone, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, CA: Cancer antigen, hCG: Human chorionic gonadotropin

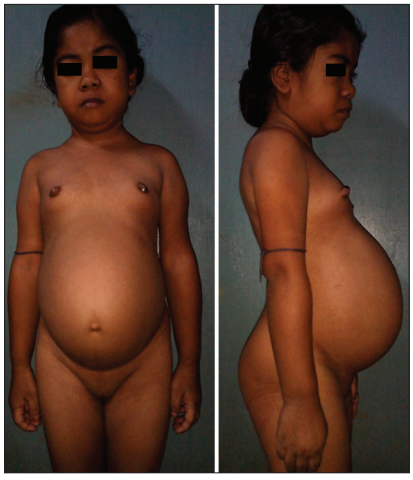

Figure 1: Photograph showing abdominal distension and galactorrhea from left breast

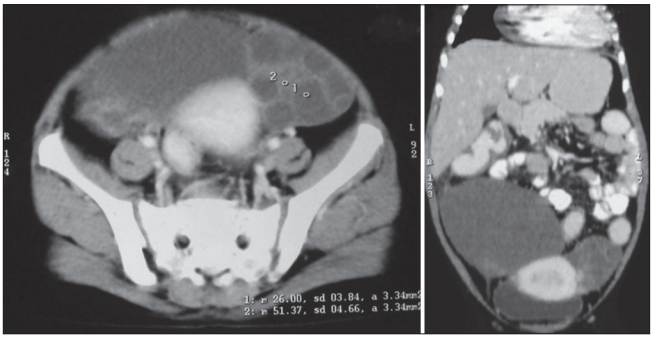

Figure 2: Computed tomography showing right unilocular ovarian cyst and left multicystic ovary

hormone (TRH) in primary hypothyroid patients.[1] The isolated rise in FSH is believed to be due to the slowing of the gonadotropin-releasing hormone (GnRH) pulse frequency in primary hypothyroidism. Low LH may also be explained by the presence of hyperprolactinemia due to increased TRH which can lead to decreased GnRH secretion.[7] A third possible mechanism has been hypothesized to be due to FSHR activating mutations permitting or amplifying the effect of hCG or TSH on the follicles.[8] Fourthly, TSH may have some sensitizing effect on ovaries to gonadotropin stimulation by stimulation of thyroid nuclear receptors in the granulosa cells.[9] Also interference in steroidogenesis by myxedematous-type infiltration of ovaries in hypothyroidism might contribute to cystic changes in ovaries.

Our patient had a high level of CA-125. Such high levels have been documented in hypothyroid patients without any malignancy.[10] Failure to diagnose hypothyroidism in patients ovarian cysts and elevated CA-125 levels may lead to misdiagnosis of ovarian carcinoma and inadvertent treatment. Such patients respond to thyroid hormone replacement with normalization of CA-125 post levothyroxine supplementation.

Conclusion

Bilateral ovarian cysts in adults are a rare presentation of juvenile hypothyroidism. They may mimic ovarian carcinoma in the presence of elevated CA-125 levels. It is necessary to screen for primary hypothyroidism in patients presenting with bilateral ovarian cysts to prevent unnecessary evaluation and treatment.

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