Undiagnosed Hypothyroidism Presenting as Recurrent Bilateral Large Ovarian Cyst in an Early Adolescent Girl - A Rare Case Report

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ABSTRACT

Hypothyroidism may manifest as large ovarian cyst formation with precocious puberty in young pre-pubertal girls, which frequently regress upon starting thyroxin supplementation. We present a case report of a 10 year old girl who had undergone unnecessary laparoscopic cystectomy for bilateral large ovarian cyst as the diagnosis of hypothyroidism was missed. She again had recurrence of bilateral ovarian cyst which regressed upon thyroxin supplementation.

Key words: hypothyroidism, ovarian cyst, precocious puberty

INTRODUCTION

Van Wyk and Grumbach in the year 1960, first described a syndrome characterised by breast development, uterine bleeding and multi-cystic ovaries in the presence of longstanding primary hypothyroidism.[1] Extensive work-up including laparotomy is often resorted in many of these patients because of lack of proper work-up. It is important to recognise this syndrome because unnecessary ovarian surgery can be avoided as the clinical features, in particular ovarian enlargement, can be reversed with thyroxine replacement alone.[2,3] We describe a case of spontaneous resolution of recurrence of bilateral large ovarian cyst in a 10 years old girl with juvenile hypothyroidism associated with precocious puberty with thyroid hormone therapy.

CASE REPORT

A 10 years old girl was referred from Gynaecology unit of our hospital to our Paediatric OPD for evaluation of recurrent large ovarian cyst. She had history of laparoscopic cystectomy for bilateral large ovarian cyst four months back. Her documents revealed that she had then presented to gynaecologist with pain abdomen of 10 days and two episodes of vaginal bleeding one month apart. Her CT scan before surgery showed well defined, large, thin walled, multilocular cyst with fine internal septation in bilateral adnexal region (Right: 9.4 X 9.3 X 8.2 cm; Left: 8.9 X 9.2 X 10.1 cm) and uterus was normal in size for age (figure 1). Histopathology study after surgery of both side cyst walls showed features of simple serous cyst. After three months of surgery, her mother noticed progressively increasing abdominal distension when she again visited the same gynaecology unit. This time she was evaluated with abdominal ultrasound which again showed bilateral multiloculated anechoic cystic structure of 8.6 X 5.4 cm (Right) and 12.7 X 9.3 cm (Left) with soap bubble appearance (Figure 2). She was then again planned for re-laparoscopic surgery. Meanwhile she was then referred to us for expert opinion regarding recurrent ovarian cyst.

During our evaluation, her mother complained that the girl is lethargic, sleepy most of the time and has chronic constipation since last six months besides her increasing abdominal distension. On examination her skin was coarse and dry, she seemed to be inactive. She had short stature (Height < 3rd centile) and her weight was 35 kg. There was breast enlargement but no pubic or axillary hair growth and she had two episodes of vaginal bleeding (B3 P1 M1). Her vaginal examination showed pink vagina. We suspected juvenile hypothyroidism with precocious puberty and

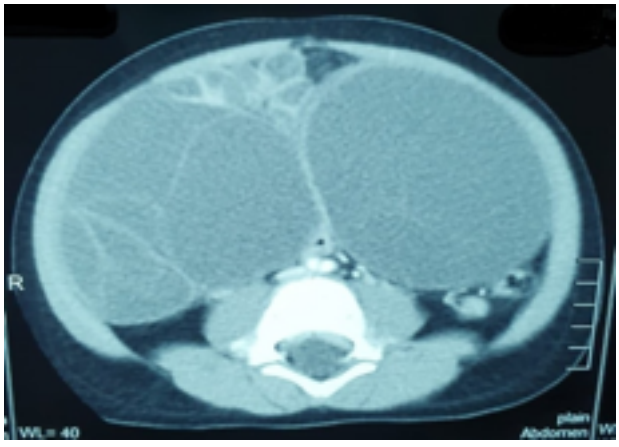

Figure 1. Figure 1. Transabdominal CT scan image s/o well defined large, thin walled multilocular cystic mass measuring 9.4 X 9.3 X 8.2 cm with multiple fine internal septae in right adnexae and mass of 8.9 X 9.2 X 10.1 cm of similar nature in left adnexae likely serous cystadenoma.

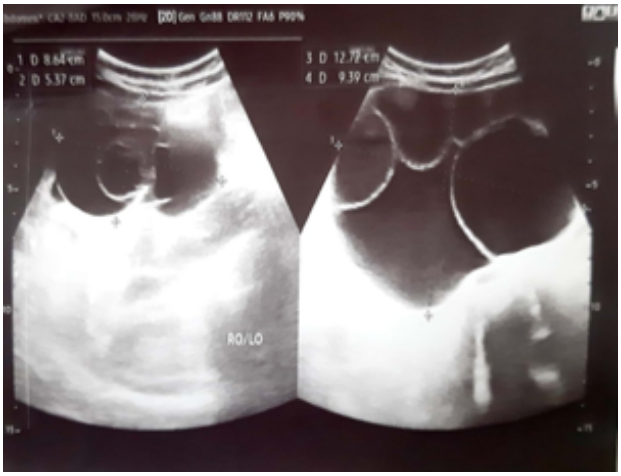

Figure 2. Abdominal ultrasound shows bilateral multiloculated anechoic cystic structure of 8.6 X5.4 cm (Right ovary) and 12.7 X 9.3 cm (Left ovary) with soap bubble appearance.

ordered for thyroid function test (TFT), leutinizing hormone (LH), follicle stimulating hormone (FSH) and anti- TPO antibody, bone age. Her TFT showed, very high thyroid stimulating hormone (TSH) level (188.6 µIU/ml) and low total triiodthyronine (T3) and total thyroxine (T4) (54 ng/dl and 0.9 µg/dl respectively). Her Anti-TPO was high to the range of 128.0 U/ml. Her FSH, LH and estradiol was in pre pubertal range. Her bone age was retarded corresponding to seven years of age. This confirmed our diagnosis and she was then started purposely with low dose of thyroxine (1.5 µgm / kg), 50 µg once a day and increased gradually to 75 and then 100 µg (3 µgm / kg) at her latest visit in four months of starting with thyroxine.

She had no further episodes of vaginal bleeding, and all her TFT returned to normal / expected values with TSH : 0.66 micro IU/ml. Her pelvic ultrasonography show left ovary (3.9 X 2.8 x 2.5 cm) and right ovary (3 X 2.5 x 1.5 cm) with a dominant follicle. Her constipation has resolved and she has become active normally as her mother compares with her other siblings. She is still under our follow up.

DISCUSSION

Hypothyroidism is a frequently encountered endocrine disorder, and severe untreated juvenile hypothyroidism may manifest as precocious puberty with ovarian enlargement. Any pre-pubertal child presenting with ovarian masses should be examined for signs of precocious puberty and tested for hypothyroidism. The pathophysiology of sexual precocity in juvenile hypothyroidism is not yet clear. It has recently been shown that TSH could interact directly with the FSH receptor to elicit gonadal stimulation resulting in ovarian cysts formations.[4] This is probably due to the ‘‘spill-over effect’’ of the glucoprotein hormones: TSH, which is markedly increased in hypothyroidism, and has a small FSH- and LH-like effect. This stimulation of the FSH receptor resulting in the subsequent development of multiple ovarian cysts and the production of high levels of estradiol stimulate the development of secondary sexual characteristics in prepubescent girls. Adrenal hormonogenesis is not increased, therefore pubic and axillary hairs are usually absent or sparse as also found in our patient.

However the response of the FSH receptor to TSH is assumed to be dose dependent, as only very few children, all with extremely high TSH levels, are affected. The glycoproteins TSH, FSH, LH and hCG share a common α-subunit but have a unique β-subunit that is specific to each hormone. They each act through transmembrane GPCRs to activate adenylate cyclase and stimulate cAMP production.[8] Anasti et al. showed that recombinant human TSH elicited a dose-dependent response at the human FSH receptor. The TSH concentration required was several orders of magnitude higher than FSH, demonstrating that the FSH-like activity of TSH is very low. They went on to show that TSH and FSH are acting through the same receptor and that TSH competitively antagonises FSH. This response was not generic for all glycoproteins as adenylate cyclase activity in transfected cells was unresponsive to hCG.[4]

Phenotypically, these girls show the classical ‘hypothyroid’ appearance, delayed growth; FSH mediated secondary sexual characteristics with breast development with or without galactorrhoea; uterine bleeding but absence of significant pubic or axillary hair development. Imaging studies typically reveal enlarged multicystic ovaries with follicular development, a pubertal uterus, enlarged pituitary gland, and unique to this cause of sexual precocity, delayed bone age. There is evidence that ovarian cysts associated with juvenile hypothyroidism disappear spontaneously after the institution of thyroid hormone therapy and improve final height achieved. Most cases in the literature are secondary to autoimmune thyroid disease but

there are some case reports where the syndrome is secondary to unrecognised congenital hypothyroidism.[3,6] Chen et al. reported a case of ectopic thyroid with congenital hypothyroidism presenting with bilateral multicystic ovaries without marked precocity.[7] The cystic ovaries disappeared dramatically after thyroid hormone therapy. In our patient too, the bilateral ovarian cyst as well as other features of precocity disappeared rapidly after therapy and this avoided unnecessary repeat invasive surgical procedure.

CONCLUSIONS

Here we highlight the importance of working up for hypothyroidism in the evaluation of sexual precocity with cystic ovaries and an expectant management of the ovarian cysts along with thyroid hormone therapy is recommended which obviates the need for extensive diagnostic work-up and invasive procedures.

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