**Case Report**

**True hermaphrodite presenting as primary amenorrhea**

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**ABSTRACT**

True hermaphrodite is one of the rare variety of disorders of sex development. Most of them are genotypically females (46 XX) and present as under virilized males. Features of hyperandrogenism are present in those reared as females. The commonest histological variety of gonad found in them is ovotestis, which is at risk for malignancy. We report a girl with 46 XY true hermaphrodite without ovotestis presenting as primary amenorrhea and isolated clitoromegaly in the absence of any other features of virilization.

**Key words:** Disorders of sex development, true hermaphrodite, ovotestis

**INTRODUCTION**

Ovotesticular disorder of sex development (DSD) is a rare disease. Most commonly, they present with genital ambiguity. However, the phenotype may vary from normal female to normal male appearance. Here, we are describing a case of 46 XY Ovotesticular DSD who presented as primary amenorrhea.

**CASE REPORT**

The index case, a 21-year-old female came to gynecology OPD with complaint of primary amenorrhea (pubarche: 15 yrs and thelarche: 18 yrs). She weighed 69 kg and her height was 160 cm. General physical examination was within normal limits (no features suggestive of hypothyroidism, Cushing’s syndrome, or Acromegaly). Her Tanner staging was B2P5A2. External genitalia examination revealed clitoromegaly (5 cm), separate vagina, and urethra openings. There was no labial fusion. Vagina was admitting one finger, but cervix could not be felt. No gonad was palpable in labia or inguinal regions. She was born out of non-consanguineous marriage and ante-natal history was not contributory. There was no similar complaint in the family.

In view of primary amenorrhea with clitoromegaly, serum total testosterone, LH, FSH, 17-OH Progesterone, DHEAS, thyroid profile, and prolactin were measured. All of the above hormone investigations were normal except raised serum total testosterone [4.78 ng/ml (0.15 to 0.81)], LH [20 mIU/ml (0.80 to 7.6)], and FSH [30 mIU/ml (0.7 to 11.1)]. Ultrasound pelvis revealed hypoplastic uterus (4.8 cm × 1.65 cm × 0.847 cm) and bilateral ill-defined gonad like structures high up in pelvis. At this point of time, mosaic Turner’s syndrome (45 X/46 XY) was kept as the first possibility. But the Karyotype revealed 46 XY, so the clinical diagnosis was changed to partial gonadal dysgenesis. MRI abdomen and pelvis was advised to locate the gonads precisely. However, the patient was lost to follow up after that.

The patient came only after 3 years at the age of 24 years. This time, she was more concerned about clitoromegaly rather than primary amenorrhea. Anthropometry revealed: height: 168 cm, weight: 75 kg, BMI: 26.60 kg/m², upper segment: 74 cm, lower segment: 94 cm, and arm span: 180 cm.
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Tanner staging was B2P4A1 and clitoromegaly had regressed from 5 to 4 cm. Hormone investigations revealed a decrease in serum total testosterone from 4.78 to 0.93 ng/ml and a further increase in gonadotrophins (LH: 31.4 mIU/ml and FSH: 53.3 mIU/ml). MRI showed hypoplastic uterus with thin endometrial cavity but could not localize gonads. So, diagnostic laparoscopy was planned. Intraoperatively, vaginal length was 10 cm, cervix and uterus were hypoplastic with B/L normal fallopian tubes in situ, left side showed tubular gonad and right side had spherical gonad. B/L gonadectomy and clitoral resection were carried out in the same sitting. Histopathology of left and right gonad revealed ovarian follicle with flattened cuboidal lining epithelium [Figure 1] and hyalinized seminiferous tubules with Leydig cells [Figure 2], respectively. Finally, she was diagnosed as true hermaphrodite. Post-operative period was uneventful. At discharge from hospital, she was started on estrogen replacement and the plan was to add progesterone after breakthrough bleeding.

**DISCUSSION**

The disorders of sex development (DSD) is an uncommon disorder with an incidence of 1:4500 to 1:5000 live births. True hermaphrodite (Ovotesticular DSD) is responsible for 4% to 10% of cases of DSD but this is the most common type of intersex disorder among South African blacks. The frequency of different Karyotype found among true hermaphrodite are 46 XX (60%), 46 XX/46 XY (30%), and 46 XY (<10%). In a study by Bhansali et al. from a tertiary care center in India, only one case of 46 XY Ovotesticular DSD was detected among seven true hermaphrodite patients over 10 years. Our patient belongs to this rare category.

Patients with Ovotesticular DSD are classified according to the type and location of the gonads. Lateral cases (20%) have a testis on one side and an ovary on the other. Bilateral cases (30%) have testicular and ovarian tissue present bilaterally, usually as ovotestis. Unilateral cases (50%) have an ovotestis present on one side and an ovary or testis on the other. The ovary is more frequently found on the left side, whereas the testis is found more often on the right like in our patient (lateral variety of Ovotesticular DSD).

A majority of true hermaphrodite patients present with genital ambiguity with or without palpable gonads and most of them are reared as males. However, the appearance of external genitalia varies from normal female with mild clitoromegaly to normal male. The index case had clitoromegaly without any ambiguity or palpable gonad. This feature is suggestive of more severe dysgenesis of gonad and is also supported by the presence of mullerian structures adjacent to testicular tissue (Rt. Side). An unusual feature of this patient was the absence of hirsutism in spite of increased serum testosterone level and clitoromegaly. This can be explained by the differential sensitivity of pilosebaceous units (PSUs) to serum androgen in different patients.

Another interesting finding in our patient was the progressive decrease in functional testicular tissue over time (a decrease in serum testosterone from 4.78 to 0.93 ng/ml with mild regression of clitoromegaly over 3 years). Similar reports have been described in the literature. Because of this phenomenon, the gonads which were initially visible in ultrasound could not be localized in MRI after 3 years. The important issue related to intra-abdominal testicular tissue is the risk of development of gonadal tumor, e.g. gonadoblastoma. The risk is more in case of gonadal dysgenetic syndromes compared to true hermaphrodite (15% to 35% vs. 0.2% to 0.4%). As the true hermaphrodite is itself a rare disease and most of the cases have 46 XX...
Karyotype, the exact risk of development of gonadal tumor among 46 XY Ovotesticular DSD (e.g. the index case) is not known. In most of the patients with true hermaphrodite, the diagnosis is made by the pathologist only after gonadectomy like in our patient. However, it is important to retain at least the ovarian tissue in case of true hermaphrodite patients with uterus as few cases with successful pregnancy are there in the literature.[10]

In summary, true hermaphrodite should be kept as one of the differential diagnosis of primary amenorrhea particularly in the presence of hyperandrogenism. Not all patients develop cutaneous manifestations of androgen excess, e.g. hirsutism because of differential sensitivity to androgens. Detailed physical examination and step-wise investigations including karyotype will pick up these cases. Various factors including the possible diagnosis (gonadal dysgenesis vs. true hermaphrodite), presence of Y-chromosome, sex of rearing and the scope of fertility should be taken into consideration before doing gonadectomy.

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