

CASE REPORTS

46 XX, SRY Negative Ovotesticular DSD

Prashant Kaduskar¹, KM Suryanarayana², Prakash Babu³, Vijaya Mysorekar⁴**Abstract**

46 XX ovotesticular DSD is a rare disorder. It presents with cryptorchidism, hypospadias or ambiguous genitalia at birth, gynaecomastia in adolescent stage or infertility in adult age. We report here a 20 year old phenotypically male who presented with gynaecomastia and found to have testis on right side and left inguinoscrotal swelling consisting of ovary, uterus and fallopian tubes. Evaluation revealed SRY negative 46 XX karyotype. He underwent surgical removal of ovary and mullerian structures. The highlight of case is development of testicular tissue in absence of SRY gene.

Introduction

Ovotesticular DSD (Disordered sexual differentiation) is an uncommon disorder of sexual development and approximately 500 cases have been reported world-wide in literature.¹ The diagnosis of this disorder requires presence of ovarian and testicular tissue in same or opposite gonad. Differentiation of genital tract and development of secondary sex characters vary in different individuals but usually follows the gonad which is dominant. Hemi uterus or rudimentary uterus is often present on side of the ovary or ovotestis. In addition breast development, cryptorchidism and hypospadias are common manifestations.

Case Report

A 20 year old patient reared as a male presented to endocrinology OPD with history of left inguinoscrotal swelling of 1 month duration and gynaecomastia (Figure 1) of 6 months duration. At the age of 2 years, patient's mother had noticed two streams of urine. He underwent two corrective surgical procedures, between 8 and 10 years of age following which he became asymptomatic. There was no significant contributory family history. Due to poor scholastic performance he discontinued studies after class 7. His gender identity, role and sexual orientation were like a male. There was no history nocturnal penile tumescence.

On examination: Vitals were normal. Height: 175 cm, Arm span: 184 cm, Upper segment: 86 cm, Lower segment: 89 cm, US: LS: 0.87, Weight: 60 kgs, BMI: 19.60 kg/m². SPL – 8 cm, 2 opening visible on ventral aspect, right testicular volume – 8 ml. Left inguinoscrotal swelling: Two separate swellings palpable-Upper swelling 2 x 2 cm, soft, non-tender, extending from left inguinal region up to base of scrotum with positive cough impulse. Lower swelling 1x1 cm, fluctuating, non-tender. His SMR A3, P4. He had grade 4 gynaecomastia (Figures 1 and 2). Systemic examination was within normal limits.

Investigations

CBC : Hb : 12.4 gm/dl, TLC : 9610 (4000-11,000), DLC : Normal ESR : 23 mm at the end of 1 hour (0-20), Platelet count : 3,24,000/mm³ (1,50,000-4,00,000), FBS : 80 mg/dl (70-110) PPBS : 85 mg/dl (70-140)

Hormonal profile : T3 : 1.32 ng / dl (1.23-3.23), T4 : 87.63 ug / dl(59-135), TSH : 0.899 uIU / ml (0.5-4.3), FSH : 10 mIU/ ml (1.5 – 12.4), LH : 12.06 mIU/ ml (1.7 – 8.6), Testosterone : 3.85 ng /ml (1.8 – 7.63), Estradiol : 40.49 pg / ml (< 39.8)

USG pelvis: Well-defined hypoechoic area measuring 31 x 15 mm in left scrotum suggestive of ovary, Right

scrotal sac shows testis measuring 25 x 11 mm. A well-defined cystic area adjacent to ovary measuring 11 mm.

MRI pelvis: Testes is seen in the scrotal sac on right side, inguinal hernia on left side with herniation of structure that looks like ovary. Inferiorly loculated fluid collection that measures 19 X 20 X 12 mm suggestive of encysted hydrocele. Uterus not identified; prostate not visualized (Figures 3 and 4).

Chromosomal and FISH analysis: Chromosomal analysis of cultured peripheral blood from male patient revealed female 46 XX chromosome complement (Figure 5). Patient sample confirmed presence of two X chromosomes and absence of SRY (Sex determining Region on Y chromosome) – Negative for SRY gene

Patient underwent surgery for left inguinoscrotal swelling. Surgical repair of hernia was done. Hernial sac examination revealed uterus, fallopian tube and ovary (Figure 6). He has been advised reduction mammoplasty for gynaecomastia.

Histopathology

Gross examination: Uterus with ovary with fallopian tube were seen. Uterus measured 5 x 2 x 2 cm ; endometrial thickness was 1 mm ; Left ovary measured : 3.5 x 1.5 x 1 cm; fallopian tube was measuring 2 cm.

Microscopic examination: Sections from the uterus showed tubular endometrial glands. Sections from the ovary showed predominantly showed fibrotic areas. The fallopian tube showed mucosal plicae.

Discussion

Ovotesticular DSD is rare disorder. It has 3 types: 1. Lateral-(20%) have a testis on one side and an ovary on the other 2. Bilateral - (30%) have testicular



Fig. 1: Gynaecomastia



Fig. 2: Female type pubic hair distribution

and ovarian tissue present bilaterally, usually as ovotestes. 3. Unilateral- (50%) have an ovotestis present on one side and an ovary or testis on the other. It is a rare condition, with a frequency of 1:20,000-25,000 male newborns and was first described by La Chapelle and cols. in 1964.² On basis of the analysis and detection of SRY gene, 46, XX male patients can be clinically divided into **SRY-positive** and the **SRY-negative** group. SRY region was thought to be necessary for determining maleness. However, presence of normal males without SRY region on X chromosome proves that other factors apart from SRY also contribute to maleness of a person.

SRY-positive individuals: 90% of 46 XX ovotesticular DSD are SRY positive. Patients in this group have normal male genitalia, small azoospermic testes and hypergonadotropic hypogonadism.³ Most carry the SRY gene translocated to X chromosome.⁴ Diagnosis is achieved in adulthood during infertility investigation.

SRY- negative individuals – 10 % of 46 ovotesticular XX DSD are SRY negative. This group includes patients with ovotesticular DSD : presence of both testicular and ovarian tissue in the gonads of the same individual in absence of SRY on X chromosome.⁵ Development of the testis and normal male genitalia in SRY-negative 46,XX males suggests existence of other



Fig. 3: MRI: Upper arrow → ovary, lower arrow → hydrocele



Fig. 4: MRI: Right scrotal sac → testis

autosomal or X-linked genes in the sex-determining pathway. The maleness in the absence of SRY gene is explained by several mechanisms. The up-regulation or super-expression of some members of SOX family (SRY-related HMG-box) has been proposed as one of the mechanisms. McElreavey *et al.* (1993) proposed that SRY acts by inhibiting a regulatory autosomal recessive gene, termed 'Z', whose product normally inhibits the male pathway.⁶ Two different studies have shown the duplication of a region of the long arm of chromosome 22 in a XX true hermaphrodite.⁷

In this particular case, the diagnosis was done only when patient had inguinoscrotal swelling and gynecomastia at an adult age. In a recent case series of ovotesticular DSD from India⁸ inguinoscrotal swelling and genital ambiguity before puberty and gynecomastia and cyclical hematuria after puberty were common presentations in ovotesticular DSD cases. Ovotesticular DSD should be considered as one of the differential diagnoses in any case of ambiguous genitalia with nonpalpable or asymmetrical gonads, pubertal gynecomastia, and cyclical hematuria.

Conclusion

46 XX ovotesticular DSD is a rare case. Such patients need timely diagnosis and management by a



Fig. 5: Karyotype

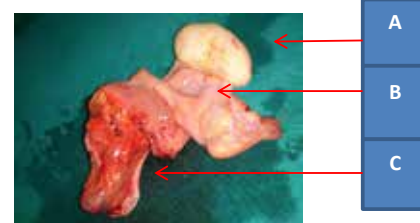


Fig. 6: Operative specimen: Uterus, fallopian tube and ovary

multidisciplinary team consisting of endocrinologist, pathologist, urologist, surgeon, psychiatrist and geneticist for better health.

Acknowledgements

We are sincerely grateful to Dr. K. M. Suryanarayana, Senior Professor and Head of Department of Endocrinology for evaluating this case.

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