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Swyer Syndrome: A Rare Cause of Primary Amenorrhoea

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Abstract
Swyer syndrome, which is pure XY gonadal dysgenesis, is an extremely rare condition, presents with primary amenorrhea, female phenotype and male genotype with fibrous streak gonads. We report a case of Swyer syndrome in a 20 year old girl who presented with primary amenorrhoea and poorly developed secondary sexual characters. Investigations revealed normal thyroid and prolactin levels, high levels of gonadotropins and low levels of estrogen and testosterone. Karyotyping revealed 46 XY. After counseling, the girl underwent diagnostic laparoscopy and bilateralgonadectomy in view of high chance of malignancy in the streak gonads. Histopathology of the streak gonads showed bilateral gonadoblastoma with dysgerminoma. The girl was put on hormone replacement therapy and is on regular follow up. The importance of this condition is its rarity leading to delay in diagnosis, the high risk of malignancy in streak gonads necessitating gonadectomy, the need for hormone replacement therapy for life and the chance of conception by in vitro fertilization as the uterus is retained.
Key words: *Swyer syndrome, primary amenorrhoea, 46XY karyotype*

Introduction

Genetic females and males in humans are characterized by the presence of an XX or XY karyotype. Swyer syndrome is characterized by XY karyotype with female phenotype. Dr. GimSwyer first recognized this condition. He described this in two women with 46XY karyotype with primary amenorrhoea. (1)

It is a rare condition, the subjects are reared as females and there is a high chance of malignancy in the streak gonads. We describe a case of Swyer syndrome presenting with primary amenorrhoea.

Case Report

A 20 year old girl presented to our outpatient department with primary amenorrhoea and delayed development of secondary sexual characters. There was no similar history in the family members. She gave history of tubercular lymphadenitis 3 years back for which she had received anti tubercular drugs for 6 months. There was no history of cyclical pain abdomen, exposure to radiation or chemotherapy, no features of anosmia, headache or visual symptoms. On examination, she was 152 cm tall, weighing 44

kgs with female phenotype. There was no evidence of acne, hirsutism or goiter. Breast development was tanner stage 2, she had scant axillary hair and pubic hair development was tanner stage 3. There were no features of Turners syndrome. External genitalia showed normal development of labia majora and minora. There was no swelling felt within labia majora or inguinal region suggestive of undescended testis. Hymen was intact without any bulge to show internal collection.

Ultrasound examination revealed infantile uterus with streak ovaries. MRI was done which confirmed the same. Hormonal analysis showed normal thyroid hormone and prolactin levels. Serum gonadotropin levels were elevated.(Follicle stimulating hormone - 60.55 mIU/ml, Luteinizing hormone - 30 mIU/ml) Estradiol and Testosterone levels were low. (15pg/ml, 0.045ng/ml) A karyotype was done which showed 46XY genotype. In view of 46 XY karyotype and presence of streak gonads, tumour markers were done. Serum alpha feto protein, lactate dehydrogenase and beta hcg were within normal limits. As there is high risk of malignancy in streak gonads, it was decided for bilateral gonadectomy. The patient and the family members were counselled regarding the condition and the need for gonadectomy was explained. The girl needed psychiatric counselling. It took 6 months for the family members to give consent for gonadectomy. She underwent laparoscopic bilateral salphingogonadectomy. Intra operative findings were: uterus was small with normal fallopian tubes. Gonads were normal in position but streak. (Pic 1, 2 and 3) Histopathology of the gonads showed features of gonadoblastoma with dysgerminoma and extensive calcification. (Pic 4 and 5). The girl was started on hormone replacement therapy. She is on regular followup from 10 months and is doing well. Breast development has improved to tanner stage 3.

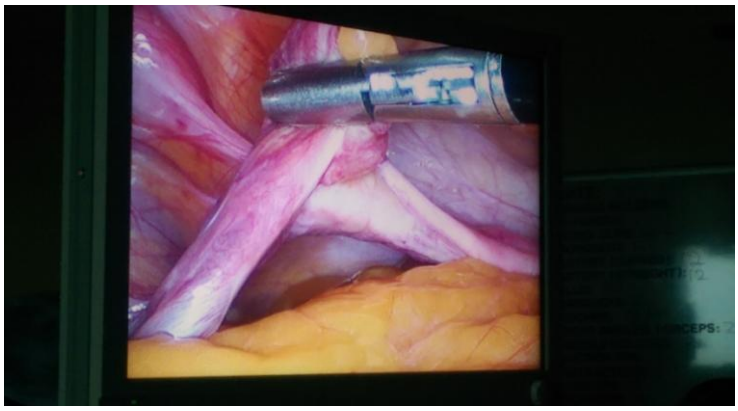

Fig 1: Laparoscopic picture of tube and streak gonad

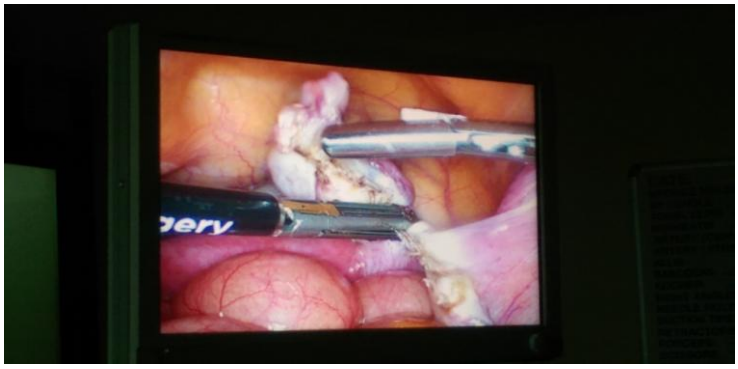

Fig 2: Laparoscopic Gonadectomy

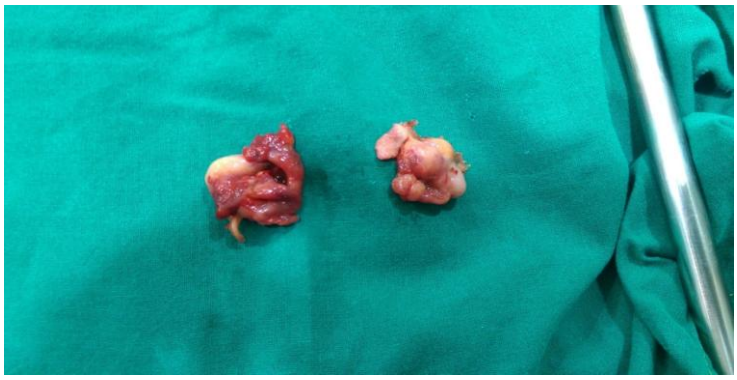

Fig 3: Bilateral streak gonads with normal tubes

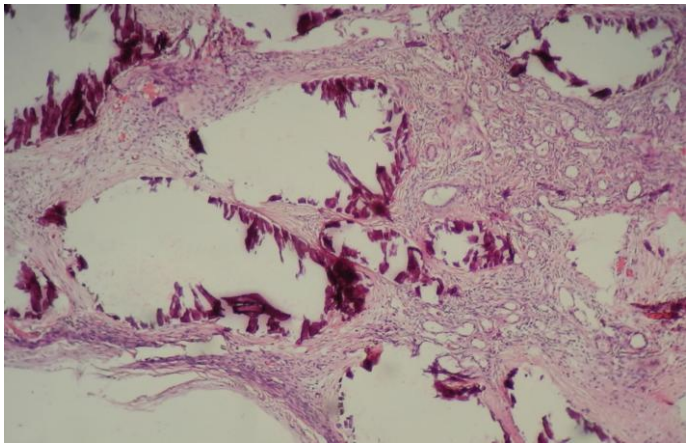

Fig 4: Sertoli component

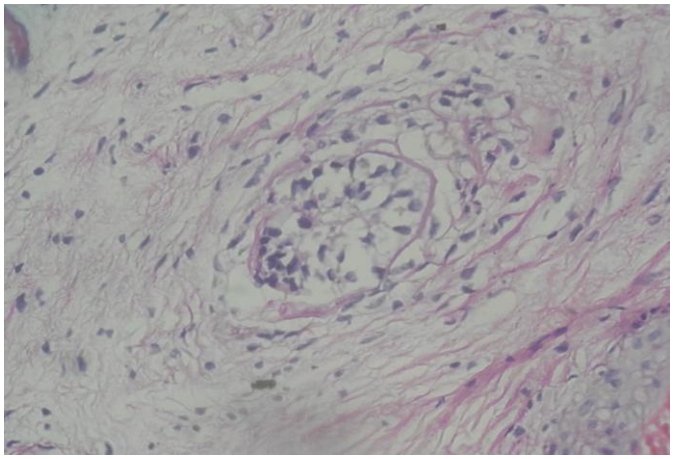

Fig 5: Tubular component

Discussion

Swyer syndrome is an uncommon form of 46 XY gonadal dysgenesis, causing primary amenorrhoea. It is a form of pure gonadal dysgenesis. The first step of sexual differentiation of a normal XY fetus is the development of testes. The early stages of testicular formation in the second month of gestation requires the action of several genes most important is SRY, the sex determining region of the Y chromosome. [(2)] Swyer syndrome arises from an abnormality in testicular differentiation and is thought to be due to a deletion or mutation involving the sex determining region of the Y chromosome [(3)]. It occurs in 1/100000 people [(4)]. The condition first becomes apparent in adolescence with delayed puberty and primary amenorrhoea. Despite having XY chromosomes, the patient with Swyer syndrome appears female and has functional female genitalia and structures including a vagina, uterus and fallopian tubes. In the absence of testes, no testosterone or antimullerian hormone is produced. Without testosterone, the external genitalia fail to virilise, resulting in normal female genitalia. Without anti mullerian hormone, the mullerian ducts develop into normal internal female organs (uterus, fallopian tubes, cervix and upper vagina). [(4)] The child has non functional streak gonads. Because of the inability of the streak gonads to produce sex hormones, most of the secondary sex characters do not develop. Adrenal gland is not affected and can produce androgens and most of these persons will develop pubic hair, though it often remains sparse. [(2)] Upon diagnosis of complete gonadal dysgenesis, the clinician must be aware that there are at least four possibilities of XY females: Androgen insensitivity syndrome, complete gonadal dysgenesis, mixed gonadal dysgenesis and partial gonadal dysgenesis. Distinguishing between these categories can often be quite challenging. [(5)]

Swyer syndrome can be differentiated from complete androgen insensitivity syndrome where the karyotyping is also XY, but there is absence of mullerianstrutures, presence of testes in the path of its descent and high serum levels of testosterone. The individuals are reared as females as phenotypically they appear like females. In Swyer syndrome, disturbances of gonadal differentiation during the early intrauterine development period result in insufficient secretion of testosterone and anti mullerian factor and hence the evolution of internal and external genitalia as female. In 10 – 15% of the cases mutation in the SRY (Sex Determining Region ofY chromosome) gene is the cause. [(6)]

The prompt diagnosis has a crucial importance for several reasons like the early institution of hormone replacement therapy and close monitoring, because of the risk of gonadal malignancy. The major risk is the development of gonadoblastoma.[(7)] The incidence of malignant gondoblastoma in patients with dysgenetic gonads is as high as 25 – 35%. [(2)]The risk increases with age; it is reported that the risk is 50 – 70% in the third decade while being as high as80% in the fourth.[(8)] The overall survival is 90 to 100% in cases diagnosed in the early stages but decreases to 54% in those diagnosed in the advanced stages. [(9)] Hence it is necessary to do early bilateral gonadectomy. Also hormone replacement is necessary to prevent osteoporosis and for development and maintenance of secondary sexual characters.

Another important aspect to be considered here is the psychosocial effect of the condition on the girl and the family. In our case, the family members

were unable to accept the diagnosis. They insisted on reconfirmation of karyotype, which was repeated in another reputed laboratory.

One aspect that is promising in Swyer syndromeis the preservation of uterus and a chance of having pregnancy in future by invitro fertilization. These patients can have a normal sexual life. Creatsasetal reported a case of successful pregnancy in a 35 year old with Swyersyndrome by in vitro fertilization and embryo transfer using donor oocyte. [10]

Conclusion

Swyer syndrome, which is pure XY gonadal dysgenesis is an extremely rare condition. The reason for presenting this case is that there can be delay in diagnosis because of its rarity and the need for early and prompt diagnosis in order to start hormone replacement therapy to initiate and maintain puberty and the need for early gonadectomy to prevent malignancy. Also we wish to highlight the psychosocial effect of XY female on the girl as well as the family and the need to do karyotyping in girls presenting with primary amenorrhoea.

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