Case Report

Swyer syndrome: Reports of 2 cases

Chowdhury TS[a], Ruman U[b], Chowdhury TA[c]

Abstract

Swyer syndrome is a form of pure 46 XY gonodal dysgenesis in which individuals have male chromosomal pattern (46XY) but a female phenotype. One out of five women with the Swyer syndrome have a deletion in the DNA-binding region of the SRY gene, while in the remaining 80–90% of cases, the SRY gene is normal and mutations in other testis determining factors are probably implicated. Early diagnosis is crucial for a number of reasons: first, the risk of gonadal malignancy, second, the early institution of estrogen therapy for induction of puberty and third, to allow for adequate hormone replacement to improve bone mineral density. We present two cases of Swyer syndrome with different presentation

Key words: *Swyer syndrome; gonodal dysgenesis; SRY gene.*

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Introduction

Swyer syndrome is a type of XY chromosomal dysgenesis where the genetic pattern is male even though the affected person is phenotypically female. Jim Swyer first described the condition in medical literature in 1955.[1] The incidence of Swyer syndrome is approximately 1:100 000.[2,3] This condition can occur as a result of a new gene mutation or can be inherited in an autosomal dominant, autosomal recessive, X-linked or Y-linked manner. Mutation of SRY gene is associated in Swyer syndrome in 15 to 20 % of individuals. Mutation in other genes like NR5A1, NR0B1, WNT4 and DHH may also be associated with this condition.[4] These mutations prevent production of the sex-determining region Y protein or result in the production of a nonfunctioning protein. A fetus whose cells do not produce functional sex-determining region Y protein will develop as a female, despite having a Y chromosome. So, the patients' mesonephric ducts are atrophic but paramesonephric ducts develop with the formation of uterus, fallopian tubes and part of the vagina as a result of lack testosterone and antimullerian hormone. Minimal breast enlargement reflects peripheral aromatization of androgens.

Author Informations

a. Dr. Tanzeem S Chowdhury, MBBS, FCPS, MRCOG, Assistant Professor, Dept. of Obstetrics and Gynecology, BIRDEM General Hospital, Dhaka

b. Dr. Umme Ruman, MBBS, FCPS, Classified specialist, Dept. of Obstetrics and Gynecology, Dhaka CMH

c. Prof. T A Chowdhury, FCPS, FRCOG, FRCS, FRCP, Chief Consultant, Dept. of Obstetrics and Gynecology, BIRDEM General Hospital, Dhaka

Address of correspondence: Dr Tanzeem S Chowdhury, Dept. of Obstetrics and Gynecology, BIRDEM General Hospital-2, 1/A, Ibrahim Sarani, Shegun Bagicha, Dhaka- 1000. Email: tanzeemsc@gmail.com

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Case Reports

Case 1

A 16-year-old girl presented with the complaints of primary amenorrhea, hoarseness of voice and hirsutism for one and half years. She was the daughter of a non consanguous parents.Physical examination revealed a phenotypic female measuring 164 cm in height and 60 kg in weight. Her breast devolvement was in Tanner stage 3.Her axillary hair was absent and pubic hair was of female pattern. There was marked clitoromegaly (Figure 1).Vaginal examination revealed a blind vagina.

Ultrasonography (USG) of whole abdomen showed a small uterus (48 mm X 20 mm X 38 mm) with no endometrial interface. There was small right ovary (13 mm X 6 mm) with non visualization of left ovary. Both kidneys and urinary bladder were normal. Detailed hormonal analysis revealed serum FSH- 53.98 mIU/ml (raised than normal range), LH - 6.06 mIU/ml (normal range), Testosterone - 1.43 ng/mL (raised from normal range)and 17-OH Progesterone- 0.35 ng/ml (reduced

Figure 1. *Clitoromegaly in case 1*

from normal range) Chromosomal aneuploidy check was consistent with normal diploid complement of chromosome 13, 18, 21 with a XY genotype and a female phenotype. So, the interpretation was Swyer syndrome or XY gonadal dysgenesis.

Decision was taken to perform laparoscopy. On laparoscopic examination a rudimentary uterus was found in the midline. Gonads were present on both sides together with the proximal parts of the fallopian tubes. Both gonads were small and smooth. Gonads with attached fallopian tubes were removed. Histopathological examination of both gonads revealed testicular tissue and the tubular structures suggestive of epididymal tissue and fallopian tube. No malignancy was detected. The patient came back for follow-up after 7 days and she was prescribed conjugated equine estrogen 0.625mg with cyclic medroxy progesterone acetate andcalcium tablet. Her parents had a detailed counseling session regarding her future reproductive and sexual life and advice was given about the need for vaginoplasty and clitoridectomy in future.

Case 2

A 31-year-old woman presented with the complaints of primary infertility for two years.Her history revealed that her menstruation had not started spontaneously until she started to take estradiolvalerate which was prescribed by a doctor when she was 16 years old. She was treated with oral estrogen for withdrawl bleeding and development of breast since then.

On examination, she was of average body built with average height and weight (152 cm and 62 kg). There was no hirsutism. Axillary hair distribution was normal and breast development was in Tanner stage 4. There was no palpable mass in the inguinal region. She had female distribution of pubic hair and there was no clitiromegaly. External genitalia looked normal and there was no labial swelling. Vagina was well capacious and cervix was normal but hypoplastic.

USG of lower abdomen showed smaller sized uterus. Transvaginal sonography also revealed same findings along with thin endometrium and homogenous myometrium. Right ovary was normal but no follicle was seen. Her serum FSH was 52.47 mIU/l and LH was13.50 mIU/l.TSH, androgen and serum prolactin levels were within normal range.

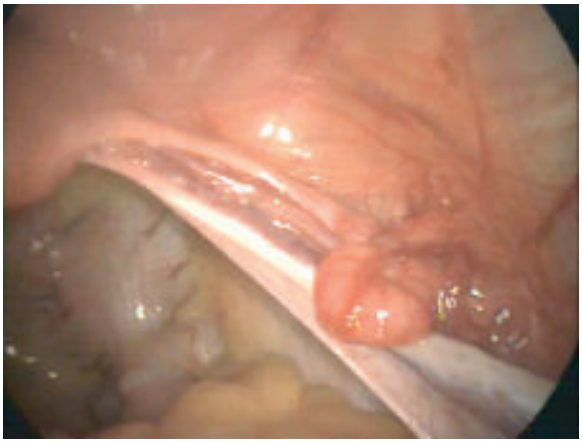

Figure 2a. *Laparoscopic picture of streak gonads in case 2*

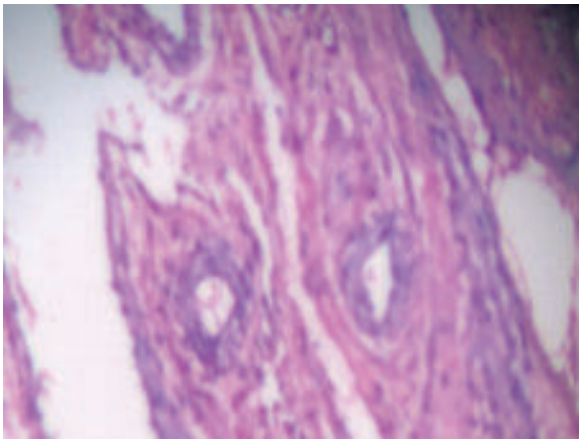

Figure 2b. *Microscopic view of streak gonads in case 2*

The result of chromosomal aneuploidy check was consistent with normal diploid complement of chromosome 13, 18 and 21, with a XY genotype and a female phenotype and the diagnosis was Swyer syndrome.

Laparoscopy and gondal biopsy was planned. On laparoscopy uterus was found to be small but normal in shape, both fallopian tubes were present with bilateral streak gonads (Figure 2a). Biopsy was taken from left gonad. Histopathology revealed fibrocollagenous tissue partly lined by mesothelial cells (Figure 2b). No ovarian follicle, seminiferous tubules or epididymal ducts were seen, so gonadectomy was not considered. She was given combined estrogen and progesterone pills and tablet calcium post operatively. She was counseled about the diagnosis and was advised strongly for regular yearly follow up for detection of any early signs of malignancy

Discussion

The diagnosis of Swyer syndrome is made on detailed patient history, systemic clinical evaluation including height and a variety of investigations including imaging of abdominal structures and hormonal assay. Individuals with Swyer syndrome exhibit female phenotypes and are typically tall girls with minimal secondary sex characteristics. These individuals are generally diagnosed in adolescence when they seek medical assistance for amenorrhea and the absence of secondary sex characteristics.[5]

Patients suffering from Swyer syndrome are first subjected to laboratory tests which include measurements of electrolytes and of the hormones FSH, LH, prolactin, thyroid-stimulating hormone, free T_4, sex hormone-binding globulin, androstenedione, estradiol, and testosterone. In the described cases, FSH and LH levels were elevated and estradiol levels were low; these findings are indicative of hypogonadotropic hypogonadism, a condition consistent with descriptions of Swyer syndrome in literature. Karyotype is the key investigation which reveals a male genotype. Cytogenetic analyses of these patients reveal a nonmosaic karyotype of 46, XY. In addition, patients can be tested for levels of anti-Müllerian hormone and inhibin, although these tests are not mandatory.[6]

Diagnosis of this rare form of gonodal dysgenesis is necessary as there is a risk of gonodal malignancy in future if they are not removed early. The risk of malignancy in Swyer syndrome is quitehigh. An incidence of 20-30% has been reported, the commonest one being gonadoblastoma.[3,8]Gonadoblastomas are benign tumours with no metastatic potential; however, they can be precursors to germ cell malignancies, such as dysgerminomas, which is the most commonly associated malignancy, or teratomas, embryonal carcinomas and endodermal sinus tumours.[9,10] So bilateral gonadectomy should be advised as early as possible followed by early institution of hormonal therapy which may help in induction of puberty and menstruation and prevention of osteoporosis in future.

Successful pregnancies have been achieved in a small group of patients through assisted reproductive technology with oocyte donation after hormonal treatment. It has been seen that the presence of XY genotype and the H-Y antigen does not affect the normal uterine and endometrial response during pregnancy. So there is a possibility, even though minuscule for pregnancy and it further confirms the physiological ability of the uterus to accommodate and maintain pregnancy in patients with XY dysgenesis.In fact, several cases of pregnancy among Swyer syndrome patients have been described since 1988; the prognosis for these pregnancies is similar to the prognosis for the pregnancies of 46, XX patients with ovarian failure.[11]

Conclusion

Swyer syndrome is a rare form of primary amenorrhea which should be evaluated early by a multi disciplinary team so that the patient can be treated with care to prevent future malignancy and osteoporosis,and for induction of puberty and pregnancy, if desired. However, proper counseling and psychological support to the patient and her family is the most important aspect of management of patients with Swyer syndrome.

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Medical Quiz: Image

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Islam MR[a], Rahman T[b]

A 35- year-old diabetic right handed lady got admitted in BIRDEM General Hospital with the complaints of altered level of consciousness for 12 days which was gradual on onset associated with confusion, drowsiness, behavioral changes, difficulty in swallowing and vomiting. It was not associated with fever, headache, loss of consciousness & convulsion. She gave history of vomiting for 15 days which was projectile, containing undigested food materials. It was not mixed with blood or bile. On examination, she was ill looking, nasogastric tube in situ disoriented, apathetic, decreased responsiveness to external stimuli, GCS 8/15, generalized hypertonia, exaggerated deep tendon reflexes including bilateral extensor plantar responses. Other systemic examination was normal. MRI of brain is available (Fig A, B, C, D)

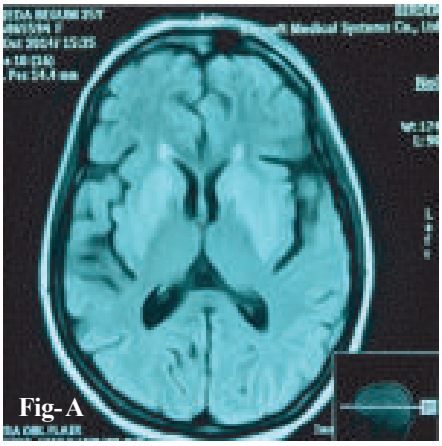

Fig- A

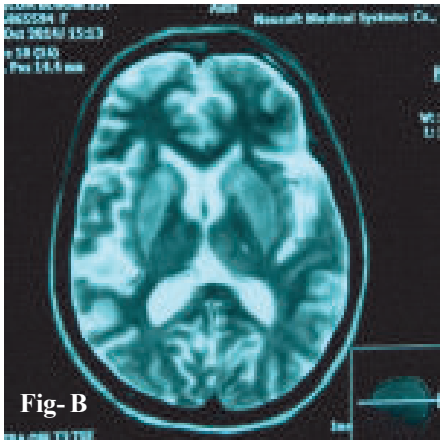

Fig- B

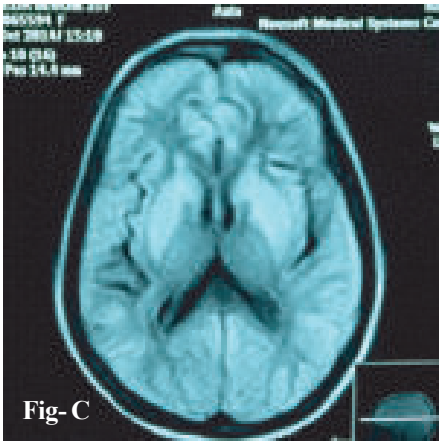

Fig- C

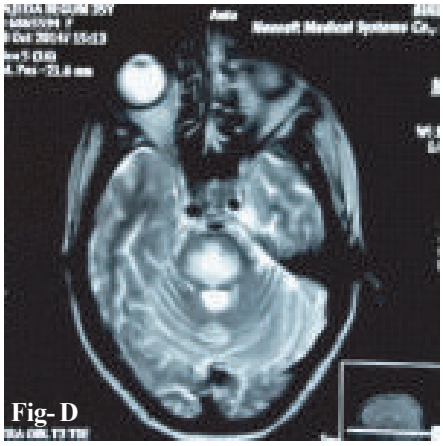

Fig- D

1. What are findings on MRI of brain?
2. What is the most likely diagnosis?
3. What is the probable cause?
4. Name two differential diagnoses

a. Dr Md Rashedul Islam, FCPS (Medicine), MRCP (UK), FACP (USA). Registrar, Neurology, BIRDEM General Hospital, Shahbag, Dhaka, Bangladesh

b. Dr Tanbin Rahman, MBBS. MD 2nd Part student, Dhaka Medical College, Bangladesh

Address of correspondence: Dr Md Rashedul Islam, FCPS (Medicine), MRCP (UK), FACP (USA). Registrar, Neurology, BIRDEM General Hospital, Shahbag, Dhaka-1000, Bangladesh