ANDROGEN INSENSITIVITY SYNDROME

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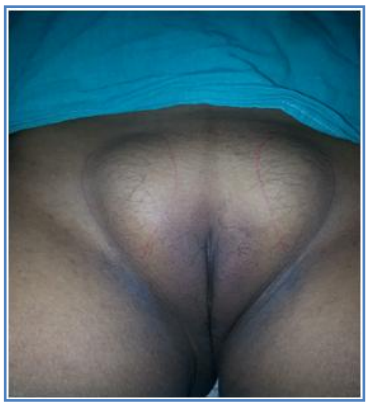
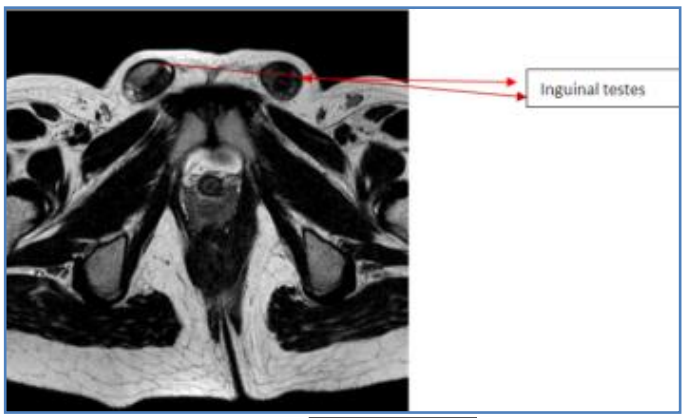
BACKGROUND: The condition is inherited as X-linked recessive gene[1]. The underlying pathology is the inability of end organs to respond to androgens. These cases are phenotypically and psychologically female with adequate breast development, normal external genitalia, a vagina with variable depth, absent /sparse pubic hair and axillary hair. The exact incidence in India is not known but the reported incidence is 1 in 2, 000 to 1 in 62,400 worldwide. These patients have male karyotyping (XY) with negative sex chromatin with undescended gonads. These cases are rarely diagnosed before puberty. Though rare, these are extremely distressing to the concerned individuals requiring expert handling. Management should include psychological counseling not only to determine the sexual mentation but also to help those individuals to cope with their problems. The chance of malignancy developing in the gonad with Y chromosome are about 20%.Surgical removal of the gonad is mandatory but can be delayed till 18 years to permit breast development and epiphyseal closure. The aim of presenting this case is to develop awareness regarding this rare syndrome X-linked genetic disorder which runs in families.
KEYWORDS: Androgen insensitivity syndrome, Primary Amenorrheoea

CASE PRESENTATION: A 25 years old married phenotypic female came with history of primary amenorrhea. She had noticed bilateral swelling in groin region since 4 yrs. She had normal sexual life. She had 4 sisters, she being the youngest one. One of her elder sisters also had complaints of primary amenorrhea but was not investigated regarding the same till date. On examination, her height is 158 cm and weight is 58 Kg, she had normal breast development (Tanner's stage IV) with absent axillary hair and sparse pubic hair(Tanner's stage I).On local examination, bilateral inguinal masses were noted along with normal female external genitalia. On per vaginal examination, uterus was absent with blind vaginal pouch of 3 cm. On investigations, USG study showed agenesis of uterus with non visualization of ovaries. For confirmation MRI was done. Report showed absence of uterus and ovaries but bilateral well-formed testes in inguinal region. Endocrinological analysis showed normal FSH, LH, PRL levels with extremely high level of testosterone >1500 ng/dl and raised levels of and rosteindione 6.21ng/ml with TSH 2.9mIU/ml. In view of MRI and endocrinological analysis karyotyping was done and suggestive of 46XY(Male Genome){ISCN-2009}.Both the testes were removed surgically and submitted for histopathology which showed atrophic seminiferous tubules along with marked Leydig hyperplasia in both testes.

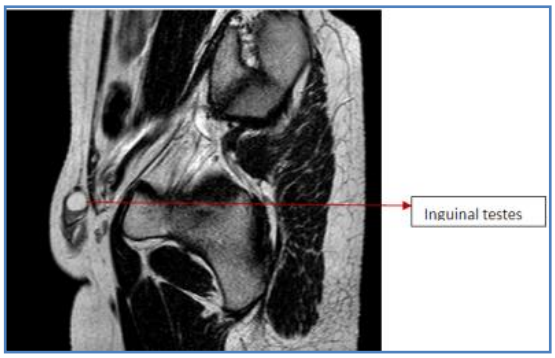
Breast development: Tanner stage IV with absence of axillary hair.



Bilateral inguinal masses with sparse pubic hair

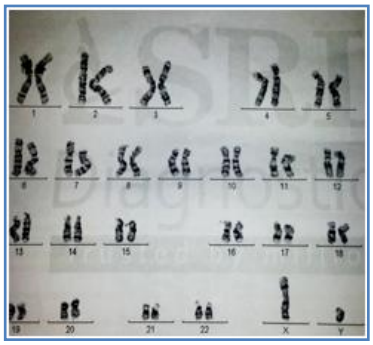


Axial MRI



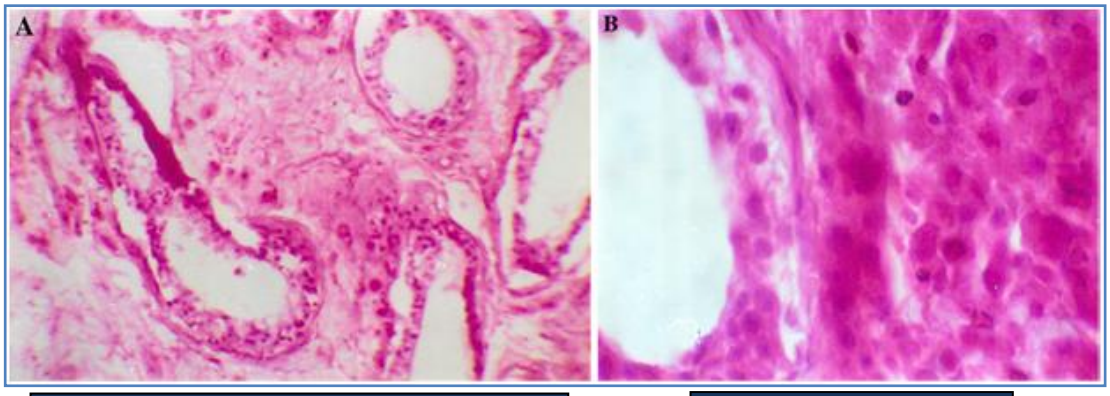
Sagital MRI

A



B

A and B Metaphase plate and karyotype of the subject.



Atrophied seminiferous tubules with thickened basement membrane (1009).

Leydig cell hyperplasia

Sr.No.	Diagnosis	Secondary sexual Characters	uterus	Investigations
1	Utero-vaginal agenesis	Normal	Absent	Karyotyping-46XX
2	Androgen insensitivity	Normal	Absent	Karyotyping-46XY
3	Outflow obstruction	Normal	Present	MRI
4	Constitutional delay, PCOS, Prolactinoma	Normal	Present	FSH, LH, PRL analysis
Differential Diagnosis				

Treatment: Counseling was done regarding need for long term hormone therapy, normal sexual function but inability to bear a child or menstruate. Gonadectomy followed by hormone replacement therapy was started and asked to continue this up to the age of 50 years in the form of COC pills till the axillary and pubic hair growth is achieved followed by Premarin 0.625 mg daily.

DISCUSSION: The incidence of testicular feminization syndrome is reported to range between one in 2, 000 to one in 62, 400 [2].Androgen insensitivity syndrome is extremely distressing to the concerned individuals and requires sympathetic handling. These patients can be helped to live good quality of life. The syndrome is divided into 2 main categories- complete & incomplete. The outcome of complete AIS is good if testicular tissue is removed at the right time, for incomplete AIS the outcome will depend on the appearance of genitals. Ahmed et al[3]reported a database in the United Kingdom of individuals with AIS, with 105 cases of complete AISand 173 cases of partial AIS[4]. This syndrome demands careful investigations of other affected family members & pedigree analysis. Apparent sisters of affected individual have1 in 3 chance of being XY & female offspring of a normal sister of an affected individual have 1 in 6 chance of being XY. About 1/3rd patients have negative family history & represents new mutation.2/3rd of all case mutations are inherited from mother while the rest occur as a result of spontaneous mutation in egg/zygote.(AIS support group UK 1999). Velidedeoglu et al[4] also reported three sisters with incomplete AIS. Our patient had 4 sisters, she being the youngest one. One of her elder sisters also has complaints of primary amenorrhea and having

normal sexual function. On repeated request she is not willing to come to the hospital for investigation.

As this syndrome runs in families we should advise genetic counseling to family members along with psychological support. After 11 weeks of pregnancy AIS can be diagnosed by chorionic villous sampling. After 15 weeks of pregnancy amniocentesis can be performed.

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