

Seminoma in Androgen Insensitivity Syndrome: A case report
Salah Ismail 1, Waleed Mudathir2, Amir Yahea Gamal 3

Introduction
Androgen insensitivity Syndrome (AIS) (testicular feminization syndrome) is a rare X-linked recessive condition. These patients characteristically have a 46 XY Karyotype and present with a spectrum of phenotypic abnormalities. AIS may be complete (CAIS), that is phenotypically normal women with adequate breast development normal external genitalia, vagina of variable depth, absent uterus, and coarse or absent pubic hair and axillary hair. They are male karyotype with negative sex chromatin.

Partial Androgen Insensitivity Syndrome (PAIS), phenotype range from mildly virilized female with external genitalia (clitorimegaly) to mildly undervirilized male external genitalia (hypospadius or diminished penile size). The gonad (undescended) testes may be intraabdominal, inguinal or labial. Malignant transformation of the testis is rare1.

Here we present a case of a young lady with seminoma arising in CAIS

Case Report
A 30- years old unmarried woman presented to our unit Where?? complaining of primary amenorrhea and abdominal mass for two months. On examination the patient looked feminine, height of 164cm and weight of 57kg, the breasts were well developed but with sparse pubic and axillary hair. On abdominal examination there was a mass about 15 week's pregnancy, firm, slightly mobile, mainly on the right side. On vaginal examination the vulva was circumcised, short blind vagina about 4-5 cm long, uterus and cervix were not felt.

Abdominal ultrasound showed a right sided solid mass with whorled apearance,about 10X12X15cm, uterus is not seen, no ascites, early right hydronephrosis. Renal function was normal.

Laparotomy revealed right sided solid tumor 10X12X15cm with minimal intestinal adhesion, attached by a pedicle to the posterior abdominal wall.

There was a small mass (gonad) attached to posterior abdominal wall, there was no uterus, pouch of Douglas was empty but there was no evidence of intraabdominal metastasis. The tumour and biopsies from the small mass (gonad) were sent for histopathology.

Histopathology reported seminoma and normal testis on the other side.

Discussion
The first medical report on AIS was published in 1953 by JM Morris an American Gynecologist. Androgen Insensitivity Syndrome AIS or Testicular Feminization Syndrome (TFS) also known as Morris Syndrome is a rare syndrome characterized by primary amenorrhea, 46XY karyotype, female phenotype and presence of testes rather than ovaries1. The incidence of AIS or TFS was reported as 1:200002 to 1:620003. It accounts for approximately 10% of cases of primary amenorrhea, ranking third after gonadal dysgenesis and congenital absence of the vagina3.

Table: Result of hormonal analysis

<table>
<thead>
<tr>
<th>Result</th>
<th>Normal ranges</th>
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<tbody>
<tr>
<td>5.9mlu/l FSH</td>
<td>F(2-48) M(2-14)</td>
</tr>
<tr>
<td>37 mlu/l LH</td>
<td>F (1.5-12) M (1-15)</td>
</tr>
<tr>
<td>Luteal (2-20)</td>
<td>Progesterone</td>
</tr>
<tr>
<td>6.0 nmol/l</td>
<td>F(0.35-3.5)</td>
</tr>
<tr>
<td>14 nmol/l Testosterone</td>
<td>M (9-37)</td>
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Fig 1: Histopathology of the mass showing seminoma

AIS is a disorder of androgen receptor function and represent the most common detectable cause of male pseudohermaphroditism5. The pathogenesis of CAIS involves a defective androgen receptor (AR) gene and end organ insensitivity to androgen, but that of PAIS involves a decrease number or qualitative defect of the AR gene6. The human AR gene has been mapped to chromosome Xq11-127. It is a large protein of at least 910 amino acids.
At present more than 100 mutations at the androgen receptor AR gene were reported. The probable explanation of the syndrome is the absence of the cytosol androgen b (binding protein receptor that is normally present in the androgen sensitive tissue). Affected individuals have normal testes with normal production of testosterone and normal conversion of dihydrotosterone (DHT) which differentiate this condition from 5 alpha-reductase deficiency. Despite normal levels of androgen synthesis the typical post receptor events that mediate the effects of hormones on tissues do not occur. This result in undervirilization of the external genitalia, absence of pubic hair and axillary hair, lack of acne and absence of voice changes at puberty. Because the testes produce normal amounts of Mullerian inhibitory factor (MIF), affected individuals do not have fallopian tubes, uterus or a proximal (upper) vagina, absence of Wolffian duct derivatives (epidydemis, vas deferens seminal vesicles and absence of prostate) but they have well developed breast as a result of conversion of testosterone to oestradiol. Testes are bilaterally retained either in the abdominal 50-70%, in inguinal region 20% or located both in the abdomen on one side and in the inguinal region on the other side 10-30%, and occasionally the testes may be even in the retro peritoneum.

In AIS bilateral undescended testes carry a high risk for malignancy, the best evidence suggests that women with CAIS or PAIS retaining their testes after puberty have 25% chance of developing benign tumors, and a 4-9% chance of malignancy. The risk of gonadal malignancy increases with age. Typically patients older than 30 years are at great risk reaching 33% in patients older than 50 years.

Our patient was 30 years therefore is at high risk of developing malignancy. The patient was circumcised. Circumcision is a bad habit widely practiced in Sudan. Such operation may change the normal anatomy of the external genitalia producing some confusion in diagnosing abnormalities of external genitalia.

Testicular tumors seen in this syndrome are hamartomas, germ cell tumors (seminoma) and sex cord tumors, Sertoli cell tumors and leydig cell tumors. Orchidectomy is recommended to avoid malignant changes within the intraabdominal testis, but the surgery deferred because such malignancy is quite uncommon before puberty delaying surgery until after puberty allows endogenous estrogen to stimulate development of secondary sex characteristics in the patient.

Testicular biopsy can be taken as soon as the syndrome is diagnosed and finding of in situ seminoma indicates immediate orchidectomy. After orchidectomy estrogen replacement therapy should be started to initiate puberty, maintain feminization and avoid osteoporosis. Progesterone is not needed because there is no uterus. Vaginal length may be sufficiently short to require dilatation.

Most women are satisfied with their psychosexual development, sexual function and satisfied with having been raised as females.

Our conclusion is that patients with CAIS should undergo post-puberty gonadectomy because of an increase risk of malignant transformation of the testes seen after puberty. Early testicular biopsy can be offered if CAIS is diagnosed early.

Attention to psychological consideration in such patients is important. The nature of the disease should be discussed clearly and the problem of primary amenorrhea and infertility explained and that they can have a normal sexual satisfaction.

References