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Case Report

Complete androgen insensitivity syndrome – A rare case report

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Abstract

Complete androgen insensitivity syndrome is a rare X linked recessive androgen receptor disorder. The prevalence is estimated at between 1 in 20,000 live male births and 1 in 60,000 live births. This condition involves genotypic males that present with phenotypic characteristics of females.. In patients with this syndrome testicular tumors especially seminoma may develop after puberty. Gonadal malignancies like sertoli cell tumor, yolk sac tumor and sex cord tumors are rare in these patients.

We came across a case in which 16 yrs old girl presented with complaint of bilateral inguinal swelling and primary amenorrhea . Subsequent investigations were done revealing absence of female internal genitalia and presence of bilateral inguinal mass possibly testes. Gonadectomy was performed and hormone replacement therapy was advised for life long.

Keywords: Androgen insensitivity syndrome , Primary Amenorrhea

1. Introduction

Complete androgen insensitivity syndrome a third most common cause of primary amenorrhea after gonadal dysgenesis and mullerian agenesis. This is also known as testicular feminization syndrome is one of the rare developmental abnormalities which result from the point mutation [2]. The affected individuals exhibit female phenotype in conjunction to XY karyotype. In these individuals, failure of masculanisation occurs because of resistance to the action of testosterone at the cellular level. This insensitivity allows the estrogen to take over and hence the female phenotype develops.[1]

Clinically this condition is difficult to diagnose in childhood but suspicion should be raised when a female patient presents with primary amenorrhea. The absolute risk of developing testicular neoplasm in subjects with this syndrome is estimated to be 3.6 % at the age of 25yrs.[3]

Laboratory evaluation will reveal a 46, XY genotype, a testosterone level in the low to normal male range, and a relatively elevated LH level. The karyoptype and elevated testosterone level are used to differentiate androgen insensitivity syndrome from mullerian agenesis, which can present with a similar phenotype. [4]

2. Case Report

16 yrs old girl was admitted in our hospital with complaints of swelling in the bilateral inguinal region with primary amenorrhea. According to the patient the size of swelling was slowly increasing and she did not encounter any pain in the swelling unless she exerted herself.

On general physical examination the patient was lean figured with normal vitals. Significant findings included scanty body hairs, scanty pubic and axillary hairs bilateral breast (Tanner III) with nipple areola complex were normal.(FIG. 1) External genitalia were normal with small labia but vagina ended in a blind pouch of approximate 2 inch length with intact hymen. There was no evidence of uterus on per rectal examination.

There was a non tender mass in bilateral inguinal region of size 3 x 4 cm which was firm in consistency and was irreducible. No Cough impulse was present.

All routine blood investigations like CBC, blood sugar, LFT , KFT were within normal limits.

Ultrasound abdo- pelvis reveals evidence of soft tissue mass in bilateral inguinal region canal showing central oval hypoechoic lesion measuring 3.68 x1.53 cms. No evidence of any follicle. No evidence of any herniation. Uterus and bilateral ovaries not visualized.

On hormonal analysis Serum FSH and LH values were 7.8 m IU /ml and 67.38 m IU / ml respectively Serum Testesterone was 578.62 ng/dl.

Serum DHEA-S value was 254.2 and Estradiol (E2) was 42. 51 pg/ml

Chromosomal analysis revealed XY KARYOTYPE.

Patient was counseled about the risk of malignant transformation of inguinal testes. Patient was consulted to undergo gonadectomy. With written informed consent patient was posted for bilateral gonadectomy. Gonads were found in inguinal canal. Bilateral gonadectomy was done without any intra operative or immediate post op complications. (Fig 2, Fig 3)

Histopathological examination of both removed gonads showed testis with fallopian tubes. no Epididymis or Vas present. Patient discharged on life long hormonal replacement therapy and calcium supplement .

Fig. 1 : showing normal breast development and scanty axillary hairs



Fig 2. Intraoperative photo showing testes



Fig. 3 Post operative specimen



3. Discussion

Complete androgen insensitivity syndrome is characterized by phenotypic female with 46XY karyotype, having primary amenorrhoea and adequate breast development but absence or scanty pubic or axillary hair. The vagina may be shorter than normal.[5]

In our condition all the criteria were met. As in most of the cases, our case got diagnosed in postpubertal stage due to primary amenorrhoea. Sometimes inguinal hernia may be associated with the condition. But in our case, it was not seen.

The gene responsible for creating the AIS phenotype has been localized to the proximal, long arm of the X chromosome at Xq11-12. There are four functional subsections, and eight exons, within the 110-kDa androgen receptor (AR) protein. Approximately 70% of AR mutations are X-linked recessive[6]. Knoke *et al*[7] reported two siblings with CAIS, Sertoli cell tumors, and an A (870) E mutation of the AR gene. They suggested that the A (870) E mutation in the AR gene could be the cause of the development of Sertoli cell tumor. Women with mullerian agenesis also presents with primary amenorrhoea but they have normally developed ovaries and pubic and axillary hair[8]. Various locations of testes have been mentioned in patients with CAIS. One study showed that out of 52 patients with the complete androgen insensitivity syndrome diagnosed 35 (67%) had abdominal, 16 had inguinal and 1 had labial testes[9].

In our case, both the testes were present in the inguinal regions. Magnetic Resonance Imaging (MRI) is considered as the gold standard investigation in cases of CAIS. But ultrasound abdomen and pelvis (USG) has got important role as the first line of investigation. USG can detect developmental abnormalities like absence of uterus and cervix and presence of testes in the abnormal location. High resolution USG can also detect intratesticular lesions like seminoma. Beside these findings, USG is also helpful in detecting congenital abnormalities of the renal system which may be associated with CAIS. In our case, due to the cost factor of MRI, only USG abdomen and pelvis was done which showed the above mentioned features without any renal abnormality.[10]

3.1 Gonadectomy

The most important issue in management is whether it is necessary to remove the testes and what shoud be the optimal timing of removal. The advantage of leaving testes till puberty allows pubertal changes to happen "naturally," without hormone replacement. The primary concept favoring removal is that testes when left in the abdomen throughout life may develop benign or malignant tumors and confer little benefit. The testicular cancer risk in CAIS appears to be higher than that which occurs with men with undescended intraabdominal testes, and rare cases of testicular cancer occurring in adolescents with CAIS have been reported. Unfortunately, it is difficult to quantify the risk of malignancy because of rare incidence of CAIS and also because the number of women who have not had testes removed is also very less. The best evidence suggests that women with CAIS and PAIS retaining their testes after puberty have a 25% chance of developing benign tumors and a 4-9% chance of malignancy. The only known benefit provided by retained testes in CAIS is that it can produce estradiol from testosterone, which can be replaced pharmaceutically.

For the treatment of vaginal hypoplasia, one can consider dilation. It is done by applying pressure to expand the tissue over an extended period of time. If dilation fails, a new vagina can be constructed using plastic surgical techniques.

3.2 Estrogen replacement

Once the testes have been removed, in order to support pubertal development, bone development, and completion of growth estrogen supplementation is necessary. Usually estrogen is given orally, but transdermal patches are gaining popularity. Since the uterus is absent, progesterone is not considered necessary.

Females with CAIS possess customary feminine appearance and their proper management can give them a normal life, despite a major chromosomal discrepancy. This case is presented in view of the rarity of the condition and the importance of early diagnosis and management considering the social and personal implications of this condition.

3.3 Chances of inheritance

Apparent sisters of affected individual have a one in three chance of being XY and female offspring of a normal sister of an affected individual have one in six chance of being XY[4].

Many of the affected individual have atypical karyotyping[11]. About a third of the patients of AIS have negative family histories and presumably represent new mutations. In two-thirds of all cases, these mutations are inherited from the mother, while the rest occur as a result of a spontaneous mutation in the egg/zygote (AIS support group UK 1999)[12].

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