ANDROGEN INSENSITIVITY SYNDROME – A CASE REPORT

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Abstract

Background: AIS is one of the most commonly diagnosed XY DSD, with an estimated prevalence of 2:100,000 to 5:100,000¹ and an incidence of 1:20,000² to 1:99,000³. The name testicular feminization syndrome was coined by John McLean Morris of Yale University in 1953. The first description of this syndrome dates back to 1817, as quoted by Morris⁴. It is the third most common cause of primary amenorrhea after gonadal dysgenesis and Mullerian agenesis⁵.

Case Report and Discussion: A 15-year-old phenotypic girl was evaluated for primary amenorrhea to find Complete Androgen Insensitivity Syndrome (CAIS) and underwent bilateral orchidectomy with plan for vaginoplasty at AIMS, Hyderabad.

Review of Literature: The treatment of AIS is based on the reinforcement sexual identity, gender identity plan and hormone replacement therapy. The prognosis is good, if the testicular tissue is resected at proper time.

Conclusion: CAIS should be considered as important differential diagnosis in delayed menarche while evaluation for primary amenorrhea and early gonadectomy can avoid gender identity disorder (GID) / psychological issues

Keywords: CAIS, GID

Introduction

Androgen insensitivity syndrome (AIS), which is also known as testicular feminization, encompasses a wide range of phenotypes that are caused by numerous different mutations in the androgen receptor gene.

AIS is an X-linked recessive disorder that is classified as complete, partial, or mild based on the phenotypic presentation. The clinical findings include a female type of external genitalia, 46-XY karyotype, absence of Mullerian structures, presence of Wolffian structures to various degree, and normal to high testosterone and gonadotropin levels.

Hereby we present a case of 15-year-old phenotypic girl with CAIS who underwent orchidectomy.

Case and Discussion

A 15-year-old female presented with complaints of pain in the groin region for 3 days. The patient has not attained menarche yet. She had no history of bleeding per vaginum, white discharge and burning micturition. She had no gastrointestinal and genitourinary symptoms. She is born to a nonconsanguineous

marriage. The birth history was normal, and the child attained normal milestones

On examinations, the patient built is normal, with minimal hair on the body and no axillary and pubic hair. Labia majora and vagina are present. The abdomen was soft, nontender. A swelling of 2 x 1 cm was palpable bilaterally. AIS was suspected based on the history and phenotypical appearance and an ultrasound abdomen was done. Ultrasonography showed agenesis of uterus and ovaries and bilateral undescended testes seen in inguinal canal close to deep ring with multiple hypoechoic nodule-? Malignancy. The ultrasound findings were further confirmed with karyotype analysis which showed 46 XY. Based on the clinical, sonographic and karyotype analysis, a diagnosis of Androgen Insensitivity syndrome is confirmed.

The patient underwent bilateral orchidectomy. Well-formed testis was found bilaterally at the deep inguinal ring. The testis is dissected bilaterally and sent for histopathology. The Histopathology of Testis

showed features consistent with Sertoli cell nodular hyperplasia, without any evidence of malignancy. Counselling was done and Vaginoplasty with Estrogen

therapy was planned after confirming the psychological gender by psychiatrist.

PHENOTYPE.

USG

KARYOTYPE

Right testis

Left testis

AIS is one of the most commonly diagnosed XY DSD, with an estimated prevalence of 2:100.000 to 5:100.000¹ and an incidence of 1:20.000² to 1:99.000³. It consists in the partial or complete inability of the cell to respond to androgens⁶: this cellular inability can lead to the wrong development of primary and secondary sexual characteristics. CAIS is characterized by the presence of female external genitalia in a 46, XY individual with normal testis development but undescended testes, due to complete unresponsiveness of the cells toward androgens². The CAIS phenotype is associated with an AR gene mutation that completely disrupts receptor's function; target cells do not respond to testosterone or DHT. An AR gene mutation is found in more than 95% of patients with CAIS, 70% of them being inherited and 30% *de novo* mutations⁷. This androgen insensitivity is diagnosed in 1/20.000 live male birth² and allows the estrogen to take over; hence, the female appearance and development of female external genitalia. However, the presence of the anti Müllerian hormone, produced by primordial testis, suppresses the formation of female genital organs. The lower part of the vagina, instead, is completely developed because it is not a Müllerian duct derivative; however, it is shorter than normal and presents a blind ending⁹. The complete absence of any sign of masculinization in external genitalia and of any typical secondary masculine characteristic is the reason why these individuals are always raised as females, have a female gender identity, and are anatomically and legally women. As a consequence of patient's apparently normal female habitus, CAIS is very rarely diagnosed in childhood. The typical presentation of this syndrome is during puberty in the form of primary amenorrhea. The presence of estradiol, in addition to the insensitivity to testosterone, promotes the formation of typical female features in puberty: there are normal breast development, normal reshaping of the

pelvis, redistribution of body fat, little or no appearance of pubic or other androgenic hair and rare appearance of facial acne². A feature that is more frequently observed in individuals with CAIS is the slightly increased height compared to average females; the reason for tallness appears to be the presence of the Y chromosome, which may have an effect on growth, independently of hormonal changes². PAIS is a DSD that results in the partial inability of the cell to respond to androgens

The diagnosis of AIS is confirmed by karyotyping with the support of ultrasound findings and phenotypical features. During childhood, no treatment is needed because these patients have normal female hormonal levels⁷. Successful management of CAIS patients requires gonadectomy, vaginal enlargement, estrogen replacement, and genetic counselling⁸. Gonadectomy is usually recommended only in early adulthood¹⁰ because the testosterone produced by the testes is converted to estrogen in the body tissues and that entails an advantage in this way pubertal changes will happen naturally, without hormone replacement. Gonadectomy is usually suggested because undescended testicular tissue presents increased risk of malignant transformation after puberty. 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 malignancy¹¹. One of the most important measures to implement is the planning of psychological support because of the distress that AIS produces in patients¹².

Conclusion

AIS should be considered as a differential diagnosis in primary amenorrhea with screening of sibling and gonadectomy should be the treatment at appropriate time (on diagnosis) with psychological counselling and Hormone replacement therapy.

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