A Case of Androgen Insensitivity Syndrome

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PRESENTATION AND HISTORY

A 24-year-old lady from a neighboring country presented with the main complaint of primary amenorrhea. She was never sexually active. She had commenced basic investigations in her country when she was 17 years of age but did not arrive at a diagnosis. Seven years later she attended our practice for a second opinion. She was otherwise healthy with no other past medical history.

EXAMINATION

The patient was phenotypically female, 1.8 metres tall and weighed 60kg. Breast examination revealed small breasts. Normal distribution of axillary and pubic hair was noted, although sparse. Examination of the external genitalia revealed a well-developed labia majora, clitoris and labia minora. The vagina was normal in appearance but with a blind ending. Urethral orifice and anus were normal. Palpation of the abdomen was unremarkable.

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CLINICAL AND LABORATORY EXAMINATION

The first step in our investigation was to perform a pelvic ultrasound which confirmed the absence of uterus and bilateral ovaries. Hematological investigations were then ordered which revealed a normal thyroid function. FSH was 24.9IU/L (age related reference range 2.5 – 10.2 IU/L) and LH was 34.51 IU/L. (age related reference range 1.90 -12.50 IU/L). Prolactin level was normal.

DIAGNOSIS

A serum karyotype was next performed which returned as 46XY. A provisional diagnosis of Androgen Insensitivity syndrome was made. A CT abdomen and pelvis was then ordered and revealed soft tissue nodules in the right and left groin measuring 2.9 x 1.0 x 2.1cm and 2.9cm x 1.3cm x 1.5cm respectively which were likely to represent undescended testis.

TREATMENT

The patient was counseled for surgical removal of bilateral testes in view of the potential risk of malignancy. An uncomplicated open bilateral gonadectomy was performed (See figure 1 and 2 below). Intra-operative findings revealed a right abdominal testis and a left inguinal testis. The final histopathological report returned as bilateral atrophic testes with Sertoli cell nodules.

The patient declined any psychological management after coming to terms with the diagnosis. A baseline bone mineral density test was performed and was normal. She was started on hormonal replacement therapy for maintenance of secondary sexual characteristics and for prevention of osteoporosis.

DISCUSSION

Androgen Insensitivity Syndrome (AIS) is a rare clinical entity that gynecologists may seldom encounter in clinical practice. This X-linked recessive disorder of testosterone resistance is characterized by a female phenotype with an XY karyotype and testes producing age-appropriate normal concentrations of androgens[1]. Complete androgen insensitivity syndrome (CAIS) is defined when the external genitalia is that of a normal female. Partial androgen insensitivity syndrome (PAIS) is defined when the external genitalia is partially but not fully masculinized. Our subject of interest is Complete AIS (CAIS) as illustrated in our case study. Individuals with CAIS have female external genitalia, female breast development, a blind vagina, absent uterus, female adnexae and abdominal or inguinal testes. The incidence of AIS was reported as 1:20000 to 1:62000[2].

The diagnosis of CAIS has health and psychological implications. Individuals with CAIS, like in other disorders of sexual development (DSD), face the potential problem of malignant transformation of the male gonads and the need for hormone replacement therapy after gonadectomy for maintenance of secondary sexual characteristics and prevention of osteoporosis. Sexual reassignment is not usually a problem in CAIS due to an obviously female phenotype and genitalia, with a vast majority of patients seeing themselves as women[3]. However, psychosexual identity issues may still impact the functioning of the individual and affect their social performance.

A study of 150 AIS patients[4] found several unique issues in relation to management of the patients including the problem of late presentation of the AIS cases, little awareness among patients and family members, no consensus on the age of performing gonadectomy, and reluctance of patients to undergo recommended surgery. The authors concluded that these issues need immediate attention to improve management of AIS cases and aimed to spread awareness among patients and clinicians.

PRESENTATION OF COMPLETE AIS

Patients with CAIS often come to specialist attention with the presentation of presumed inguinal hernia, or for the investigation of primary amenorrhea.

DIAGNOSIS OF COMPLETE AIS

A common presentation in adolescent AIS patients is primary amenorrhea. Part of the workup will include laboratory hormonal analysis including FSH, LH as well as testosterone levels.

Karyotyping is one of the investigations performed in the workup of primary amenorrhea. The finding of a 46XY karyotype raises the differential diagnoses of Androgen Insensitivity syndrome and Swyer Syndrome (46XY gonadal dysgenesis), which are further distinguished from each other by other clinical features.

Imaging is an important mainstay in diagnosis of CAIS patients. Ultrasonography confirms the absence of uterus and ovaries and may incidentally find inguinal or abdominal testes. However, when it comes to surgical intervention, Magnetic Resonance Imaging (MRI) provides better localization of the gonads and pre-surgical planning[5]. MRI is also useful for watchful waiting of patients who choose to defer gonadectomy, although MRI cannot depict premalignant changes[6].

MANAGEMENT OF AIS

In addition to physical and psychological disturbances, the most important clinical problem in CAIS includes the risk of gonadal tumor development. The timing of gonadectomy remains controversial. In the past, early gonadectomy had been recommended. However in a recent review prevalence of germ cell tumors is low in complete AIS[7]. Gonadol tumor risk is 0.8% -2% during prepubertal period and rises up to 30% during late adulthood[8]. In patients with pre-pubertal diagnoses, gonadectomy is recommended to be delayed until breast development is completed as aromatization of the androgens into estrogens yield normal breast development, given the low risk of malignancy[9] during puberty. For adult patients, gonadectomy may be considered if the gonad is palpable in the inguinal area causing discomfort and an unpleasant appearance. Open and laparoscopic approach for gonadectomy had both been described[10]

It was thought that patients with CAIS are at risk of psychological issues. However, not all women with AIS are affected socially. A study of 43 women in Italy including 34 women with AIS[11] showed that these women were well

adapted and were higher achievers than controls both in educational and professional life. They showed good quality of life scores but appeared to have higher scores for depression and anxiety. This emphasized the fact that psychological support is important in this unique group of women.

For patients who have their gonads removed, hormone replacement therapy is essential for preservation of female secondary sexual characteristics, optimize bone mass accrual, and to promote overall physical and social well-being[12]. Estrogens are usually used for this purpose as for other persons with DSD reared as females. An alternative therapy for women with ascertained CAIS could be testosterone but this approach requires further studies.

Patients with CAIS can choose to be sexually active but may require vaginal dilatation in view of their small blind vaginal opening. Dilatation by vaginal dilators and coital dilatation have been described[13]. Surgical vaginoplasty is an alternative if there is non-compliance to vaginal dilatation or if the technique fails[14]. Sexual satisfaction may be a problem for women with CAIS. Problems with desire, arousal, and dyspareunia were found to be significant in a group of women with XY disorders of sex development, most of which were due to CAIS[15].

CONCLUSION

AIS is a form of disorder of sexual development. Patients with AIS face multiple complex long-term health and psychosocial issues. A multidisciplinary input is necessary for such individuals involving gynecologists, urologists, psychiatrists, psychologists as well as endocrinologists for joint management.

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Figure 1: Right Abdominal Testis

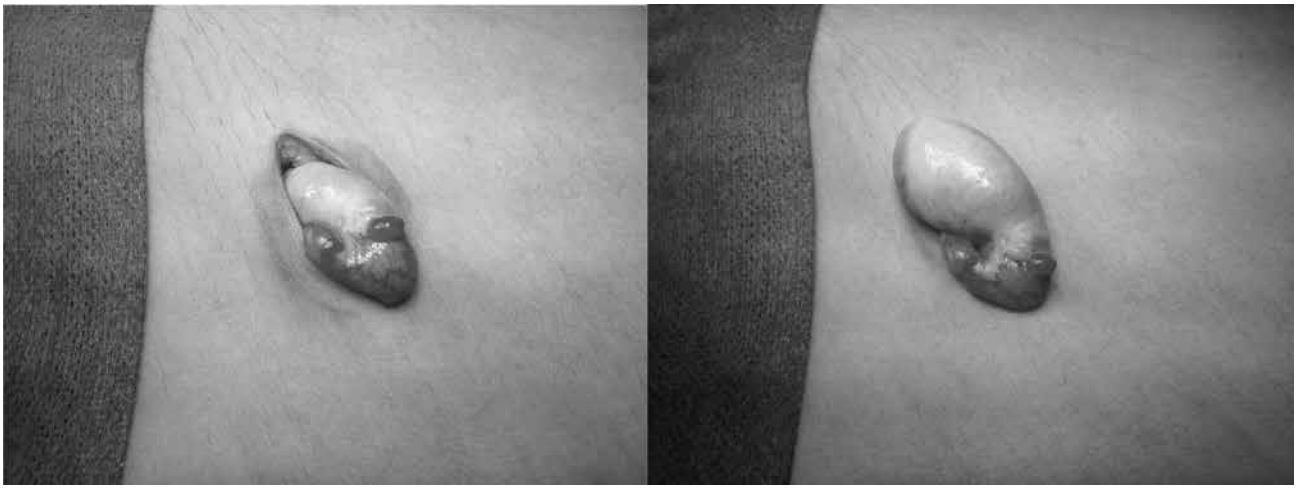

Figure 2: Open Bilateral Gonadectomy