A Rare Case of Bilateral Sertoli Cell Adenoma in Gonads Associated with Unilateral Serous Cyst in a Patient with Complete Androgen Insensitivity Syndrome

Abstract

Complete androgen insensitivity syndrome (CAIS) is an extremely infrequent disease. The patients exhibit female phenotype because of insensitivity to the androgen receptor and may develop tumors, especially in their undescended gonads. We present here a case of CAIS with bilateral Sertoli cell adenoma along with unilateral serous cyst in a 16-year-old patient.

Keywords: *Complete androgen insensitivity syndrome, serous cyst, Sertoli cell adenoma*

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Introduction

Complete androgen insensitivity syndrome (CAIS – previously called testicular feminization) is specified by a 46 XY karyotype, bilateral undescended testes, female genitalia appearance, and lack of Mullerian derivatives. The patient is phenotypically female without uterus and a blind shortened vagina.[1] The incidence of this condition is 1 in 99,000–1 in 20,000 female births.[2] It is caused by X-linked mutations in the androgen receptor (AR) gene that expresses a variety of phenotypes ranging from male infertility to completely normal female external genitalia. AR is expressed from 8 weeks of gestation. In male embryo, testes begin to secrete testosterone at 9 weeks of gestation which peaks around 11 and 18 weeks.[3] This stimulates differentiation of the Wolffian duct system into epididymis, vas deferens, and seminal vesicles. Another more powerful androgen, dihydrotestosterone, originates from action of the enzyme 5alpha-reductase type 2 on testosterone. It stimulates differentiation of the primordial external genitalia. Mild androgen insensitivity syndrome (MAIS), which is associated with a (normal) male phenotype, is often undiagnosed. Patients usually present with infertility, gynecomastia, hypospadias, etc. Genetic tests are needed at this point to diagnosis this condition.[4] More severe forms of CAIS present with different degrees of genital ambiguity, at birth. CAIS is overlooked at birth as there is normal female phenotype of the child and is usually diagnosed at puberty when the patient presents with primary amenorrhea.[5] In patients with this syndrome, testicular neoplasms may develop after puberty with seminoma being the most common histological type.[6]

We report a case of bilateral Sertoli cell adenoma tumor with unilateral serous cyst in the testis of a 16-year-old patient with CAIS. Literature search shows that only once such case has been reported in a 30 year old female who also presented with bilateral sertoli cell adenoma and serous cyst.[7]

Case Report

A 16-year-old patient presented with complains of primary amenorrhea. On physical examination, there was scant body hair with absent pubic hair. Breast development was normal. There were bilateral inguinal swellings measuring 4 cm × 2 cm and 2 cm × 1 cm soft in consistency. Vaginal examination was not done and external genitalia were underdeveloped. Ultrasonography of the pelvic and inguinal region revealed the absence of uterus, fallopian tubes, and ovaries. Inguinal region showed bilateral masses measuring 4 cm × 2.5 cm and 2 cm × 2 cm with homogeneous echogenicity. Provisional diagnosis of bilateral testis in the inguinal region was given.

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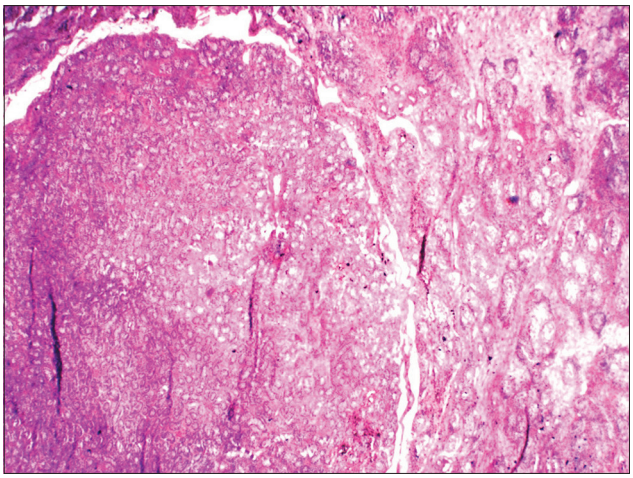

Figure 1: Microscopic examination shows well-circumscribed nodules revealing small tubules separated by thin vascular septa and Leydig cell in the stroma (H and E, ×40)

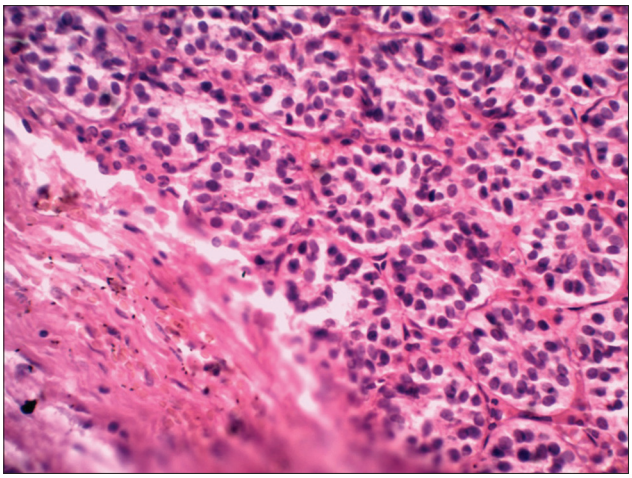

Figure 2: Microscopic examination of nodules in both testis revealed small tubules lined by Sertoli cells having round hyperchromatic nuclei, inconspicuous nucleoli, and eosinophilic-to-clear cytoplasm separated by thin vascular septa. Mitotic activity and necrosis were not seen (H and E, ×400)

Grossly we received specimen of bilateral testis, larger measuring 4.5x2.5x2cm and the smaller measuring 2x1.5x1cm. In addition the smaller testis showed two cystic structures measuring 2x1x1 cm and 1x1x1 cm respectively attached on the outer surface. Cut section of the larger testis showed a homogenous yellow-tan nodule measuring 0.5 in diameter. Cut section of the smaller testis also showed two well circumscribed yellow tan nodules measuring 1cm and 0.3 cm respectively. Both the cystic masses had a smooth brownish translucent surface and were filled with serous fluid. Microscopic examination of both testis showed wellcircumscribed nodules revealing small tubules separated by thin vascular septa and Leydig cell in the stroma [Figure 1]. Tubules were lined by sertoli cells having round hyperchromatic nuclei, inconspicuous nucleoli and eosinophilic to clear cytoplasm separated by thin vascular septa and leydig cell in the stroma [Figure 2]. Mitotic activity and necrosis were not seen. Histopathological examination of the gonads in non-neoplastic region showed prepubertal immature tubules lined by sertoli cells along with leydig cell hyperplasia in the stroma [Figure 3].

Cystic fibrous wall lined by flat cuboidal epithelium with congested blood vessels and inflammatory cell infiltrate.

Thus, a diagnosis of bilateral Sertoli cell adenoma with a unilateral benign serous cyst was made.

Discussion

CAIS previously referred to as testicular feminization syndrome is the most common form of male pseudohermaphroditism. It is an X-linked recessive disorder caused by a mutation of Xq11-q12 at the AR gene. Patients present with phenotypes that vary from women with normal female external genitalia, in CAIS, to genital ambiguity, in the partial androgen insensitivity (PAIS), to men with normal male genitalia but infertility, in MAIS. At puberty, in some cases, MAIS patients can have alteration in the spermatogenesis, impotence, and gynecomastia. Endocrine features of CAIS and PAIS are the same. There is normal or overproduction of serum luteinizing hormone (LH) and Testosterone (T) during the first 3 months of life, which are usually in the normal range until the puberty. At puberty, there are elevated serum levels of T and LH, due to the androgen insensitivity and the lack of negative feedback by sex hormone on hypothalamus and hypophysis. Testosterone is converted to estrogen by enzyme aromatase, which causes CAIS patients to have higher estrogen levels than normal male leading to good development of the breast.[3] The complete form is 10 times more common than the incomplete form. The complete form is characterized by a 46 XY karyotype, usually abdominal testes, female external genitalia, and absence or scant pubic and axillary hair with normal breast development.[8]

Like our case, most of the cases are diagnosed in postpubertal stage when the patient presents with primary amenorrhea.

Complete AIS is accompanied with abnormal testicular development and increased risk of germ cell malignancy beginning after puberty.

The risk of developing a testicular neoplasm in participants with this syndrome is estimated to be 3.6% at the age of 25 years.[9]

Unfortunately, because of rare incidence of CAIS, it is difficult to quantify the exact risk of malignancy. The malignant tumors often associated with this syndrome are seminomas and gonadoblastomas, and other histological forms such as teratomas, choriocarcinomas, yolk sac tumors, and embryonal tumors may also be present. Likewise, benign tumors such as adenomas, Leydig cell, and/or Sertoli cell tumors are other possible findings.[10]

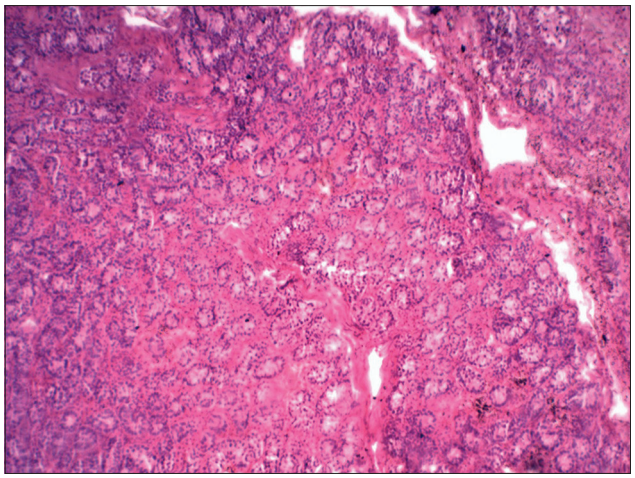

Figure 3: Microscopic examination of nonneoplastic region showed prepubertal immature tubules lined by Sertoli cells along with Leydig cell hyperplasia in the stroma (H and E, ×100)

The prevalence of Sertoli cell tumors in both gonads is low in the population, representing 0.4%–1.5% of testicular tumors in adults and 4% in children.[10,11]

For these reasons, prophylactic gonadectomy is advised in the prepubertal period to avoid potential malignant transformation.[12]

In a case series of 43 patients with AIS by Rutgers and Scully, 63% hamartomas, 23% Sertoli cell adenomas, and 9% malignant tumors including two seminomas and one intratubular germ cell neoplasm with early stromal invasion and a malignant sex cord tumor were reported.[13]

CAIS is often associated with Sertoli cell tumor. Sharma *et al*. stated that in their case report, 21 cases of Sertoli cell tumor in patients of the age group of 17–82 years associated with CAIS. Out of the 21 cases, 20 were reported to be of benign variety and 1 was advanced malignant disease.[6]

Asl Zare *et al*. reviewed the previous articles on gonadal tumors in CAIS patients. They found out that most cases were of unilateral Sertoli adenoma or tumor. They also found out that only one case of bilateral Sertoli cell adenoma had been reported.[2,7]

Treatment should not just be restricted to gonadectomy but demands multidisciplinary management in an attempt to minimize the psychological impact since there is discordance between the individual's 46 × Y genotype and female phenotype.[14,15] Guidance with respect to sexuality and the impossibility of reproduction is also important aspects and cannot be neglected.

Conclusion

CAIS is a rare clinical entity. The occurrence of Sertoli cell adenoma is still rarer. Most of the reported cases in literature are of unilateral Sertoli cell adenoma or tumor. Herein, we reported a case of CAIS with bilateral Sertoli cell adenoma associated with a unilateral serous cyst.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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