TFS or complete androgen insensitivity is a familial inherited form of male pseudohermaphroditism which was described by Morris in 1953 (1-7). The inheritance is X-linked recessive or sex limited autosomal dominant (2,7). This syndrome may result from the absence of the androgen receptor or qualitative defect or be due to a postreceptor defect affecting the nuclear binding of the steroid-receptor complex. It may also result from a defect in transcription (2).

The incidence of TFS is reported to range between 1 in 2000 to 1 in 62,400. More than 200 cases have been reported since 1973 (2,4).

The complete form of the syndrome is characterized by a female phenotype and the affected patients show normal female external genitalia except the vagina is shorter than normal and ends blindly (1,2,4,5,7,8). The other outstanding features of this syndrome, such as the status of the breasts and the distribution of body hair, are also well described by Morris (1). At puberty female secondary sexual characteristics are normally developed, but menarche does not ensue. These patients have undescended bilateral testes. The testes are aspermic and are located usually in the inguinal channel, sometimes intraabdominal or in the labia. Rare spermatogonias are described in 28 % of cases (9). Patients usually have inguinal hernias if the gonads are in the inguinal region.

The uterus and other female internal genital organs are absent or rudimentary (1-10). However, at least one fallopian tube was present in 35 % of the cases (9).

Although seminomas, dysgerminomas, teratomas and arrhenoblastomas were reported in TFS, tubular adenomas were described as a frequent histopathological finding in these patients (1,4-7,9,10). Since histological features of testicular tubular adenoma and Sertoli cell tumor have not been clearly differentiated, we used these terms as synonyms, as reported by O’Connell (4).

Case 1: An 18-year-old phenotypic woman applied to the general surgery outpatients clinic with bilateral inguinal hernias. Her karyotype was 46 XY. TFS was diagnosed before we examined the patient. Her family history revealed that one of her sisters, two aunts and a cousin have the same complaints. Bilateral gonadectomy and bilateral inguinal herniorrhaphy were performed. The postoperative course of the patient was unremarkable.

Case 2: The younger sister of the first case was a 16-year-old woman, who also had never menstruated like her elder sister (case 1), her two aunts and one of her cousins. She was examined by the Gynaecology and Genetic departments and was diagnosed TFS, before we evaluated her. She also had bilateral inguinal hernias. Bilateral gonadectomy and inguinal herniorrhaphy were performed.
Both of them were discharged without any problem. The patients were referred to the Obstetrics and Gynecology department prior to their discharge. Regular follow up and supportive hormonal therapy was planned.

**HISTOPATHOLOGICAL FINDINGS**

**Case 1:**

**Gross:** The left testis measured 7x4x3 cm with spermatic cord. The cut sections included six gray-white nodules which were well circumscribed. In addition, two paratesticular cysts were observed. The right testis and spermatic cord were 7x3x2 cm and the cut sections showed only one well circumscribed nodule.

**Microscopy:** The left and right testes had the same microscopic features showing nodular tumors surrounded by a thin fibrous capsule and composed of immature tubules lined by Sertoli cells. Large fibrous septas were seen in tumoral areas (Figures 1, 2). Leydig cells were not seen in the tumor. Paratesticular cysts, which were lined by ciliated prismatic epithelium, were also seen. Also immature seminiferous tubules with rare spermatogenetic activity and interstitial Leydig cells were seen in normal looking testes, adjacent to the tumoral nodules (Figure 3).

**Case 2:** The right and left testes were approximately 3.5x3x2 cm in greatest dimensions. Gross and microscopic views of these testes were similar to her older sister’s (case 1) as described above, except for the large collagen bundles in the tumor observed as a striking microscopic feature.

The term “testicular feminization” was described by Morris in phenotypic females with 46 XY karyotype, presenting primary amenorrhea, adequate breast development, and absent or scanty pubic or axillary hair. The vagina may be shorter than normal and ends blindly (1,2,3,7). Gonads consist of seminiferous tubules usually without spermatogenesis (1,9). The testes also show interstitial cell hyperplasia and ovarian-like stroma (2,9). Electron microscopic studies have shown that the gonadal ultrastructure resembles that of the fetal testis with primitive germ cells and Sertoli cells lining the seminiferous tubules (4). This syndrome should be considered in the differential diagnosis of a postpubertal girl who has never menstruated and also has an inguinal hernia (7), as in both our cases.

Hamartomatous nodules are reported in 63 % of cases of TFS (9). This type of nodule is seen in adults and adolescents. Grossly the nodules are described as multiple, bilateral, tan-yellow or white in appearance, and up to 24 cm in diameter. Histopathologically hamartomas are composed of immature Sertoli cells, germ cells, Leydig cells and ovarian type stroma. The multinodular tubular pattern in TFS is suggestive of Sertoli cell hyperplasia rather than adenoma according to some authors (9). But in general, if the nodules are composed of only Sertoli cells, the lesion is recognized as “Sertoli cell adenoma” rather than hamartoma (2,9). The lack of

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Figure 1. Well circumscribed tumor with large collagen bundles and ovarian like stroma.

Figure 2. Immature tubules lined by Sertoli cells in tumor.
germ cells and interstitial Leydig cells supports the diagnosis of testicular tubular adenoma (Sertoli cell tumor) (4). In the present case since we did not see any germ cells or Leydig cells in the tumoral nodules, our diagnosis was Sertoli cell tumor. Malignant transformation in Sertoli cell tumors also have been reported, although these tumors are considered benign by several authors (1). The high coincidence of the Sertoli cell tumor in patients with TFS and its malignant potential, and the removal of the gonads should frequently be considered in these patients.

The timing of prophylactic gonadectomy has been the subject of some controversy (4). Manuel et al. found that the incidence of tumors, including the other types, is 3.6% at the age of 25 years and reaches 33% at the age of 50 (6). The delay in the removal of the gonads in the patients with TFS until puberty allows spontaneous feminization. Most authors recommend gonadectomy at postpuberty (4,6). In our two sibs, gonadectomy was performed after puberty and secondary sexual characteristics were well developed.

We presented these two cases because of the rarity of TFS and the interesting family history.

References


