Seminoma arising in androgen insensitivity syndrome (testicular feminization syndrome): A case report

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Androgen insensitivity (testicular feminization) syndrome is a rare inherited form of male pseudohermaphroditism that occurs in phenotypically normal woman with male karyotype (XY). The undescended testis may go into malignant transformation. The androgen insensitivity syndrome with malignant testicular disorder is very rare. A thirty-one year old female was admitted to the hospital with the complaint of primary amenorrhea. Clinical and laboratory investigation revealed testicular feminization syndrome with seminoma developed from intraabdominal undescended testis. Primary removal of the mass and postoperative radiotherapy were treatment of choice for the patient. [Turk J Cancer 2001;31(4):168-171]

Key words: Androgen insensitivity syndrome, testicular feminization syndrome, seminoma, radiotherapy

Androgen insensitivity (testicular feminization) syndrome is a rare inherited form of male pseudohermaphroditism that occurs in phenotypically normal woman with adequate breast development, normal external genitalia, a vagina of variable depth, absent uterus, and sparse or absent pubic hair and axillary hair. These patients have male karyotype (XY) and negative sex chromatin. The gonad (undescended testes) may be intraabdominal, inguinal, or labial. Malignant transformation of the testis is a distinct possibility in these patients. It is a relatively rare syndrome with the association of malignancy even more rare (1). This paper is a case presentation of a young woman with seminoma arising in testicular feminization syndrome.

Case Report

A 31-year-old female was admitted to Hacettepe University hospital for investigation of primary amenorrhea. Physical examination revealed a female with normal external genitalia with the absence of uterus and cervix. The blind vagina was 3 cm long. Digital rectal examination revealed a large firm mass in
the mid-pelvis. The remainder of the patient's history was significant, as she had two sisters with primary amenorrhea who were diagnosed as testicular feminization syndrome. Cytogenetically, they were reported to have 46 XY karyotypes with no evidence of mosaicism. One of her sisters who was 33 year-old was operated for removal of inguinal masses. Histopathological examination revealed testicular tissue with hamartomatous nodules. They have one brother who was married with two children.

A computerized tomography of the pelvis showed a solid mass measured 11x12 cm in mid-pelvis (Figure 1). The β-subunit of human chorionic gonadotropin was abnormally high, 253 mIU/ml. Alpha-fetoprotein and other tumor markers were within normal ranges. A karyotype was also performed which revealed a 46 XY complement (Figure 2). In view of these findings testicular feminization syndrome was diagnosed, complicated by probable neoplastic mass within the pelvis.

Exploratory laparotomy revealed a solid right gonadal mass measured 10x13x8 cm and left atrophic gonad in the left pelvic wall with 2x2x3 cm size. There was no evidence of female internal genitalia. Histologically right gonadal mass was typical of a seminoma. The left adnexal mass was an immature testis with hamartomatous foci.

Fig 1. Computerized tomography of the patient showing large mass within the mid-pelvis
The patient was treated with radiation therapy as for a stage I testicular seminoma. A 6 MV linear accelerator was used to deliver a total dose of 2000 cGy to the pelvic and paraaortic lymphatic fields in 10 fractions.

**Discussion**

Testicular feminization, is considered to be the most common form of male pseudohermaphroditism with an incidence of 1 in 25,000 to 60,000 females (2). It accounts for approximately 10% of cases of primary amenorrhea, ranking third after gonadal dysgenesis and congenital absence of the vagina (3).

Androgen insensitivity syndrome (AIS) results from an androgen receptor defect (4). The probable explanation of the syndrome is the absence of the cytosal androgen binding protein receptor that is normally present in the androgen responsive tissue. So, the male fetus is not stimulated by normal levels of circulating androgens. As a result, there is no fusion of the genital folds to form scrotum and penis and no posterior migration of the labioscrotal folds (5).

The risk of malignancy in AIS is considerably lower and occurs at a later age than with other intersex disorders. In the literature, a general trend for malignant transformation is noted and is age related (6). Typically, patients older than 30 year are at greatest risk (7). Our patient was also 31 year-old at time of diagnosis. Morris and Mahesh (8) reported a 22% incidence of malignant gonadal tumors in 181 AIS patients. All, but 3 of their cases were at their thirties and majority of malignancies were of germ cell origin. On the other hand, Dewhurst (9) found no malignancy in 82 patients with this syndrome. He estimated the chance of malignancy in AIS to be approximately 5%.
calculate the potential for the development of gonadal tumors in patients with AIS, Manuel et al. (10) combined a series of 23 cases of patients with Dewhurst series and determined that expectancy of tumors is 3.6% at age 25 and 33% at age 50.

Many authors believe this to be a relatively low incidence which allows for safe postponement of gonadectomy after puberty. In one study conducted on 12 patients with AIS, gonadal biopsy was performed to investigate whether carcinomatous changes could be seen in children; three of 12 patients had intratubular neoplasia, which was considered premalignant (11). Carcinoma in situ was diagnosed in the testes of three of eight consecutive patients with AIS at 2 months and at 13 and 14 years. The authors concluded that testicular biopsy is warranted as soon as the syndrome is diagnosed and that finding of in situ seminoma should indicate immediate orchidectomy. Most authors suggest that at least one gonad be left until puberty to allow for the endogenous estrogen to result in secondary sex characteristics (12).

References