Adult type granulosa cell tumor in adult testis: report of a case and review of the literature

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Abstract

Granulosa cell tumors can be classified into juvenile and adult types and more commonly occur in ovaries. Adult testicular granulosa cell tumors are extremely rare and only 29 cases of adult type have previously been reported. We report here a 28-year old Caucasian man with a left testicular adult type granulosa cell tumor. The tumor measured 2.6 x 2.6 x 2.5 cm and was mitotically active (10/10 HPF). Immunohistochemical stains showed the tumor diffusely positive for inhibin and vimentin, and negative for epithelial membrane antigen, cytokeratins, synaptophysin, HMB-45, OCT-4, placental-like alkaline phosphatase and lymphoid markers. The reported granulosa cell tumors in adult testis were briefly reviewed.

Introduction

Granulosa cell tumors can be classified into juvenile and adult types. Juvenile type is usually benign. However, the clinical behavior of adult type granulosa cell tumors is difficult to predict. Testicular granulosa cell tumors are extremely rare. Only 29 adult type granulosa cell tumors in adult testis have been reported. Analysis of the previous reported cases shows only tumor size of >5 cm reaches statistical significance in association with adverse clinical behavior. We report a new case of adult type granulosa cell tumor in the testis and briefly review the previously published literature.

Case Report

The patient is a 28-year-old Caucasian male who presented for urological evaluation after noting a firm lump in the left testicle. He complained of mild left sided scrotal discomfort. He denied decreased libido or erectile dysfunction. Physical examination was normal except for an enlarged hard left testicle. Of note, no gynecomasia was noted. A trans-scrotal ultrasound confirmed a solid mass in left testicle. Serum alpha-fetoprotein and human chorionic gonadotropin levels were within normal limits. Computed tomography (CT) scans of chest, abdomen, pelvis showed no evidence of metastatic disease; however, an enhancing mass in left hemiscrotum was identified (Figure 1). The patient underwent a left inguinal orchectomy. He recovered from his procedure uneventfully. Macroscopically, the testicle and epididymis measured 5 cm in length and 1 cm in diameter. There was a 2.6 x 2.5 x 2.5 cm well-circumscribed mass in the testicle. On cut surface, the tumor was tan with a slight red pallor. No hemorrhage or necrosis was seen.

Microscopically, the tumor was well circumscribed with focal infiltration of testicular parenchyma (Figure 2A,B). No involvement of tunica albuginea was seen. The tumor was composed of solid sheets of cells with fine chromatin and inconspicuous nuclei. Focal nuclear grooves were seen. The mitosis was brisk and averaged 10/10 high power fields (HPF). No atypical mitosis was seen. No necrosis or lymphovascular invasion was identified. The rete testis, epididymis, and spermatic cord were not involved.

To further characterize the tumor, immunohistochemical stains were performed (Figure 2C/D). The tumor was strongly positive for inhibin and vimentin, negative for epithelial membrane antigen (EMA), cytokeratins (AE1/3, CAM5.2), germ cell tumor markers (OCT-4, placental-like alkaline phosphatase), melanocytic markers (S100, HMB45), lymphoma markers (LCA, CD3, CD5, CD20, CD79a, CD21, CD35).

The combined findings of morphology and immunohistochemistry supported the diagnosis of primary testicular adult type granulosa cell tumor.

Discussion

Granulosa cell tumor is a sex-cord stromal tumor which more commonly occurs in the ovary. Granulosa cell tumor is extremely rare in the adult testicle. Only 29 cases of testicular adult type granulosa cell tumor have been previously reported. A testicular granulosa cell tumor usually presents as a painless mass in the testicle. A small portion of patients may present with gynecomasia. The average age at presentation is 45 years (range 16-77 years).

Granulosa cell tumor of the testicle, like its ovarian counterpart, can be classified into juvenile or adult types. juvenile type granulosa cell tumor usually occurs in children, but very rarely it can occur in an adult. The tumor is usually multicystic, and lacks the morphological features of the adult type granulosa cell tumor such as Call-Exner bodies or coffee-bean nuclei. Most testicular granulosa cell tumors in adults are adult type. Testicular granulosa cell tumors usually do not invade the tunica albuginea. Focal infiltration of the testicular parenchyma can be present. No lymphovascular invasion is usually seen. The tumor can grow in multiple patterns, including trabecular, insular, macrofollicular, mifoilocular and gyrosform patterns. The nuclei are elongated, sometimes with nuclear grooves. No prominent nucleioli are seen. Mitosis is highly variable, ranging from 2 per 50 HPF to 5 per HPF. Call-Exner bodies may be present.

The differential diagnosis for a testicular granulosa cell tumor includes subtyping the tumors into adult or juvenile type; type 2 germ cell tumors, especially yolk sac tumor; metastatic carcinoma; carcinoid tumors; and, non-Hodgkin’s lymphoma. Adult type granulosa cell tumors can be differentiated from the juvenile type by the presence of Call-Exner bodies and/or coffee-bean nuclei. In contrast, juvenile type is usually multicystic, and lacks the characteristic features of adult type.

Immunohistochemically granulosa cell tumor is positive for inhibin, vimentin and calcitonin, negative for epithelial membrane antigen (EMA), placental alkaline phosphatase, synaptophysin and lymphoid markers. Yolk sac tumor (YST) of mixed malignant germ cell tumors can show multiple growth patterns. However, YST is usually positive for PLAP, cytokeratin and AFP, albeit it can also be positive for inhibin. Granulosa cell tumors need to be differentiated from hematopoietic malignan-
cy because these tumors can be quite mitotically active and only focally show the characteristic coffee-bean nuclear feature. Immunohistochemical stain for leukocyte common antigen usually is helpful in this distinction. Cytokeratin and synaptophysin stain is usually negative in granulosa cell tumors, which is helpful in excluding metastatic carcinoma or carcinoid tumors.

Juvenile type granulosa cell tumor is usually benign, typically presenting as an asymptomatic scrotal mass. In contrast, adult type of granulosa cell tumor has malignant potential. From the 30 reported cases of testicular adult type granulosa cell tumors including all previously reported cases and the current case, 6 patients had metastatic disease. The tumor can metastasize to retroperitoneal lymph nodes, liver, bone and lung.

The morphological features associated with malignant behaviors have not been well defined. Jimenez-Quintero et al reviewed 52 cases of testicular sex-cord-stromal tumors, in which there were 7 cases of adult type granulosa cell tumors. They found that many malignant tumors had the following features: size >7.0 cm, lymphovascular invasion, tumor necrosis, and hemorrhage. Hanson et al reviewed all the reported cases of adult testicular granulosa cell tumors and found that only size greater than 5.0 cm reached statistical significance in association with malignancy. Mitotic count and tumor necrosis did not reach statistical significance in predicting the tumor clinical behavior. More cases may be needed to refine the morphological features that may predict for the clinical behavior of the tumor.

The initial treatment for all reported cases was radical or inguinal orchiectomy. There is no evidence to support additional therapy in patients with disease clinically confined to testicle. There is no consensus regarding the treatment for metastatic disease, which may include chemotherapy and/or radiation. Interestingly, Harrison et al reported an advanced testicular granulosa cell tumor partially responding to an angiogenesis inhibitor after initially resisting to cytotoxic chemotherapy. Long term follow-up with a sufficient number of cases may be needed to define optimal treatment options for patients with this rare tumor.

References

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