Sertoli-Leydig cell gonadal stroma tumors in the Dr. Manuel Gea González General Hospital


ABSTRACT

Gonadal stroma tumors are rare and include Leydig cell, Sertoli cell, mixed and non-classified tumors. Leydig cell tumors make up 1-3% of testicular tumors in the adult and 3% in the child. They are the most common type of gonadal stroma tumor. Approximately 10% are malignant and 30% present with gynecomastia. Three cases of gonadal stroma tumor are presented: a Sertoli-Leydig cell tumor, a large-cell calcifying Sertoli cell tumor and a Leydig cell tumor.

Key words: Tumor, Sertoli, Leydig, Mexico.

INTRODUCTION

Gonadal stroma tumors are rare and include Leydig cell, Sertoli cell, mixed and non-classified tumors. Leydig cell tumors are the most common of the gonadal stroma tumors. They represent 1-3% of testicular tumors in the adult and 3% of tumors in children. They are more common between the third and sixth decade of life in adults and between 3-9 years of age in children. Three percent of Leydig cell tumors are bilateral, solid and measure approximately 5 cm and 30% present with hemorrhage or necrosis. Under the microscope their cells are polygonal with eosinophilic cytoplasm and Reinke’s crystals. Approximately 10% are malignant and characterized by tumor ≥ 5 cm, cytologic...
atypia, increased mitotic activity, necrosis, vascular invasion, infiltrative margins, extension beyond the testicular parenchyma and DNA aneuploidy. They can present with testicular pain during ultrasonography (USG).

Estrogen and estradiol serum levels are elevated in 80% of cases and testosterone levels are reduced. Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) may be increased and germ cell tumor markers are negative. Thirty percent of these tumors present with gynecomastia and cause metastasis to lymph nodes, lung, liver and bone. When stroma tumors show signs of malignancy, radical orchiectomy and lymphadenectomy should be performed. These types of tumors respond poorly to chemotherapy and radiotherapy.1,2

Sertoli cell tumors present in ≤ 1% of gonadal stroma tumors and affect men at a mean age of 45 years. They rarely present in patients with Peutz-Jeghers syndrome or androgen insensitivity syndrome. The tumor is well-defined with a mean 3.5 cm diameter. Under the microscope its cells are eosinophilic with vacuolated cytoplasm and cell arrangement is tubular or solid. They express vimentin, cytokeratins, inhibin (40%) and S-100 protein (30%). Malignancy range is 10-22% (fewer than 50 reported cases).

Signs of malignancy are size ≥ 5 cm, pleomorphic nucleus with prominent nucleolus, increased mitotic activity, necrosis and vascular invasion. These tumors are classified as classic Sertoli cell tumor, large cell calcifying tumor and sclerosing tumor (rare). Tumor markers are always negative. Large cell calcifying tumors present in young men and are associated with genetic syndromes (Carney, Peutz-Jeghers). Approximately 40% of cases present with endocrine disorders.2 Forty-four percent are bilateral and 28% are multifocal.

This type of tumor may present with precocious pseudopuberty with signs of virilization. In the adult, 40% present with feminization, serum estradiol and testosterone level elevation with normal FSH and LH levels. Ten percent are malignant and are associated with cryptorchidism (9%), sexual ambiguity, pseudohermaphroditism, gynecomastia and Klinefelter’s syndrome.3

Three cases from our institution are presented.

### CLINICAL CASE 1

The patient is a 35-year-old man whose illness had begun 2 months before seeking medical attention for increased volume in the right testicle accompanied with moderate steady pain and a sensation of heaviness. Upon urologic examination, an increase in volume and consistency was observed in the right scrotal sac. Palpation produced pain. There were no alterations in the left testicle. Preoperative study results were alpha-fetoprotein (AFP) 4.1 ng/ml, human chorionic gonadotropin (hCG) β subunit 0.26 mIU/ml and lactic acid dehydrogenase (LDH) 116 mIU/ml. Ultrasonogram of the testicle showed hypervascular and heterogeneous echographic changes (Image 1).

Chest X-ray did not show any alterations. Right radical orchiectomy was performed. Histopathological report revealed 7 x 4.5 x 5 cm Sertoli-Leydig tumor affecting the tunica albuginea without vascular affection. Epididymis and spermatic cord were
tumor-free (Images 2 and 3). Abdominal computed axial tomography (CAT) showed no postoperative complications (Image 4).

At 2-year follow-up the patient has had no changes in tumor markers, chest X-ray and abdominal CAT.

**CLINICAL CASE 2**

The patient is a 19-year-old man whose illness had begun 18 months prior to being seen for an increase of volume in the left testicle accompanied with moderate pain. Urological examination revealed increase in volume and consistency in the left scrotal sac that was painful when palpated. There were no alterations in the right testicle.

Laboratory work-up showed AFP 4 ng/ml, hCG-β fraction 0.3 mIU/ml, LDH 161 mIU/ml. Ultrasound revealed heterogeneous left testicular tumor (Image 5). Chest X-ray showed no alterations. Left radical orchiectomy was performed and histopathological report described 1.4 cm large cell calcifying Sertoli cell tumor with surgical margin free from neoplastic activity. At 2-year follow-up, patient presents with negative tumor markers and chest X-ray and abdominal CAT show no signs of malignancy.

**DISCUSSION**

In relation to frequency, these types of tumors present as Sertoli cell tumors in 1%, Leydig cell tumors in 1-3% and mixed tumors in 0.2%. Currently there are approximately 50 cases of Sertoli or Leydig cell tumor and 23 cases of Leydig-Sertoli cell tumor reported in the literature, making the presentation of the case series from our institution relevant. Metastasis is the only criterion for malignancy. Suspicion criteria includes tumor ≥ 5 cm, cellular pleomorphism, elevated mitotic index, tumor necrosis and capsular, vascular and cord invasion. These tumors grow slowly, with dissemination to the lymph nodes (iliac and retroperitoneal) and pulmonary, liver and bone metastases. At the time of malignancy diagnosis, 25% of tumors present with lymph node metastasis. Diagnosis is difficult because presentation can correspond to any histological type.
Surveillance should be long-term due to the infrequency and low percentage of malignancy of these tumors and standard treatment is radical orchiectomy.  

**CONCLUSIONS**

This type of tumor is infrequent and the majority of cases are benign. Approximately 25% of tumors are malignant at time of diagnosis and therefore standard treatment should be radical surgery and surveillance as stipulated by international guidelines.

**BIBLIOGRAPHY**