JOURNAL OF HEALTH SCIENCES AND MEDICINE

Sağlık Bilimleri ve Tıp Dergisi

J Health Sci Med 2019; 2(2): 72-74

Case Report / Olgu Sunumu

Pure Leydig cell tumor: a rare case report

Saf Leydig hücresi tümörü: nadir bir olgu sunumu

Mehmet Zengin

Kırıkkale University Faculty of Medicine, Department of Pathology, Kırıkkale, Turkey

ABSTRACT

Leydig cell tumors are rare tumors and constitute 1-3% of all testicular tumors. The pure form of these tumors, which are often found in mixed form with Sertoli cells, is extremely rare. It is very difficult to determine the malignancy potential in Leydig cell tumors most commonly manifested by a testicular mass or endocrine symptoms. In this study, clinical, histological and prognostic features of a pure form of Leydig cell tumors are presented in the light of literature information.

Keywords: Leydig cell tumor, testicular tumors, endocrine manifestation

ÖZ

Leydig hücre tümörleri nadir tümörler olup tüm testiküler tümörlerin% 1-3'ünü oluşturur. Sıklıkla Sertoli hücreleri ile karışık formda bulunan bu tümörlerin saf formu son derece nadirdir. Testiküler kitle veya endokrin semptomları ile en sık görülen Leydig hücresi tümörlerinde malignite potansiyelini belirlemek çok zordur. Bu çalışmada, saf Leydig hücre tümörleri formunun klinik, histolojik ve prognostik özellikleri literatür bilgileri ışığında sunulmuştur.

Anahtar Kelimeler: Leydig hücre tümörü, testis tümörleri, endokrin tezahürü

INTRODUCTION

According to the different series, non-germ cell tumors are 5-6% of all testicular tumors. Mixed tumors, sex cord / stromal tumors (commonly Leydig / Stromal cell tumors), mesenchymal or hematopoietic neoplasias are found in this group (1). Leydig hücre tümörleri (LCT) is a rare neoplasm arising from the gonadal stroma. They are often found in mixed form with Sertoli cells (2). In the last few years, the incidence of LCT has risen far beyond estimates (approximately 14.7% of the testicular neoplasias). Increased use of imaging technology and increased detection of small nodules are possible explanations for this finding (2,3). The aim of our study is to emphasize the clinical, histological and prognostic qualities of this rare tumor.

CASE REPORT

A male patient of 48-year-old presented to the urology polyclinic with painless, slowly enlarging left testicular mass. There was no anamnesis of scrotal pain, cryptorchidism, loss of weight, hereditary disease or trauma. On physical examination, unilateral testicle enlargement was observed. In the palpation,

Corresponding Author: Mehmet Zengin, Kırıkkale University, School of Medicine, Department of Pathology Kırıkkale, Turkey

E-mail: mz1379@hotmail.com

Receiveed: 2018.08.14 **Accepted:** 2018.09.16 **Doi:** 10.32322/jhsm.453515

Cite this article as: Zengin M. Pure leydig cell tumor: a rare case report. J Health Sci Med 2019; 2(2): 72-74.

an elastic-hard, well-defined, painless left testicular mass was detected and inguinal lymph nodes could not be palpated. Ultrasonography showed a well-defined, 2x1 cm solid tumor lesion with homogeneous echogenicity. Lactate dehydrogenase, alpha-fetoprotein and beta-human chorionic gonadotropin were in normal limits. No evidence of lymphadenopathy or metastasis favored in the upper and lower abdominal computerized tomography. Clinically preoperative diagnosis was probability of classical seminoma. The patient was accepted as first stage and left orchiectomy was applied.

In the macroscopic investigation, left testis was a 7x4 cm size and there was significant swelling, no testis attachments were observed. The sections showed 2x1 cm sized, well-defined, pale gray-white colored tumoral lesion within the testis. Tunica vaginalis, tunica albigunea, skin and testis attachments were not invasive. Histological examination revealed that the tumor formed diffuse patterns or small asiner structures **(Figure a)**. It was noted that the tumor consisted of large granular eosinophilic cytoplasm cells and occasionally nucleol-containing cells. In the cytoplasm of some cells, Reinke crystals were detected. Mitosis, necrosis, pleomorphism, atypia were not observed **(Figure b-c)**. Immunohistochemically, it was shown that the inhibin alpha **(Figure d)**, calretinin, vimentin positive and pancreatin, CD30, placenta-like alkaline phosphatase (PLAP) were negative. Immunohistochemical and histological findings revealed a case of Leydig cell tumor. Since no different component was observed in the sections, it was accepted as pure form. Patient was followed without further treatment and loco-regional metastasis was not occured 18 months after the surgery.

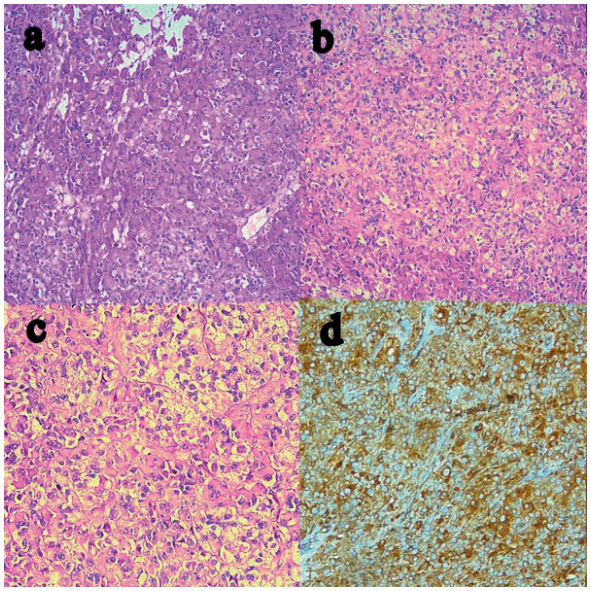

Figure. Representative examples of hematoxylin and eosin (*H&E)* and İnhibin with Leydig cell tumour (LCT).

LCT is characterized by the arrangement of cells, resembling normally leydig cells of testis, in layers and cords. **a.** LCT formed diffuse patterns or small asiner structures (H&Ex200) **b-c.** SS showing a characteristic mixture of cells with large granular eosinophilic cytoplasm and occasionally nucleol-containin cells (H&Ex200/400) **d**. Positivity of tumoral cells for İnhibin antibody (x400).

DISCUSSION

Most common non-germ cell testicular tumor is the LCT and %10 of the LCT cases are bilateral (1). Approximately quaternary cases appear in the prepubertal period although a majority of cases have been reported to develop from undescended testes between 20 and 60 years of age (2). LCTs are always good prognosis at children (2). Clinical presentation may be asymptomatic during testicular growth, gynecomastia, and sexual dysfunction, or asymptomatic during testicular ultrasonography (3). Increased estradiol levels and reduced testosterone levels are observed in adults with feminization and childhood masculinisation in % 20 of cases (3). Endocrinologic disorders are the most common presentation and palpable testicles precede the immune system and can lead to oligozoospermia, cryptoazoospermia or azoospermia. Most of these tumors are hypoechoic and hypervascularized on ultrasonography (4). MR may also detect small LCT cases not seen on ultrasonography. As with all intra-scrotal lesions, the ultimate diagnosis is based on histopathological findings. Clinical and hormonal manifestations after orchiectomy are reduced by 90% . For follow-up to detect tumor recurrence, endocrinologic changes are useful (5).

Metastasis in LCT is very rare. Presence of necrosis, cytologic atypia, vascular invasion, infiltrative borders, increased mitotic activity and MIB-1 activity propose potential metastatic behavior in LCTs (6). At the same time, some immunohistochemical antibodies (bcl-2, Ki-67, p53) may be valuable in identifying malignant and borderline cases in LCT. Metastases are commonly seen in retroperitoneal lymph nodes, liver, bones and liver (6).

The molecular substructure of LCTs is less demonstrated and the etiology is unknown. In the etiology of this tumor, Some studies have reported a probable role of genetic elements. Curiously, the genetic mutations determined so far in children and adults are different from other cancers (7). The somatic mutation of Guanine nucleotide binding protein has reported by some authors, a gene which is thought to lead to tumor development in adult LCTs. This acti-

vation also leads to hyperactivity of the testosterone pathway and overexpression of the inhibitory alpha subunit (8). In addition, hereditary fumarate hydratase mutation, which causes tumor growth through in adults, has also been reported. Changes in local stimuli such as müllerian channel inhibitor factor, temperature, growth factors have also been reported to be favorable conditions for tumor formation (8). Palazzo has proposed that most of LCTs are diploid and that the aneuploidy findings may be useful prognostic marker (9).

Orchiectomy with or without lymphadenectomy is the first treatment for LCT. Nowadays, authors offer a conservative treatment and suggest that testicular surgeon is a best choice as first-line treatment for small tumors and young men (10). Surgery may be curative in about 90% of patients, while chemotherapy and radiotherapy resistant metastases may develop in the remaining patients (10). Metastatic forms of LCT have potential for lymph nodes (65%), lungs, liver and bone. Metastatic type LCTs are seen only in adults and often over 40 years of age patients. The malignancy risk in undescended testes was 4 to 10 times higher than general population (11). In our case, our clinical and histological findings were consistent with the literature and no malignant course or endocrine disorder was observed in 4 year follow-up.

CONCLUSION

Testicular LCTs are rare but interesting tumors due to their potential to cause endocrine disorders. All patients should be followed for a long time because of the difficulty of determining definitive malignant differentiation. The maintenance of these rare tumors, which we encounter more often with the development of imaging modalities, will contribute to our knowledge and approach to these tumors.

DECLARATION OF CONFLICTING INTERESTS

The author declared no conflicts of interest with respect to the authorship and/or publication of this article.

REFERENCES

1. Dilworth JP, Farrow GM, Oesterling JE. Non-germ cell tumors of testis. Urology 1991; 37: 399–417.
2. Emerson RE, Ulbright TM: Morphological approach to tumours of the testis and paratestis. J Clin Pathol 2007; 60: 866–80.
3. Cheville JC: Classification and pathology of testicular germ cell and sex cord-stromal tumors. Urol Clin North Am 1999; 26: 595–609.
4. Leonhartsberger N, Ramoner R, Aigner F, et al. Increased incidence of Leydig cell tumours of the testis in the era of improved imaging techniques. BJU Int 2011; 108: 1603–07.
5. Giacaglia LR, Kohek MB da F, Carvalho FM, Fragoso MC, Mendonca B, Latronico AC. No evidence of somatic activating mutations on gonadotropin receptor genes in sex cord stromal tumors. Fertil Steril 2000; 74: 992–5.
6. Libe R, Fratticci A, Lahlou N, et al. A rare cause of hypertestosteronemia in a 68-year-old patient: a Leydig cell tumor due to a somatic GNAS (guanine nucleotide-binding protein, alpha-stimulating activity polypeptide 1)-activating mutation. J Androl 2012; 33: 578–84.
7. Carvajal-Carmona LG, Alam NA, Pollard PJ, et al. Adult leydig cell tumors of the testis caused by germline fumarate hydratase mutations. J Clin Endocrinol Metab 2006; 91: 3071–5.
8. Lejeune H, Habert R, Saez JM. Origin, proliferation and differentiation of Leydig cells. J Mol Endocrinol 1998, 20: 1–25.
9. Butruille C, Marcelli F, Ghoneim T, et al. Management of testicular lesions in a population of infertile patients. Prog Urol 2012; 22: 45–52.
10. Hekimgil M, Altay B, Yakut BD, Soydan S, Ozyurt C, Killi R. Leydig cell tumour of the testis: comparison of histopathological and immunohistochemical features of three azoospermic cases and one malignant case. Pathol Int 2001; 51: 792-6.
11. Kaufman E, Akiya F, Foucar E, Gambort F, Cartwright KC. Virilization due to Leydig cell tumor diagnosis by magnetic resonance imaging: case management report. Clin Pediatr 1990; 29: 414-7.
12. Maeda T, Itoh N, Kobayashi K, Takahashi A, Masumori N, Tsukamoto T. Elevated serum estradiol suggesting recurrence of Leydig cell tumor nine years after radical orchidectomy. Int J Urol 2002; 9: 659-61.
13. Ulbright TM, Srigley JR, Hatzianastassiou DK, Young RH. Leydig cell tumours of the testis with unusual features: adipose differentiation, calcification with ossification, and spindle-shaped tumour cells. Am J Surg Pathol 2002; 26: 1424-33.
14. Palazzo JP, Petersen RO, Young RH, Scully RE. Deoxyribonucleic acid flow cytometry of testicular Leydig cell tumors. J Urol 1994; 152: 415–7.
15. Henderson CG, Ahmed AA, Sesterhenn I, Belman AB, Rushton HG. Enucleation for prepubertal leydig cell tumor. J Urol 2006; 176: 703–5.
16. Bertram KA, Bratloff B, Hodges GF, Davidson H. Treatment of malignant Leydig cell tumor. Cancer 1991; 68: 2324–9.
17. Hekimgil M, Altay B, Yakut BD, Soydan S, Ozyurt C, Killi R. Leydig cell tumor of the testis: comparison of histopathological and immunohistochemical features of three azoospermic cases and one malignant case. Pathol Int 2001; 51: 792–6.
18. Trabert B, Zugna D, Richiardi L, McGlynn KA, Akre O. Congenital malformations and testicular germ cell tumors. Int J Cancer 2013; 133: 1900–4.