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Case Report

A peak into metastatic Leydig cell tumor: a rare case report

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ABSTRACT

Testicle tumors are a rare entity among men population, comprising 1-1.5% of all cancers. The Sex cord Stromal tumors contribute just 4% of all testicular cancers, only 10% of them are malignant. Most common sex cord-stromal tumors are the Leydig cell tumor, comprising of 75 to 80% of the total. Incidence is bimodal involving children and adults between 30 and 60 years. The commonest metastatic sites are regional lymph nodes, lung, liver, and bones. Here, we report a case of late metastatic relapsed Leydig cell tumor in a 38-year-old male. Patients with metastatic Leydig cell tumors have poor prognosis and standard treatment recommendations are unclear.

Keywords: Leydig cell tumor, Testis, Neoplasms

INTRODUCTION

Testicular neoplasms are a rare entity among men, accounting for only 1-1.5% of all male cancers. Most common tumors are germinal comprising of seminoma and nonseminoma. The incidence of germ-cell tumors (GCTs) decreases after 50 years of age, whereas the incidence of spermatocytic seminoma, primary lymph-oma, stromal tumors and metastasis increases.[1] Leydig cell tumors (LCTs), comprise of 5% of all sex cord stromal tumors (SCSTs), are the most common and originate from the Leydig cells that normally occupy the interstitium of testicles and secrete testosterone in the presence of luteinizing hormone. They are commonly benign tumors, rarely 5%-10% are found malignant. They have a bimodal distribution, peak occurring in the prepubertal age group and between the ages of 30 and 60 years.[2] It can present from being asymptomatic disease to locally invasive or metastatic disease. LCTs can be challenging to diagnose, requiring a collaboration of clinical, imaging, and histological analysis. Treatment includes surgery, with either radiation therapy or hormone therapy.[3,4] We report a rare case of a late metastatic relapsed Leydig cell tumor in a 38-year-old male, instigating the diagnostic and treatment approaches. Data shows incidence of only 1% of individuals who experience a late recurrence of testicular germ cell tumors, defined as developing more than 5 years after the initial presentation, associated with an unfavourable prognosis.[5] The purpose of this report was to emphasize into the clinical course, management and to provide an aid in the diagnostic, treatment decision-making process for all healthcare professionals.

CASE REPORT

A 38-year-old male initially was diagnosed with testicular cancer that was treated with a Right high inguinal orchidectomy at the age of 33 years. Outside Histopathology report stated an LCT, a subtype SCST measuring 6.5 x 6.0 x 5.5 cm in size and was completely encapsulated, with no lymphovascular invasion, negative for extratesticular involvement and spermatic cord

resection margin. Biochemical parameters stated LDH-2627, normal alpha-feto protein (AFP) and beta human chorionic gonadotropin (β-HCG). After doing well for 5 years, Patient presented at our centre with complain of right abdominal pain for 1-2 weeks and late semen ejaculation.

Figure 1: Gross pathology of Leydig cell tumor: the right iliac fossa mass is bisected, revealing a nodal mass approximately 11.5 cm diameter, circumscribed, heterogeneous lesion showing focal haemorrhage and necrosis.

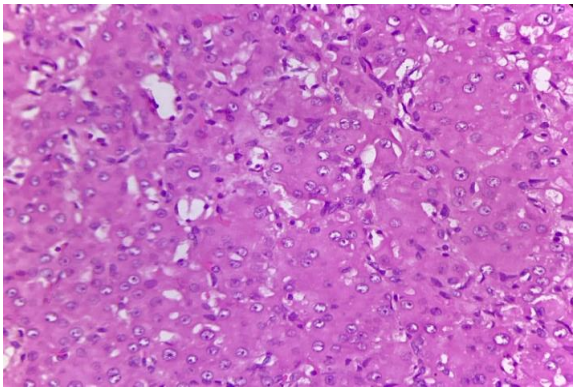

Figure 2: Haematoxylin & eosin, 200X magnification, stained section shows plump polygonal cells with abundant cytoplasm with many prominent nucleoli.

Patient underwent CECT abdomen-pelvis illustrating 11.5 cm lesion right iliac fossa, closely abutting right external iliac artery, loss of fat planes with small bowel loops, few enlarged nodes at lower preaortic, prevcaval largest measuring 1.9 cm in length and left adrenal adenoma. Biochemical parameters evaluated showed normal AFP-1.71, β-HCG-0.3. Patient underwent USG guided biopsy from Right iliac fossa mass, histopathology report stated lesion comprised of clusters & trabeculae of polygonal cells exhibiting round nuclei & vesicular chromatin surrounded by abundant eosinophilic cytoplasm, favouring Leydig cell tumor. The patient was discussed at the multidisciplinary tumor board, based on the history and diagnostic information, it was determined that the patient had metastatic relapse. Imaging of the left testicle with ultrasound was negative. Outside blocks were requested for Review at our centre, however due to some technical issues patient failed to produce the same. Patient underwent Right iliac fossa mass excision (Figure 1) along with removal of pelvic, retroperitoneal and aortic group of lymph nodes.

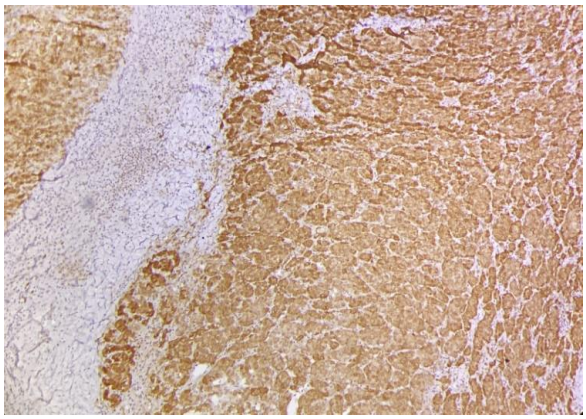

Figure 3: Immunohistochemical stain performed show positive staining for inhibin.

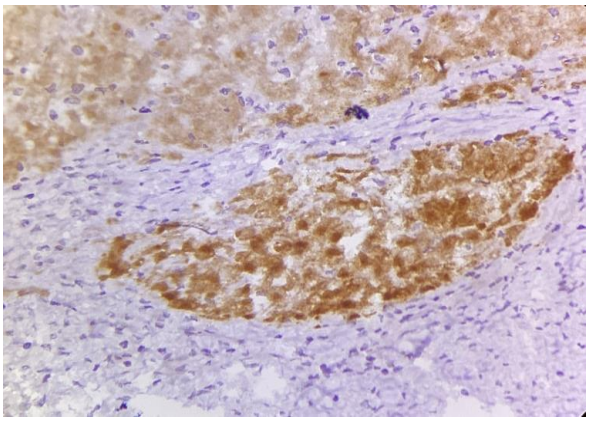

Figure 4: Immunohistochemical stain performed show positive staining for calretinin.

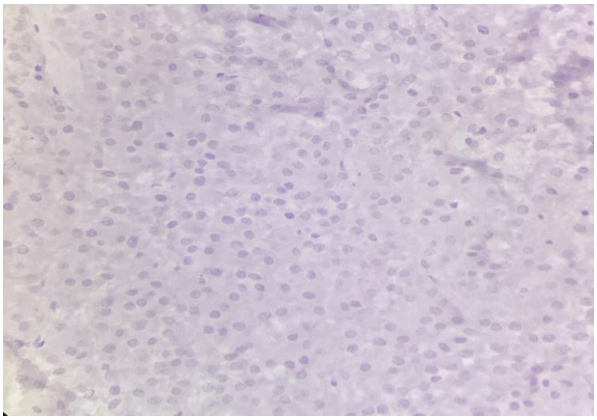

Figure 5: Immunohistochemical stain performed show negative staining for SALL 4.

Final Histopathology report stated metastatic nodal mass with sheets, clusters & nests of polygonal cells exhibiting

round nuclei & vesicular chromatin surrounded by abundant eosinophilic cytoplasm, nuclear pleomorphism ranged from mild to moderate with extensive areas of necrosis, haemorrhages and sclerosis, suggestive of metastatic malignant leydig cell tumour with four metastatic nodes (Figure 2). Immunohistochemistry performed was found consistent with LCT, tumor cells were positive for calretinin, α-inhibin, synaptophysin, vimentin, and Ki-67 proliferative index of 7% consistent with LCTs. The tumor was negative for CK 20, CK7, S100, EMA, WT1, SALL-4 and SOX10 (Figure 3-5).

DISCUSSION

Testicular neoplasms are broadly divided into two major groups: germ cell tumors and sex stromal cord tumors (SCSTs). SCSTs are derived from Leydig cells, Sertoli cells, granulosa cells, or rarely theca cells.[6] Most common among stromal tumors is the Leydig cell tumor, comprising up to 75 to 80% cases, having no association with cryptorchidism. Incidence is bimodal with peak involving children and adults between 30 and 60 years. Children account for 25% of cases. Elderly people tend to have malignant tumors.[7] The histopathological diagnosis of LCTs is usually based on tumor cells morphology. Pathologists must be familiar with the diagnostic histopathologic features, immunohistochemical panel of this tumor, and its principal differential diagnoses to prevent tumor misdiagnosis.[3] Microscopically, LCTs appear as monomorphic sheets or nests of large cells, with increased eosinophilic cytoplasm and regular nuclei with a conspicuous nucleolus. Sometimes it may show spindle-shaped cells or cytoplasm with vacuoles. In about one third of cases, Reinke's eosinophilic crystals can be observed in the cytoplasm however doesn't comprise a definite finding to indicate neoplasia.[8] The risk factors and etiology for LCT are unclear. The pathogenesis of Leydig cell tumor is poorly understood. It is hypothesisied that disruption of the hypothalamic–pituitary– testicular axis leads to excessive stimulation of Leydig cells by excess luteinizing hormone. Activating mutation in the guanine nucleotide-binding protein α gene is a cause of adult LCTs, by driving tumor development and causing hyperactivity of the testosterone biosynthetic pathway.[9] Adults commonly present with painless testicular masses, orchialgia, gynecomastia, impotence, decreased libido or infertility. Children are usually aged between 5 and 10 years old and present with testicular masses and precocious signs of virilization, including pubic hair, increased penis size and acne due to abnormal amounts of testosterone. In this age group differential diagnosis with causes of early puberty: congenital adrenal hyperplasia, adrenocortical carcinoma and isosexual precocious puberty should be made.[7] Our patient presented with late semen ejaculation along with pain at the age of 38 years. A scrotal ultrasound is said to have high sensitivity for diagnosing testicular tumors (98%-100%).[10] LCTs typically appear as hypoechoic and hypervascular lesions on ultrasound. Majority LCTs are benign tumors, rarely 5%-10% being found malignant.[11] Malignant behavior has not been described in young population. The usual metastatic sites are regional lymph nodes, the lung, liver, and bones.[12] Reported incidence is of 20% metastatic disease and 40% metastatic involvement within 2 years from the diagnosis has been found.[13] In our case, the patient was found to have late metastatic relapse ipsilateral side iliac fossa over 5 years after initial diagnosis and treatment. A late recurrence of testicular germ cell tumors, is defined as occurring more than 5 years after the original presentation, associated with a poor prognosis.[5]

Leydig cell tumor scaled score (LeSS) has been made a predictive mode to assess metastatic risk, and to pathologically differentiate between benign and malignant LCT. Kim et al examined five metastatic LCTs in adult males and found that at least four of the six major indicators of malignancy (>3 mitoses/10 high-power fields, size >50 mm, infiltrative boundaries, nuclear atypia, vascular invasion, and necrosis) were consistently present.[4] It is proposed that benign LCT stands for LeSS score <4 whereas all malignant LCTs were accurately recognized with a LeSS of >4.[14] With little information over whether this criterion was applied to our patient's initial diagnosis when the disease was localized is unclear, the outside histopathology report stated a mass of 6.5 cm in primary tumor, which was encapsulated with no lymphovascular emboli and no extratesticular involvement, these overall characteristics favour low chance for disease recurrence. This instigates for awareness among pathologists that though majority LCT have benign course, no stone should be left unturned to rule out hidden malignant features. Malignant behavior of Leydig cell tumors is exhibited by metastasis to the retroperitoneal lymph nodes, liver, lungs, and bone.[12] If metastatic disease does occur, it responds poorly to chemotherapy or radiation, leaving surgical resection (retroperitoneal lymph node dissection or RPLND) as the only treatment capable of rendering patients disease-free.[15] Regular long-term follow-up with endocrine profile and imaging investigations repeated periodically, are recommended to exclude recurrence or metastasis.[3] In current case, the expectation was for pain control and possibly improved disease control for prevention of progression of disease. On subsequent follow-up, the patient's symptoms were found to be relieved.

CONCLUSION

Patients presenting with metastatic LCT (or SCST) have poor prognosis and no standard treatment recommend-ations are described in literature. It is found to be resistant to radiation therapy and chemotherapy, with surgery as the main modality of treatment implicating complete removal of tumor. Given the rare occurrence of this malignancy, this study emphasizes the importance of evaluation of thorough histopathological characteristics and LeSS score at patient's first presentation itself so that no endeavours are left behind to search for hidden malignant features.

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REFERENCES

1. Berney DM, Warren AY, Verma M, Kudahetti S, Robson JM, Williams MW, et al. Malignant germ cell tumours in the elderly: a histopathological review of 50 cases in men aged 60 years or over. Mod Pathol. 2008;21:54-9.
2. Mooney KL and Kao CS. A contemporary review of common adult non-germ cell tumors of the testis and paratestis. Surg Pathol Clin. 2018;11:739-58.
3. Al-Agha OM and Axiotis CA. An in-depth look at Leydig cell tumor of the testis. Arch Pathol Lab Med. 2007;131:311-7.
4. Kim I, Young RH and Scully RE. Leydig cell tumors of the testis. A clinicopathological analysis of 40 cases and review of the literature. Am J Surg Pathol. 1985;9:177-92.
5. Moore JA, Slack RS, Lehner MJ. Very late recurrence in germ cell tumor of the testis: lessons and implications. Cancers. 2022;14:1127.
6. Ober WB and Sciagura C. Leydig, Sertoli, and Reinke: three anatomists who were on the ball. Pathol Ann. 1981;16(1):1-13.
7. Stephenson AJ, Gilligan,TD. Neoplasms of the Testis. In: Wein AJ, Kavoussi LR, Novick LR, Partin AW, Peters CA, editors. Campbell-Walsh urology. 11th ed. Philadelphia: Elsevier; 2016:784-814.
8. Ulbright TM, Kao C-S, Williamson SR. Tumors and tumor-like lesions of the testis and adjacent tissues. Arlington: American Registry of Pathology; 2022.
9. Boot AM, Lumbroso S, Verhoef-Post M. Mutation analysis of the LH receptor gene in Leydig cell adenoma and hyperplasia and functional and biochemical studies of activating mutations of the LH receptor gene. J Clin Endocrinol Metab. 2011; 96:E1197-205.
10. Acar C, Gurocak S and Sozen S. Current treatment of testicular sex cord-stromal tumors: critical review. Urology. 2009;73:1165-71.
11. Pomajzl AJ and Siref LE. Leydig cell cancer. Treasure Island, FL: Statpearls; 2023.
12. Rich MA and Keating MA. Leydig cell tumors and tumors associated with congenital adrenal hyperplasia. Urol Clin North Am. 2000;27:519-28.
13. Bertram KA, Bratloff B, Hodges GF. Treatment of malignant Leydig cell tumor. Cancer. 1991;68: 2324-9.
14. Colecchia M, Bertolotti A, Paolini B. The Leydig cell tumour scaled score (LeSS): a method to distinguish benign from malignant cases, with additional correlation with MDM2 and CDK4 amplification. Histopathology. 2021;78:290-9.
15. Cost NG, Maroni P, Flaig TW. Metastatic relapse after initial clinical stage I testicular Leydig cell tumor. Oncology. 2014;28(3):211-4.

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