Case Report

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Leydig cell tumor of testis- a rare case report

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ABSTRACT

Leydig cell tumors(LCTs) of testis are rare testicular tumors of male gonadal interstitium. Although rare, they are most common sex cord stromal tumors and comprise 1-3 % of all testicular neoplasms. They usually occur in fourth to sixth decade. In young patients, they are mostly benign and in adults it can be malignant in about 10 % cases. The incidence of Leydig cell tumors is gradually increasing every year which might be attributed to increased use of radiological techniques and subsequent early detection of tumors that have not been found in historical series. Here we report a case of benign Leydig cell tumor testis in a 45-year-old male who presented with left sided testicular mass. The patient subsequently underwent high inguinal orchidectomy. Histopathological examination showed benign pure Leydig cell tumor. Serological investigations revealed normal testosterone levels, DHEA and androstenedione levels. Immunohistochemical staining for inhibin showed fine granular cytoplasmic positivity and diffuse positive staining for Melan-A which further confirmed the diagnosis. The endocrine profile and imaging investigations of such patients might be normal and patients can be totally asymptomatic. However periodic follow up of endocrine profile and imaging must be done as many cases have been reported which had deranged endocrine levels and appearance of atypical symptoms even after years of unilateral orchidectomy. Our case also presents with normal hormonal levels, henceforth for a better prognosis we must identify benign LCTs and do long term follow up.

Keywords: Benign, Leydig cell tumour, Testis

INTRODUCTION

Leydig cell tumors (LCT) of testis are rare testicular tumors of male gonadal interstitium and comprise 1-3 % of all testicular neoplasms. They usually occur in fourth to sixth decade. In young patients, they are mostly benign and in adults it can be malignant in about 10 % cases. The incidence of Leydig cell tumors is gradually increasing every year which might be attributed to increased use of radiological techniques and subsequent early detection of tumors that have not been found in historical series.

An increased risk of testicular cancer is associated with male infertility, LCT, a benign neoplasm usually presents as a testicular mass, accompanied or preceded by hormonal changes, leading to either feminizing or virilizing syndromes but the endocrine profile of such patients might be normal.⁴ It is very important to identify such cases as many cases have been reported which had deranged endocrine levels and appearance of atypical symptoms even after years of unilateral orchidectomy.⁵ Our case also presents with normal hormonal levels, henceforth we must identify benign LCTs and do long term follow up.

CASE REPORT

A 45-year-old male presented with the complaint of infertility. On physical examination, a left sided testicular mass was detected. Patient had no sign of gynecomastia or palpable inguinal lymph nodes. On Ultrasound, it typically showed homogeneous hypoechoic a sonographic appearance which signifies its benign nature. Serum tumor markers AFP, HCG and LDH were found to be within normal limits. The patient subsequently underwent high inguinal orchiectomy. We received a specimen of left testis with attached spermatic cord altogether measuring 11x4x3 cm in which testis measured 4x2x2 cm. Attached spermatic cord measured 7 cm in length. On cut section, testis showed greyish white to greyish yellow circumscribed mass measuring 2x2x1.5 cm with normal testis seen at upper pole. Focal areas of hemorrhage were also seen. Tumor appeared to be reaching up to testicular capsule at lower pole. No lymph nodes were identified.



Figure 1: Cut section of testis showing greyish white to greyish yellow well circumscribed tumor mass measuring 2x2x1.5 cms with normal testis at upper pole. focal areas of haemorrhage also seen.

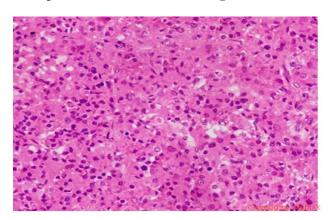


Figure 2: Tissue section showing individual tumour cells having round to polygonal shape with dense granular eosinophilic cytoplasm and round to oval vesicular nuclei with mild nuclear pleomorphism and prominent nucleoli in some. (H and E, x40).

Histopathological examination showed a well circumscribed lesion comprising of solid sheets and cords

of tumor cells. Individual tumor cells were round to polygonal in shape with dense granular eosinophilic cytoplasm and round to oval vesicular nuclei with mild nuclear pleomorphism and prominent nucleoli in some. At places, eosinophilic cytoplasmic inclusions, Rinke's crystals were identified. Mitotic activity (2-3/10 hpf) was low and there was no necrosis, nuclear atypia, atypical mitotic figures or lymphovascular invasion. Rest of the testes showed atrophy with increase in Leydig cells in the interstitium. Based on the above histopathological features diagnosis of benign Leydig cell tumour of left testis was made.

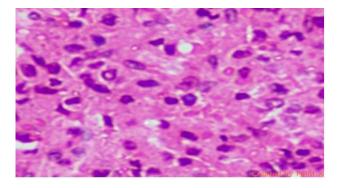


Figure 3: Tissue section showing eosinophilic cytoplasmic inclusions, Rinke's crystals at few places. (H and E, x40).

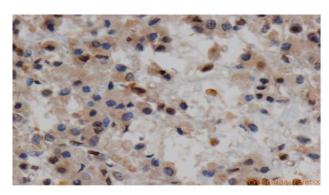


Figure 4: immunohistochemical (IHC) staining for inhibin showing cytoplasmic positivity in tumor cells. (x40).

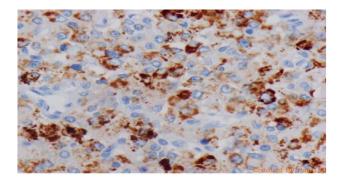


Figure 5: Immunohistochemical (IHC) staining for Melan-A showing positive staining in tumor cells. (x40)

Immunohistochemical (IHC) staining for inhibin showed fine granular cytoplasmic positivity. It also showed diffuse positive staining for Melan-A which further confirmed the diagnosis. Tumour cells were negative for Placental like alkaline phosphatase (PLAP). Serological investigations revealed normal testosterone levels, Dehydroepiandrosterone (DHEA) and androstenedione levels.

DISCUSSION

LCTs constitute 1-3% of all testicular tumors. They can occur at any age but are more common in prepubertal boys (most often between 5 and 10 years of age) and in men aged 30 to 60 years.^{6,7} They are mostly benign in children, whereas in adults they are malignant in 10% of cases.^{2,3} LCTs are hormonally active and considered as one of the steroid-secreting tumors. They produce androgens, mainly testosterone, but can produce estrogen by either direct production of estradiol or peripheral aromatization of testosterone. In androgen-secreting tumors, in adults, most patients are asymptomatic as the excess androgen rarely causes notable effects. In estrogen-secreting tumors, feminizing symptoms predominate, adults generally present with gynecomastia associated with loss of libido, erectile dysfunction, impotence, and infertility.

LCTs may be an incidental finding of a testicular mass on scrotal ultrasonography performed for other conditions.⁸ Except for the testicular tumor mass present in all cases, other signs and symptoms may be present in different degrees (pain in the testis, enlargement of a testicle, heaviness in the scrotum, and gynecomastia). Azoospermia and infertility are uncommon and, if exist they are reversible after removal of the tumor.⁹ In the present case patient presented with infertility and testicular mass was identified during his work up.

Ultrasound of scrotum is very useful to confirm the diagnosis of testicular tumor.¹⁰ In our case scrotal ultrasonography revealed a homogenous hypoechogenic tumoral mass in the left testis.

In patients with LCTs the blood tests for tumor markers (AFP, β - hCG, and lactate dehydrogenase) are negative. In our case also they were found in normal range.

The most common hormones secreted by LCTs are testosterone and oestrogen. In most cases, adults have non-functional testicular masses. In this case, hormone profile was normal initially. But the hormone levels could not be performed later as patient was lost to follow up.

The histopathological examination and IHC are essential for the diagnosis and for the next steps in treatment. In our case, no histopathological feature suggestive of malignancy was seen and the final diagnosis of benign LCT of testis was given. The results of immuno-reactive tests were consistent with the existing literature. ¹¹ IHC is

useful in confirming the diagnosis. Inhibin-α, melan-A and calretinin may be used as positive markers for Leydig cell tumours which were negative in seminomas and other non seminomatous germ cell tumors. PLAP and c-KIT negativity again helps in supporting the diagnosis and excluding the possibility of seminomas, embryonal carcinoma and yolk sac tumor. PLAP immunoreactivity is unusual for Leydig cell tumours but 27% of Sertoli cell tumours express PLAP, so PLAP immune positivity is not by itself diagnostic of germ cell neoplasia. AFP is mostly negative and cytokeratin's are negative or weak. The constraints are negative or weak. The constraints are negative or weak.

LCTs need to be differentiated from Leydig cell hyperplasia (LCH) and large cell calcifying Sertoli cell tumor (LCCSCT). LCH can be differentiated from LCT by the absence of discrete mass, and interstitial location of proliferating cells surrounding seminiferous tubules in a background of testicular atrophy. LCCSCT is characterized by more frequent calcification, intratubular growth, neutrophilic infiltrate, more abundant stroma and absence of Reinke's crystals.

While benign, LCTs have malignant potential in about 10% of cases with metastatic forms, particular to the lymph nodes, especially the retroperitoneal and inguinal nodes (70%), liver (45%), lungs (40%), and bone (25%). The metastatic type occurs exclusively in adults and is more common in older patients with an average age of more than 40 years. The risk of malignancy in the undescended testis is 4 to 10 times higher than that in the general population but the most common type of testicular cancer occurring in undescended testes is seminoma.

In our case all clinical, hormonal, immunocytochemical, and pathological findings supported the diagnosis of benign LCT.

Statistics show that malignant LCTs correlate with increasing age of the patient, tumor size (over 5 cm) and increased tumor mitotic index.¹⁵ Benign LCTs can be cured by resection, testicular dysfunction and infertility can be a serious sequel in patients with estrogen-secreting LCTs. Long-term excess of estrogen can cause impairment of spermatogenesis, most likely because of hypothalamic-pituitary inhibition as well as direct blockade at the testicular level.¹⁶ This calls for early detection and management of these tumors to preserve the reproductive capacity.

It is very important to identify such cases as many cases have been reported which had deranged endocrine levels and appearance of atypical symptoms even after years of unilateral orchidectomy.⁵ Awareness of the constellation of its clinical, pathologic features and immunohistochemistry aids in establishing the correct diagnosis and distinguishing this neoplasm from other lesions of the testis.

CONCLUSION

LCTs are rare neoplasms arising from gonadal stroma. It is critical not to overlook the possibility of this rare tumor. Based on the histopathological features, diagnosis of LCT in patient presenting with infertility was made which was confirmed by immunohistochemistry. We conclude that a diagnosis of non-germ cell tumors such as LCT should be considered in a patient presenting with infertility. A routine histopathological study complemented with immunohistochemistry, is necessary in making the correct diagnosis. According to the available literature, LCT is a rare tumor presenting as infertility and should not be overlooked.

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