

A Testicular Leydig Cell Tumor with Azoospermia; Re-visited

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ABSTRACT

Leydig tumor is relatively a rare testicular tumor but the most common non-germ cell gonadal tumor. It constitutes about 1-3% of all testicular tumors. Clinically, it is usually presented as a testicular mass or with endocrine symptoms, which include gynecomastia, increased sex hormone levels, and other correlated symptoms. Here, we report a case of Leydig cell tumor with azoospermia in a 34-year-old patient.

KEY WORDS: Germ cell, gonadal, gynecomastia, leydig cell tumor, testicular mass

INTRODUCTION

Leydig cell tumor is the most common non-germ cell testicular tumor accounting for 1-3% of all testicular malignancies.^[1] Most of them are benign, only 10% tumors are malignant.^[1] Approximately 3% of Leydig cell tumors are bilateral.^[1] They may be hormonally active, causing either feminizing or virilizing syndromes. These benign tumors usually present as a testicular mass with or without hormone related symptoms. Patients with testicular Leydig cell tumor having infertility are exposed to increased risk of testicular carcinoma.^[2] Although it may be associated with male infertility, there is paucity of literature about this tumor presenting with azoospermia in our local environment.

CASE REPORT

A 34-year-old male patient was admitted for evaluation of lump in right sided testis for 4 years. On physical examination, both the testes were normal in consistency, but a hard mass was palpable in the right testis. Semen analysis revealed azoospermia. He had no gynecomastia. Tumor markers such as α -feto protein (α FP), human chorionic gonadotropin (β -hCG), and lactate dehydrogenase (LDH) were normal. Testicular ultrasound revealed a 5.5×5 cm nonhomogenous hypoechoic testicular mass in right testis. Other findings were unremarkable. A right sided inguinal

orchidectomy was performed, and the specimen has been sent to histopathology department.

Specimen consisted [Figure 1] of right sided testis with spermatic cord measuring $12 \times 6 \times 5$ cm. Testis measured $6 \times 5.5 \times 4$ cm and spermatic cord measured 9 cm long. The cut section of the specimen also consisted of a yellowish mass measuring $5.6 \times 5 \times 4$ cm in size.

Multiple sections [Figures 2-5] revealed testicular tumor to be composed of nests, sheets, and focal microcystic growth pattern. Stroma was fibrous with prominent vascularity.

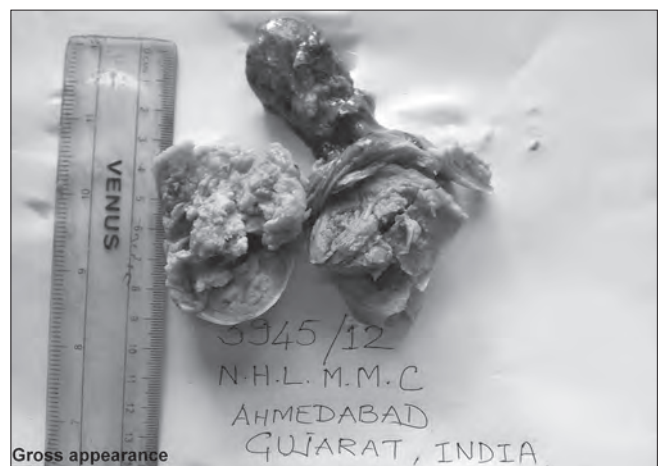


Figure 1: Specimen consisted of right sided testis with spermatic cord measuring $12 \times 6 \times 5$ cm. Testis measured $6 \times 5.5 \times 4$ cm and spermatic cord measured 9 cm long. The cut section also consisted of a yellowish mass measuring $5.6 \times 5 \times 4$ cm in size

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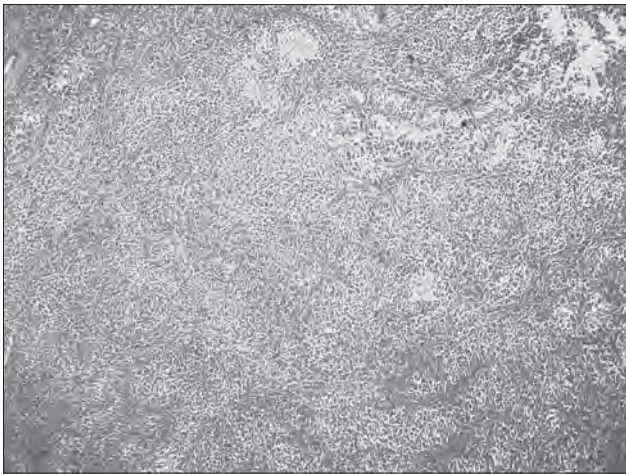


Figure 2: Testicular tumor to be composed of nests, sheets, and focal microcystic growth pattern. Stroma was fibrous with prominent vascularity. H and E, ×4

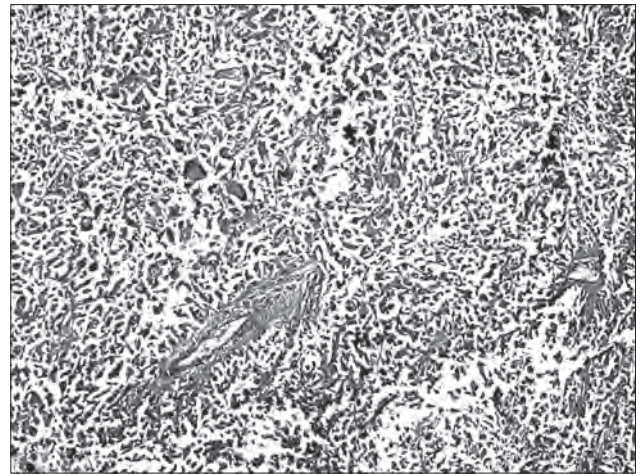


Figure 3: Testicular tumor to be composed of nests, sheets, and focal microcystic growth pattern. Stroma was fibrous with prominent vascularity. Tumor cells were large, polygonal with abundant finely granular, eosinophilic cytoplasm, indistinct cytoplasmic border and regular round nuclei. At places, bizarre giant cells were seen. No evidence of necrosis, significant mitoses, or vascular invasion was seen. H and E, ×10

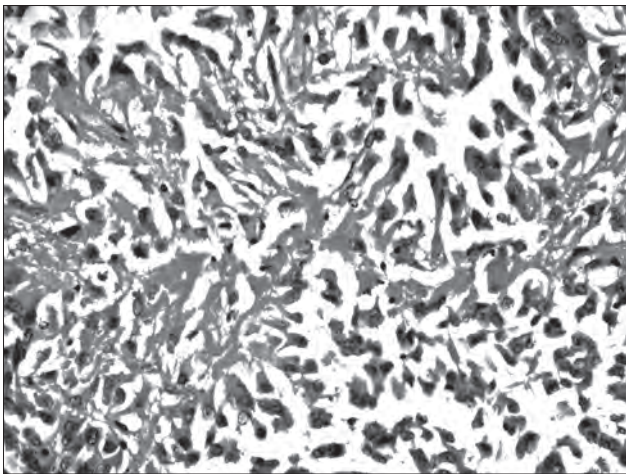


Figure 4: Reinke crystals. H and E, ×40

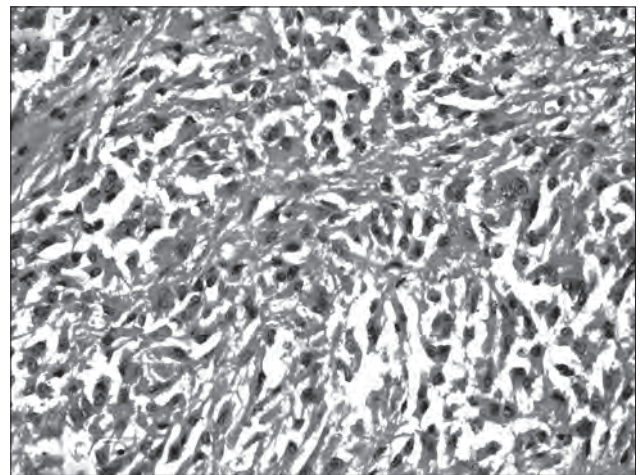


Figure 5: Tumor cells were large, polygonal with abundant finely granular, eosinophilic cytoplasm, indistinct cytoplasmic border, and regular round nuclei. H and E, ×40

Tumor cells were large, polygonal with abundant finely granular, eosinophilic cytoplasm, indistinct cytoplasmic border, and regular round nuclei. At places, bizarre giant cells were seen. No evidence of necrosis, significant mitoses or vascular invasion was seen. Tunica and distal end of spermatic cord were free from tumor cell invasion. No histopathological feature suggestive of malignancy was seen.

The final diagnosis of benign Leydig cell tumor of testis was given.

DISCUSSION

Leydig cell tumor is rare but the most common gonadal stromal tumor.^[1] It comprises of 1-3% of all testicular tumors.^[1] A total of 90% of Leydig cell tumors are benign.^[3-5] Mostly it is unilateral, but 3-9% of bilateral cases have been reported.^[6] The patients are usually between 20-60 years of

age in reported cases. However, 25% of these cases occurred before puberty.^[7] It is always benign in children and in 90% of adult patients.^[8]

The clinical manifestations include testicular mass, gynecomastia, and sexual dysfunction as well as asymptomatic masses, which are found incidentally during testicular ultrasound.^[9] Hormonally active tumor is found in approximately 20% of cases, which comprises of increased estradiol and decreased serum testosterone level, that causes feminization in adult and masculinization in child.^[8] Sometimes endocrinal symptoms appear first than the testicular mass, which is the most common presenting manifestation.^[9] Semen analysis may reveal oligospermia, cryptozoospermia, or azoospermia. It is therefore

recommended that an infertile man should be evaluated for testicular Leydig cell tumor.^[10]

Ultrasonography of the tumor shows a hypoechoic mass with hypervascularization.^[8,9] Changes in endocrinological findings are useful as follow-up markers to detect recurrence of the tumor.^[11] Histopathological criteria are important in prediction of malignant behavior of tumor that may help in differentiating malignant from benign tumor.^[12] Metastatic behavior of primary Leydig cell tumor is relatively uncommon. Presence of cytological atypia, necrosis, angiolymphatic invasion, increased mitotic activity, atypical mitotic figures, infiltrating margins, extension beyond the testicular parenchyma, DNA ploidy, and increased MIB-1 activity, all suggest potential metastatic behavior.^[12,13]

Microscopically, the Leydig cell tumor is made up of large polygonal cells with abundant eosinophilic and granular cytoplasm. Clear or vacuolated cytoplasm may also be seen.^[14] Nuclei are round and vesicular with delicate chromatin and a single prominent nucleolus. The cells usually show solid infiltrating pattern. Sometimes pseudotubular or trabecular pattern is also seen when fibrous septa are present. Crystalloids of Reinke are present in 25% of cases, which are observed on electron microscopic examination. On light microscopy, they appear as dense eosinophilic needle-like or rhomboid structures within the cytoplasm. Immunohistochemical stains like inhibin and vimentin are positive in Leydig cell tumor, while cytokeratin, CD-30, Oct3/4, or placental alkaline phosphatase are negative.

One study^[10] reported that immunohistochemical stains like Ki-67, p53 and bcl2 could be helpful in the identification of borderline and malignant cases of Leydig cell tumor.

Recently, according to some studies, testis sparing surgery can be used as an alternative to the traditional orchidectomy in cases of benign and small tumors.^[15,16] The main concern with the salvage procedure of any organ is the possibility of local tumor recurrence or distant metastasis. Surgical enucleation with testicular preservation is also described as an effective management of testicular neoplasms with adrenogenital syndromes without recurrence after 48 months of follow-up.^[15] But long term follow-up is necessary to rule out recurrence or metastasis in testis sparing surgeries. According to one large study,^[17] testis sparing surgery in patients with Leydig cell tumor showed preservation of fertility in terms of paternity after organ sparing surgery. The surgery was proven to be highly effective in patients with Leydig cell tumor that even after eight years of follow-up, there was no evidence of recurrence or metastasis.

In our case, semen analysis revealed azoospermia while all other laboratory investigations were unremarkable. Histopathological examination confirmed the benign potential of the Leydig cell tumor. It is thus critical for practitioners to be reminded not to overlook the possibility of this rare tumor while managing cases of male factor infertility especially, azoospermia.

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