



Recurrent Malignant Leydig Cell Tumor of Testis: A Case Report with Review of Literature

G.M.Bhat¹, S.N.Ahmad¹, M.I.Lone², S.Alsolami³, Q.M. Iqbal⁴

¹Department of Medical Oncology, India, ²Department of Pathology, Srinagar, ³Department of Pathology, K.S.A and ⁴Department of Internal Medicine, Srinagar.

Abstract

Malignant Testicular Leydig Cell tumors (leydigomas) are extremely rare to occur and mostly carry a bad prognosis. Here we describe the disease course of a middle aged patient with recurrent / metastatic Leydig cell tumor of testes,

who needed repeated oncosurgical intervention and chemotherapy.

Key words:

Testicular Interstitial tumor, Leydig cell tumor, Testicular cancer

Introduction

Leydig cell tumors (LCTs) are rare tumors of the male gonadal interstitium, although they are the most common type of interstitial tumors of the testes. Testicular mass, gynecomastia and breast tenderness are the commonest presenting features in adults, who may also present with infertility. In boys, Leydig cell tumor must always be considered in the differential diagnosis of precocious puberty. In majority, the testicular leydig cell tumors are, benign. Malignant variants account only for 10 % of cases (1) and overall for less than 0.2% of all testicular cancers (2). They are predominantly both chemo- and radiotherapy resistant.

Case report

A 29 years old Jordanian male was admitted through OPD in Oct.1996 with chief complaint of right scrotal swelling for one and half year prior to the presentation. The patient was completely well till one and half years back when he started to notice a small swelling in the scrotum on the right side while he was having a shower. The swelling gradually increased in size and was associated with pain. There was no history of discharge, nausea, vomiting, and loss of appetite or weight, urinary symptoms or sexually transmitted disease. Cardiovascular and chest examination was normal. On abdominal

examination, there was no visceromegaly or palpable lump. Local examination showed a hard, non-tender right scrotal mass, with irregular surface. Spermatic cord was free from nodules. Initial impression by the consulting oncology team was of seminoma stage I, was advised surveillance and meanwhile to have bipedal lymphangiography. CT scan abdomen showed right para-aortic lymphadenopathy in addition to 4 subcentimetric right inguinal lymph nodes. The patient underwent high inguinal orchiectomy with suspicion of testicular germ cell cancer. At surgery, a verbal frozen section report of seminoma was given. Histopathology of the resected tumor was consistent with diagnosis of Leydig cell tumor (Figure 1) with positive immunoreactivity to inhibin (Figure 2) but non-reactive to calretin (Figure 3).

Preoperative and serial postoperative alpha fetoprotein and HCG levels were normal. Patient was stable for 9 years when he presented with

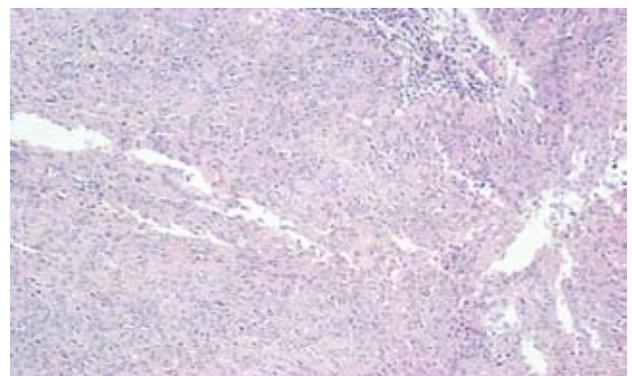


Fig. 1 : Photomicrograph showing Leydig cell tumor of testis with solid growth pattern of lipid rich polygonal cells. (H & E X10)

Correspondence to: Dr Gull Mohd Bhat, Associate Prof. Dep't. Of Medical Oncology, SKIMS, Soura, Srinagar, 190011, post bag 27, Tel: 91-194-2435825 E-mail: drgull8125@yahoo.com

complaints of pain in the right inguinal region. The pain was severe in intensity, throbbing in nature and radiated to the ipsilateral thigh.

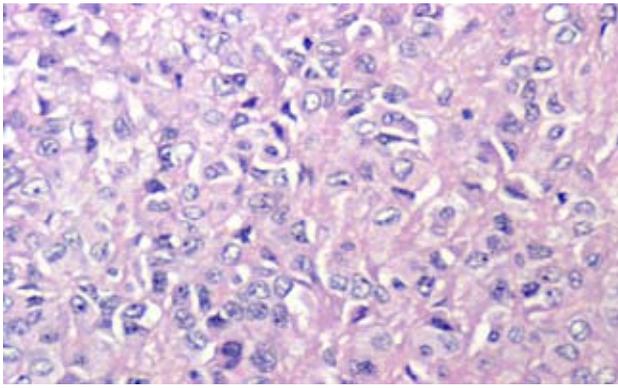


Fig. 2 : Photomicrograph showing clear cells with well outlined cytoplasm. Acidophilic granular cytoplasm and nuclear pleomorphism can also be seen. (H & E X 400)

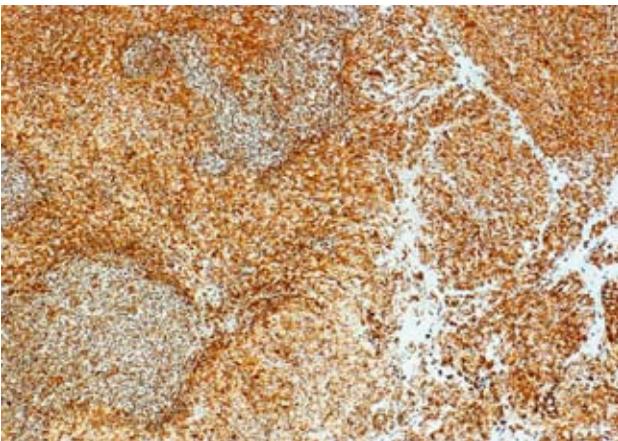


Fig. 3 : Immunohistochemistry showing tumor positivity to Inhibin.

There was also history of intermittent low-grade fever unaccompanied by any dysuria or bowel symptoms. The systematic examination was within normal limits but local examination showed tender right inguinal region with 2x1 cm fluctuant mass. Image guided aspiration showed atypical cells. On laparotomy, there was a huge recurrent tumor in close proximity to internal iliac vessels. He underwent less than complete excision of the lymph node mass even with the help of vascular surgeon. Histopathology of resected specimen was consistent with recurrent / metastatic LCT. However, patient was not given any chemotherapy after surgery. Three years later he again presented with the right inguinal painful mass measuring 4x2 cm, which was fixed to the underlying tissue and firm in consistency. The mass was mildly tender and had irregular

surface. Complete blood count, liver function tests and renal function tests were normal. Urine analysis was also normal. Evaluation for urinary tuberculosis including culture studies was negative. Tumor markers such as β HCG, serum alpha fetoprotein levels were normal. Serum estradiol levels were 37.4 pg/ml (normal values- 11-44 pg/ml). Serum testosterone level-158.5 ng/ml (normal-.5-53ng/ml). Serum FSH levels were 13.23 Miu /ml. (normal-1.37-13.58Miu/ml).LH levels were-11.79 mIU/ml (normal-1.26-10.05 mIU/ml). On exploration, there was a fungating tumor, frozen to right iliac bone and adherent to urinary bladder, encasing both internal iliac artery and vein and external iliac artery and there were numerous mesenteric and omental seedlings. Maximum palliative debulking was carried out. Post-operatively, he received several courses of cyclical cis-platinum based chemotherapy. He had a stable state for about 8 months but he developed symptomatic anemia (chemotherapy induced) which was managed with darbepoietin 500 micrograms weekly and blood transfusion support.

Discussion

Interstitial tumors of testis are also called as stromal cell or Leydig cell tumors (LCT). These neoplasms comprise 3 percent of all testicular tumors; of which 3 percent are bilateral and about, 90 percent are benign. Testicular Leydig cell tumors although rare are the most common type of interstitial tumor. Testicular mass, gynecomastia and breast tenderness are the common presenting features in adults, who may also present with infertility. In boys, a LCT must always be considered in the differential diagnosis of precocious puberty. Malignant variants (Leydig cell cancer) account for 10 % of cases⁽¹⁾. and overall for less than 0.2% of all testicular cancers. Metastatic spread or recurrence is considered the best evidence of malignancy. These Leydig cell carcinomas carry a bad prognosis with a median survival of less than 2 years^(2,3) when metastatic. On histopathology, LCT is characterized by polygonal cells with abundant granular acidophilic cytoplasm with round central nucleus and indistinct cell boundaries. The cytoplasm frequently contains lipid granules, vacuoles or

lipofuscin pigment, but most characteristic is intracytoplasmic inclusion bodies (Reinke's crystals). Diagnostic immunopanel of LCT is diffuse cytoplasmic positivity for α -inhibin, calretin, Melan-A, and vimentin and negative immunostaining for cytokeratin. The number of mitotic figures / high power field and nuclear proliferation index and pleomorphism can suggest malignant behavior of such tumors⁽¹⁾ and in another study cytologic atypia, necrosis, angiolymphatic invasion, increased mitotic activity, atypical mitotic figures, infiltrative margins, extension beyond the testicular parenchyma, DNA aneuploidy, and increased MIB-1 activity were significantly associated with metastatic behavior in LCT⁽⁴⁾. Generally metastatic spread occurs within 2 years of the primary LCT, and the patient dies within 2 years of the discovery of metastatic disease⁽³⁾. However, at times recurrence is delayed 8 years⁽³⁾ or even much delayed and could occur after 17 years from primary resection⁽⁵⁾. Surgical resection may provide prolonged relief and at recurrence, mitotane can work wonders⁽⁶⁾ but at times fails⁽³⁾. Malignant tumor can very rarely occur in association with Klinefelter's syndrome⁽⁷⁾. Malignant testicular LCT metastasizing to lung and lymph nodes⁽⁷⁾ and even to contralateral testes⁽¹⁾ has been reported. Out of 7 cases with this histology from a series of 790 cases of testicular tumor over a period of 18 years, 4 patients finally developed metastasis and succumbed to them⁽⁸⁾.

Cord compression⁽⁹⁾, diffuse lung metastasis, skin metastasis⁽¹⁰⁾, bilateral adrenal metastasis⁽¹¹⁾ have also been reported. Although mainly a tumor of the adult, it has been reported at a younger age of 25 years⁽¹²⁾ and at prepubertal age⁽¹³⁾. Bilateral metachronous⁽¹⁾ or synchronous malignant LCT associated with pseudoprecocious puberty has been described⁽¹³⁾. In either case, metastasis to the second testis needs to be carefully ruled out, which have been described in 3 cases⁽¹⁾. Cushing's syndrome due to ectopic production of cortisol heralding tumor recurrence⁽¹⁴⁾ and hypoglycemia have also been reported⁽¹⁵⁾. Estradiol levels may be elevated at the time of recurrence and can serve as a tumor marker⁽¹⁶⁾. The same is true of serum inhibin⁽¹⁷⁾. Alpha-fetoprotein and human chorionic gonadotrophin levels are always normal. Apart from germ cell tumors and adrenal hyperplasia, it is to be differentiated from Sertoli cell tumor and testicular secondaries. Primary retroperitoneal lymph node dissection should be carried out in malignant LCT. Surgical resection of recurrent lesion should form the basis of treatment since mostly this tumor is considered to be both chemo- and radio resistant^(2,3,8) although in certain situations it may be worthwhile to try cisplatin based chemotherapy or mitotane with or without surgery⁽⁴⁾. Imatinib has been tried but was found to be ineffective⁽¹⁸⁾. Efforts at exploring newer chemotherapies should continue. Cases have been reported from India as well⁽¹⁹⁾.

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