LEYDIG CELL TUMOR IN CRYPTORCHID TESTIS

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Abstract:
Leydig cell tumor of the testis is a rare (1-3 percentage), benign, interstitial tumor of sexcord stromal catgory. Cryptorchidism is a well established epidemiological risk factor of testicular germ cell tumor. However, data regarding a possible association with Leydig cell tumor are scarce. So far only 20 cases of Leydig cell tumor in cryptorchid testis have been reported. Hereby, we present a rare case of Unilateral benign Leydig cell tumor in the cryptorchid testis. A 35 year old male presented with a swelling in the right inguinal region for 2 months. CT abdomen revealed a tumor involving right ectopic undescended testis. Orchidectomy was performed. Grossly the tumor was gray-brown, measuring around 8cm. Histopathologically, differential diagnosis of Leydig cell tumor, Testicular Tumor of adrenogenital syndrome (TTAGS), Leydig cell hyperplasia were considered. Immunohistochemical study was performed and tumor cells showed positivity for Inhibin A and serum adrenocorticotropic hormone (ACTH) level was within normal limits 23.80pg per ml (normal 7.20-63.30pg per ml) postoperatively, confirming the diagnosis of Leydig cell tumor. This case has been presented for its rarity and to emphasize the importance of histopathologic features, immunohistochemical marker (Inhibin) and serum adrenocorticotropic hormone (ACTH) level for correct diagnosis since treatment protocol varies for different lesions.

Keyword: Cryptorchidism, Leydig Cell Tumor, Inhibin, ACTH

INTRODUCTION:
Testicular tumors span an amazing gamut of anatomic types. They are divided into two major categories: Germ cell tumors (90%) and sex–cord stromal tumors. Others are mixed germ cell –sex cord stromal tumors, primary tumors not specific to testis and metastatic tumors. Most germ cell tumors are aggressive neoplasms although with current therapy, most can be cured. Sex cord–stromal tumors in contrast are generally benign. Leydig cell tumor is the most common sex cord stromal tumor that comprise 1-3% of all testicular tumors. About 3% are...
bilateral. They occur in the age group of 3\textsuperscript{rd} to 6\textsuperscript{th} decade. A few have been described in cryptorchid testis and in patients with klinefelter syndrome\textsuperscript{9}. They may be hormonally active leading to feminising or virilizing syndromes. About 10\% are malignant\textsuperscript{4}. They are commonly present as testicular mass with gynecomastia. Precocious puberty occurs in childhood but without spermatocytic maturation in the non-neoplastic testis. These symptoms usually regress after removal\textsuperscript{9}. So far only 20 cases of Leydig cell tumor in cryptorchid testis have been reported\textsuperscript{7}. Here we present a rare case of unilateral Leydig cell tumor in the cryptorchid testis and treated by orchidectomy.

**CASE REPORT:**
A 35 year old married male with two children presented at Ortho OPD with complaints of pain over the right knee. On clinical examination an incidental finding of swelling in the right inguinal region was noted. Right testis was absent. Left testis was normal. Gynecomastia or any other hormonal manifestations were not present. Ultrasonogram report was normal inguinal lymphnode/? bowel lymphoma. CT abdomen revealed a tumor involving the right ectopic undescended testis. Grossly surgical specimen measured 8x7x4 cm. Cut surface was gray brown with blackish areas. (Figure 1)

**Fig. 1** GROSS - CUT SURFACE SHOWING GRAY-BROWN AREAS

**Histopathological examination** revealed compressed, atrophic testicular parenchyma with a well encapsulated tumor composed of polygonal cells with abundant granular, eosinophilic vacuolated cytoplasm, round nuclei with central nucleoli without atypia. The tumor cells were arranged in diffuse sheets, small nests and cords in a fibrous stroma, suggestive of Leydig cell tumor (Fig 2,3,4)

**Fig. 2 - SCANNER VIEW - ATROPHIC PARENCHYMA (LEFT) WITH TUMOR (RIGHT)**

**Fig. 3 - LOW POWER VIEW - ROUND TO POLYGONAL TUMOR CELLS ARRANGED IN SHEETS**

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On immunohistochemistry, tumor cells were strongly positive for Inhibin A, confirming our diagnosis of Leydig Cell Tumor (Figure 5).

To rule out the possibility of other Leydig cell lesions namely Testicular tumor of adrenogenital syndrome which constitutes the most important and difficult differential diagnosis, serum ACTH level was done postoperatively which was within normal limits, 23.80pg/ml (normal-7.20-63.30pg/ml). So the final diagnosis of Leydig cell tumor was made.

To summarise, this is a rare case of unilateral benign Leydig cell tumor in cryptorchid testis without any hormonal manifestations which was well circumscribed, gray-brown grossly. The histopathological, immunohistochemical and serum marker study confirmed the diagnosis of Leydig cell tumor.

DISCUSSION:
A thorough review of literature revealed 480 reported Leydig cell tumors in adults. However, only 20 cases were associated with cryptorchidism indicating a minimal incidence in these patients. Our case of unilateral Leydig cell tumor in cryptorchid right testis, presents the next report of such a rarity. 15 and 3 unilateral Leydig cell tumors have been reported in terms of homolateral and bilateralcryptorchidism respectively. A case with bilateral Leydig cell tumor was reported in a patient with unilateral cryptorchidism. Another case of unilateral Leydig cell tumor with contralateral undescended testis was reported.

Molecular studies have shown specific mutations to have a causative role. The mechanism of Leydig cell oncogenesis is still poorly understood. The disruption of the hypothalamic-pituitary-testicular axis leading to excessive stimulation of Leydig cells by excess luteinizing hormone is thought to play a role. However, structural changes of the luteinizing hormone receptors and G proteins in Leydig cells have been postulated to induce tumorigenesis. In contrast to germ cell tumors, there does not seem to be a definitive association with cryptorchidism. Although Testicular dysgenesis syndrome has been associated with testicular germ cell tumor, it is unclear whether the same link can be proposed for Leydig cell tumor, further studies are needed to clarify this field.

Around 41.7% of Leydig cell tumors in adults are diagnosed incidentally on USG, 29.2% present with a palpable testicular mass, 16.6% with scrotal pain and 12.5% with gynaecomastia. Our case was also diagnosed incidentally on clinical examination.
without any hormonal manifestations. About one tenth of all leydig cell tumors show evidence of malignant behaviour in the form of metastatic disease, particularly to lymph nodes, lung and liver. Malignant Leydig cell tumor occurs exclusively in adults, are usually unaccompanied by endocrine changes, are larger than benign variety (average size 7.5 cm). They are commonly infiltrative, tend to exhibit necrosis, blood vessel invasion, nuclear atypia, numerous mitosis and lack lipochrome pigment. Since the above features were not present in our case, it was diagnosed to be a case of Benign Leydig cell tumor ed out, and this emphasizes the significance of serum ACTH values post-operatively in differentiating Leydig cell tumor from TTAGS as treatment varies. Leydig cell tumor requires orchidectomy whereas TTAGS requires only hormonal therapy. Leydig Cell Hyperplasia is characteristically multifocal and less than 0.5 cm in diameter. Histopathologically it would reveal a non-destructive interstitial growth pattern that preserves the surrounding tissues. Whereas in our case, the tumor was solitary measuring 8x7x4 cm and microscopically the testicular parenchyma was mostly replaced by the tumor. Hence the diagnosis of Leydig Cell Hyperplasia was ruled out. Sometimes, when Leydig cell tumors present with prominent cytoplasmic clarity, as a result of lipid, it may be mistaken for seminoma which is the most common malignant tumor in cryptorchid testis. The absence of consistent fibrous trabeculae, lymphocytic infiltrate, Intratubular Germ Cell Neoplasia Unclassified (IGCNU), lower mitotic rate, immunomarker Inhibin +, PLAP – in Leydig cell tumor are helpful in this regard. This distinction is important because seminoma has poor prognosis and needs aggressive treatment. This case is presented for its rarity and to emphasize the importance of histopathologic features, immunohistochemical (Inhibin) and serum marker (ACTH) in proper diagnosis and for appropriate management, since the treatment protocol varies.

Reference:


8 Robbins and Cotran. Pathologic basis of Disease, 8th edition, page 987

9 Rosai and Ackerman’s surgical pathology, 9th edition, page 1436.
