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Giant Leydig Cell Tumor Presenting as Gynecomastia: A Rare Case Report and Review

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Abstract | **Case Report**

This case report describes a 67-year-old man who presented with bilateral gynecomastia and a left palpable testicular mass of 10-years, no clinical signs of hypogonadism. Hormonal evaluation found a low level of testosterone. Upon orchiectomy via an inguinal approach, a giant Leydig cell tumor of 15 cm in diameter was removed. The patient recovered favorably with a rapid reduction in breast tension without a change in the size of the gynecomastia. There was no recurrence at 8-month follow-up. This tumor was notable for its size and it's compressing effect causing a gynecomastia by a reduced secretion of Testosterone. In addition, in our case we described the state-of-art management of this rare tumor.

Keywords: Leydig Cell Tumors, Gynecomastia, Case Report.

INTRODUCTION

- Leydig cell tumors are relatively uncommon, comprising only 1-3% of all testicular tumors. Most of these tumors are benign and asymptomatic, but they can lead to hormonal disturbances, including gynecomastia.
- Gynecomastia in males can have a variety of causes (hormonal imbalances, medications, systemic diseases, etc.).
- The combination of bilateral gynecomastia and a Leydig cell tumor as the underlying cause is an unusual clinical finding,

CASE PRESENTATION

Mr. O. M., aged 67, Married, father of seven children, presented with a 10-years history of progressive left testicular swelling and tenderness. He also noted the recent development of breast enlargement and tenderness. He had normal erection, ejaculation and libido. No chronic medication.

His personal and family history is unremarkable: puberty at 14 years old, normal growth, adult height identical to that of his father.

Clinical Examination

- 75 kg for 1.75 m, eunuchoid appearance, bilateral glandular gynecomastia sensitive to pressure (Fig. 1) no galactorrhea, normal hair, normal penis,
- Right testicle of normal size (4/2/3 cm), firm, non-tender. Mass in the left testicle of 15 cm and soft.

Normal prostate on rectal examination.

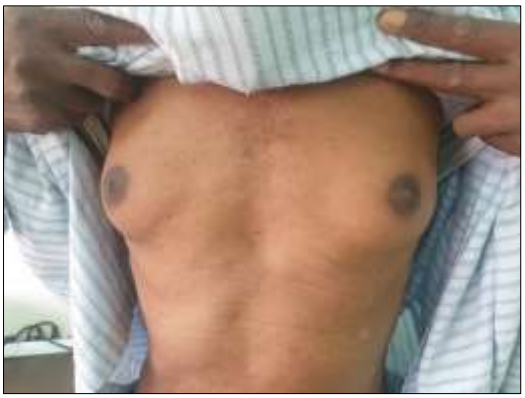

Fig. 1: A 67-year-old patient presented with bilateral gynecomastia.

Testicular ultrasound (Figure 2) revealed an ovular and echogenic left testicular mass of 103x86x74 mm in diameter, largely necrotic with a fleshy portion presenting vascularization on color Doppler.

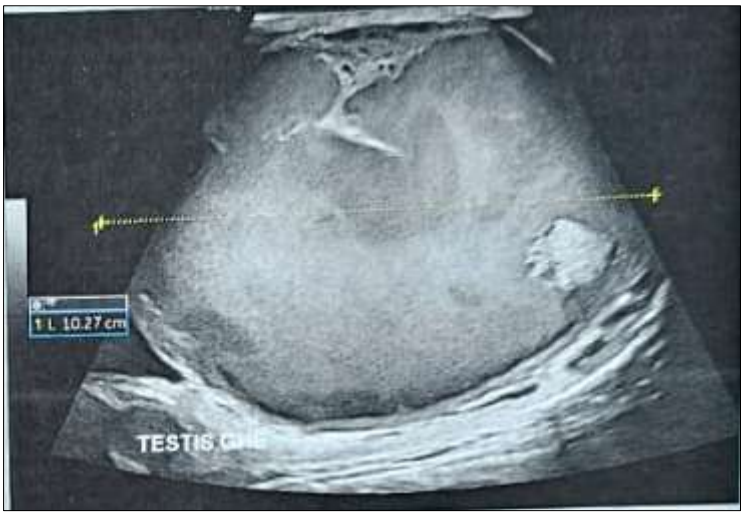

Figure 2: Large tumor mass occupying the testicle

Hormonal levels were normal except for a low testosterone:9 ng/mL (normal range, 3-10 ng/mL); estradiol, 58 pg/mL (normal range, 20-60 pg/mL); follicle stimulating hormone (FSH), 7 mU/mL (normal, 8 mU/mL); luteinizing hormone (LH), 5 mU/mL (normal 5.8 mU/mL).

Tumor markers were normal. Karyotype: 46 XY

No metastasis revealed by the following examinations: chest and abdominal CT scan centered on the retroperitoneal lymph nodes and the liver, bone scintigraphy.

Based on clinical and paraclinical results, the patient was treated with an inguinal left orchidectomy after spermatic cord clamping (Figure 3) The anatomopathological study found a well-defined tumor 15 cm in diameter within the testicular parenchyma.

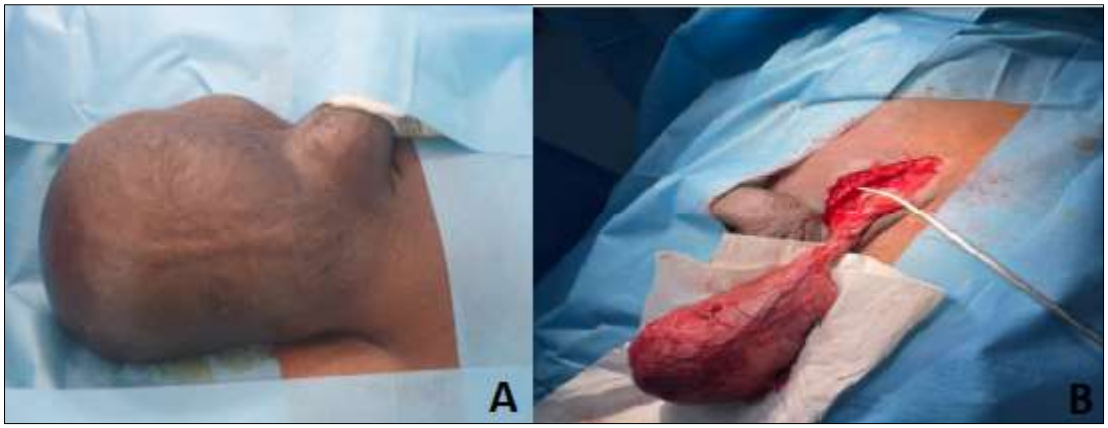

Figure 3: A: Left scrotal swelling / B: Left testicular mass and spermatic cord clamping

Microscopic examination revealed an extensive involvement and replacement of testis by an interstitial tumor of the testicle or leydigoma. The Leydig cells are eosinophilic, grouped in regular cords, containing lipid vacuoles with normal aspect and rare seminiferous tubules containing Sertoli cells, but no germ cells (Figure 4). There were no cytological character of malignancy.

On IHC, Strong expression of tumor cells by the Calretinin A antibody (Figure 5) and inhibin. Negative immunostaining with lactate dehydrogenase (LDH), AFP, and HCG.

After tumor removal, the patient recovered favorably and there was no recurrence at 8-month follow-up. Testosterone levels normalized and there was a rapid reduction in breast tension without a change in the size of the gynecomastia. The patient prefered to wait for the spontaneous gradual regression of his gynecomastia, which requires at least 1 year.

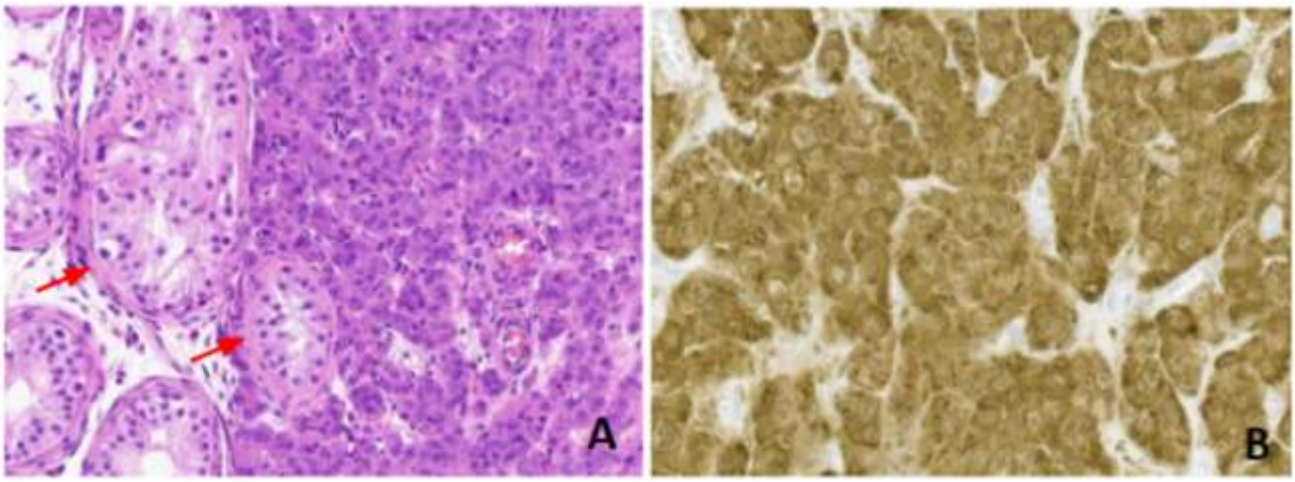

Figure 4: A Tumor proliferation made up of cells with abundant eosinophilic cytoplasm and finely nucleolated round nuclei with the presence of residual testicular parenchyma on the left (red arrows) (HE x200) B -Strong expression of tumor cells by the Calretinin A antibody (IHC x200)

DISCUSSION

Leydig cell tumors (LCT) are rare testicular neoplasms that arise from the Leydig cells responsible for testosterone production. They are representing 1%–3% of all testicular tumors in adults but they are the most common interstitial neoplasms of the testis. LCTs are usually unilateral. Although these tumors arise at any age, they are more common in men their third to sixth decade [1].

Leydig cell tumors are hormonally active and secrete a variety of hormones including testosterone, estrogen, or its derivates that can induce an imbalance in the estrogen-to-testosterone ratio. therefor, they may present endocrine abnormalities such as reduced libido, erectile dysfunction, azoospermia and Gynecomastia [2].

Gynecomastia is defined as the enlargement of breast glandular tissue and reflect an elevated circulating ratio of oestrogens to androgens due to age, disease, drugs, or idiopathic factors. Rarely it is secondary to a testicular tumour [3]. It could precede by some months to several years the appearance of the tumor at the early stages; Therefore, some authors recommend testicular ultrasound and laboratory measurements of serum tumor markers in patients presenting with gynecomastia [4].

In prepubertal patients, LCT can present as precocious puberty (accelerated skeletal and muscle growth, growth of the penis, pubic hair) [3].

These hormonal disorders are due to the fact that, in the adult, the conversion of testosterone to estradiol, It is carried out by the enzyme aromatase microsomial contained in Leydig cells (increased in tumor cells) [5]. In our case, the patient had an hypogonadism with a reduced Testosterone Secretion Due to Tumor Mass Effect; While Leydig cells typically produce testosterone, there might be cases where the tumor itself does not secrete significant amounts of testosterone especially If the tumor is large enough, it might affect normal testicular function by compressing surrounding tissue. This hypothesis is consistent with our clinical case since the tumor is very large occupying almost all the testicle with a few remaining testicular parenchyma.

As a result. The body's androgen-to-estrogen ratio is altered, even without direct estrogen secretion by the tumor, and gynecomastia could occur.

The tumorigenesis of LCT remains unclear and seems to be heterogeneous. Germline mutations have been reported to have a role in predisposition to LCTs; they induce structural changes of the luteinizing hormone receptors and G proteins, however, cryptorchidism does not increase the risk for LCT in contrast to most other testicular tumors [6].

LCT generally present as painless testicular swelling. The size of these tumors can vary, with the vast majority being smaller than 5 cm in diameter [7]. In our patient, the tumour was 15 cm of diameter occupying almost all the testicle.

If the tumor is impalpable, ultrasonography is the investigative procedure of choice. LCT of the testis typically has a homogeneous hypoechoic sonographic appearance. However, LCT are indistinguishable from a more commonly malignant germ cell tumor.

Laboratory studies in LCTs are nonspecific. The steroid secretion pattern in LCTs is variable. serum estradiol measurement is increased in cases with feminization stigmata. All the serum tumor markers testing for α-fetoprotein, β-human chorionic gonadotropin, and placental alkaline phosphatase should be within normal ranges in pure LCTs. These markers are often elevated in certain germ cell tumors.

These tumors are usually benign, but malignant variants can occur in 10 % of cases. Several authors suggested that 5 clinical features allow the identification of malignant LCT, including presence of endocrine changes, older patients (from the 5th or 6th decade), tumor size greater than 5 cm, infiltrative margins, and areas of hemorrhage and necrosis extending beyond testicular parenchyma [8]. In our current report, the tumor was 15 cm in size involving the half of the left testis, also the patient present with bilateral gynecomastia and there are no positive surgical margins and no area of hemorrhage and necrosis were presented, so only 2 features (patient's age and endocrine changes) were consistent with the above criteria.

LCT arises from the interstitial cells of Leydig adjacent to the seminiferous tubules. The pathologic diagnosis of LCT is usually made based on morphologic characteristics of the tumor cells [10]. Histologically, LCT is characterized by the proliferation of large polygonal tumor cells with granular eosinophilic cytoplasms and prominent nucleoli arranged in sheets pattern. Immunologically, The stromal origin is confirmed using immunochemistry, as 100% of LCT express inhibin A. LCT are differentiated from Sertoli cell tumors using Calretinin A (strong cytoplasmic and nuclear expression in LCT, weak and exclusively cytoplasmic in Sertoli cell tumors)., LCT is distinguished from germ cell tumors by the negative immunostaining with lactate dehydrogenase (LDH), AFP, and HCG [10]. In the presented case, the tumor cells were strongly positive for Calretinin A and inhibin and negative for pan-cytokeratin, calretinin and sinaptophysin.

Since percutaneous testicular biopsy is still not recommended, the only diagnostic criterion of malignancy is the presence of metastasis [9]. These metastases are located mainly in retroperitoneal and inguinal lymph nodes (68%), lung (45%), liver (45%) and bone (27%). Therefore, follow up of these patients through the complementary tests is essential.

LCTs were previously treated aggressively and a radical inguinal orchiectomy was classically proposed as the diagnosis of testicular germ cell tumor could be ruled out preoperatively.

Recently, conservative treatment is widely adopted ; testis-sparing surgery consisting of tumour enucleation with clear margins is considered especially in boys and young men, to maintain their fertility and avoid useless and potentially harmful [11]. Active surveillance is also proposed in some selected cases.We opted for radical orchiectomy because of the large size of the tumor in an old patient with hormonal imbalance and suspicion of malignant LCT.

Metastatic LCT responds poorly to additional systemic chemotherapy or radiation. In Malignant forms , regular long-term follow-up 10 through tumor markers, thoracic and abdominal CT, including ultrasound of the contralateral testis, to rule out possibility of metachronous cell tumors Leydig, Leydig cell hyperplasia or late metastasis. In our current case report, the 8- month postoperatively CT scan shows no local recurence and absence of distant metastasis.

CONCLUSION

We believe that the reported case has significant importance as it highlights the rare occurrence of a giant Leydig cell tumor presenting with bilateral gynecomastia and low testosterone levels. This large tumour had a compressive effect on the testes leading to the reduced testosterone secretion.

Abbreviations:
LCTs: Leydig cell tumour.
IHC: immunohistochemistry

Author Contributions

Conceptualization, O.J. and P.C.; methodology, resources, U.S., R.I. and E.T.; data curation, A.A.; writing—original draft preparation, S.I. and P.C.; writing—review and editing, G.S., S.I. and A.A.; visualization, S.I.; supervision,O J

All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

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Informed Consent Statement: Written informed consent for publication has been obtained from all subjects involved in this study.

Data Availability Statement: Data supporting the reported results are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

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