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Case Report

Bilateral testicular mixed germ cell tumor in an elderly male with generalized lymphadenopathy masquerading as testicular lymphoma: A diagnostic dilemma

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Abstract

Testicular mixed germ cell tumors (MGCTs) in elderly males are a rare entity with only a handful of cases reported in the literature. Their presentation as a bilateral testicular neoplasm is even rarer, where they can be commonly mistaken as testicular lymphomas that typically present in this age group and with bilaterality. Accurate diagnosis of MGCTs in the elderly is much required because of their highly aggressive nature as compared to those presenting in the younger age group. This case reports a similar instance of metachronous bilateral testicular tumor in a sixty-year-old male who presented with extensive nodal and lung metastasis and was clinically diagnosed as testicular lymphoma initially, but with the help of an extensive diagnostic workup, was finally diagnosed as an MGCT.

Keywords: Germ cell tumors, Yolk sac tumors, Seminoma, Embryonal carcinoma, Choriocarcinoma, Spermatocytic tumor.

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1. Introduction

More than 90% of testicular tumors are of germ cell origin. The majority of cases present in the age bracket of 15-45 years.[1] Conventionally, Germ cell tumors (GCTs) are classified as seminomatous and nonseminomatous on histology.[2] Pure forms of GCTs are rare as compared to mixed GCTs, which account for 16% of all testicular tumors.[3] GCTs are an exceedingly rare occurrence (<5%) in elderly males. They are aggressive tumors, and distant metastasis is usually present at the time of diagnosis. This makes them a challenging entity to diagnose due to clinically overlapping features with other aggressive and more commonly reported malignancies in this age group, especially testicular Non-Hodgkin Lymphomas (NHLs). We present here a case of a bilateral testicular MGCT in an elderly man with generalized lymphadenopathy, initially raising suspicion of a testicular NHL.

2. Case Presentation

A 60-year-old male presented to the surgery outpatient department with a two-month history of left scrotal swelling, followed by enlargement of the left supraclavicular and left inguinal lymph nodes, the latter to swellings appearing almost simultaneously. The patient had a previous history of right orchidectomy done one year prior, the histopathology report of which was unavailable. Suspecting him to be a case of testicular lymphoma, the patient was advised to undergo hematological examination (CBC, LFT, KFT, and Tumor markers); radiological examination (CECT) and cytological examination (FNAC)of the enlarged nodes. On physical examination, the left scrotal swelling measured 2.5 x 2.5 cm and was firm and non-tender. The left supraclavicular swelling measured (4.0 x 5.0 cm) and the left inguinal swelling measured (1.5 x 1.5 cm), both hard, fixed, and non-tender **[Figure 1a, b]**. CECT scans of the abdomen and chest revealed widespread retroperitoneal and mediastinal lymphadenopathy, which ranged from 2-4 cm in size.

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Visceral metastases were also observed, including "cannonball" lesions in the right lung **[Figure 1c, d]**.

FNAC attempts from both the supraclavicular and inguinal swellings yielded blood-mixed material. Smears prepared from this material showed a similar morphology, comprising a mixed population of medium and large cells with moderate pleomorphism, irregular margins, open chromatin, prominent nucleoli, and cytoplasmic vacuolation. Moreover, organoid structures with hyaline globules and pseudoglandular pattern were also noted, raising suspicion of a metastatic high-grade epithelial neoplasm, likely originating from a testicular germ cell tumor (GCT) **[Figure 2a-d].** Based on this, Immunocytochemistry for PLAP, AFP, CD30, and hCG was performed, where the former two turned out to be positive, whereas the latter two were negative. The diagnosis of metastatic testicular mixed germ cell tumor (MGCT) was hence confirmed.

Laboratory results also showed elevated Lactate Dehydrogenase (LDH), Alpha-Fetoprotein (AFP), and Placental Alkaline Phosphatase (PLAP) levels. Other laboratory parameters were unremarkable. On reviewing the patient's previous right-sided orchiectomy histopathology slides, a mixed GCT composed majorly of yolk sac tumor with various architectural patterns (microcystic, adenoid, and retiform along with Schiller-Duval bodies) and a minor seminomatous component showing moderately pleomorphic cells arranged in sheets and lobules separated by fibrous septae and infiltrated by chronic inflammatory infiltrates was seen. **[Figure 3a-d]**.

Because of the extensive metastatic spread, the patient was initiated on the BEP regimen of chemotherapy, but expired just after one cycle.

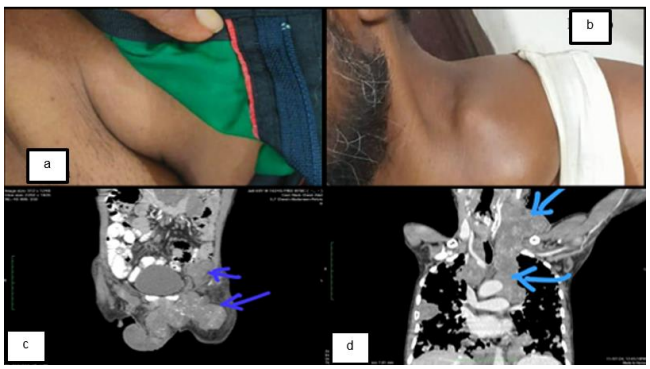

Figure 1: **a:** The palpable Left inguinal swelling measured 1.5 x 1.5 cm and was firm, fixed, and non-tender; **b:** The left supraclavicular swelling measured 4.0 x 5.0 cm and was hard, fixed, and non-tender; **c:** CECT abdomen showing left iliac and left inguinal lymphadenopathy (arrows); **d:** CECT thorax showing left-sided cervical, supraclavicular, and mediastinal lymphadenopathy; cannonball lesions in the lungs were also seen (arrows), suggestive of metastasis.

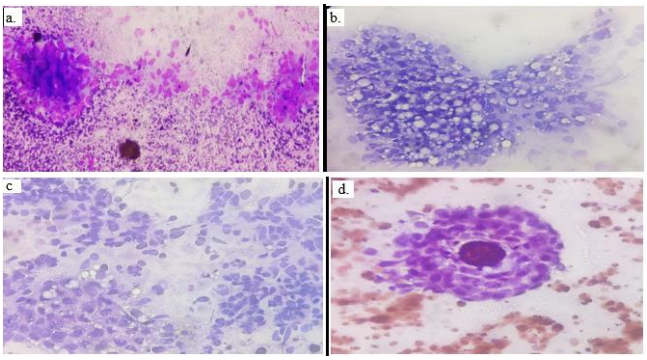

Figure 2: FNAC from left supraclavicular and inguinal lymph nodes showing: **a:** Tight and loose clusters, vague acinar pattern (MGGx10x); **b:** Large cells with prominent cytoplasmic vacoulations (PAP x10x); **c:** Pleomorphic cells with fine and coarse vacuolations (PAP x10x); d: Organoid structure with hyaline globule (PAPx40x)

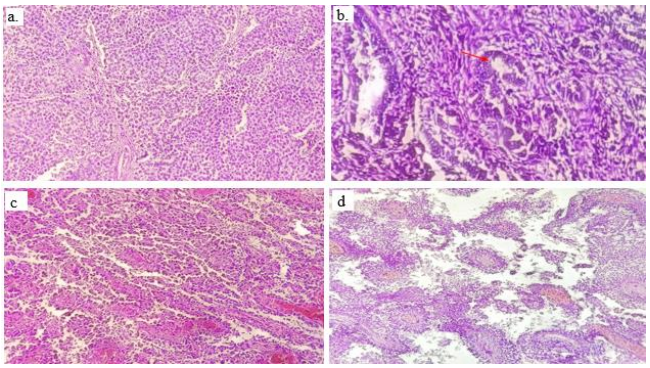

Figure 3: Review of right orchidectomy histopathology slides showed: **a:** A Classical Seminoma component [H & E x 10 x]; **b:** Glandular pattern of yolk sac component. [H & E x 10x]; **c:** Retiform pattern of yolk sac component [H & E x 10x]; **d:** Schiller Duvall bodies [H &E x 10 x]

3. Discussion

Testicular cancers account for approximately 1-1.5% of all cancers in men and 5% of all urological tumors.[4] The incidence of bilateral testicular tumors ranges between 1-5%, which can be either synchronous or metachronous.[5] Approx 50% of GCTs are seminomas and the vast majority of the remainder are either pure forms of other subtypes or mixed GCTs referred to as Non-Seminomatous Germ Cell Tumors (NSGCTs). The median patient age at diagnosis is 37 years for pure seminomas and 30 years for pure NSGCTs.[1] Mixed forms present at a slightly lower age and mainly include teratoma, embryonal carcinoma, and seminoma in various combinations. The combination of seminoma and yolk sac Tumor is rarely observed.[3]

Table 1: Various components of mixed germ cell tumors of testis

Components	Histopathology	Immunohistochemistry	Tumor markers elevated
Seminoma	Sheet and nests of tumor cells with lymphocytic infiltrates and fibrous septae; cells with abundant clear cytoplasm, defined cell boundaries, uniform nuclei containing prominent nucleoli; can be sometimes pleomorphic and in solid sheets	***PLAP, CD117***, OCT3/4, SALL4, Podoplanin	Serum hCG <1000 mIU/ml, LDH> 1.5 times the ULN, PLAP> 10 mIU/ml
Yolk Sac Tumor	Various patterns- microcystic/ reticular, glandular, myxoid and solid along with Schiller-Duval bodies, hyaline bodies.	***AFP***, Glypican3, SALL4	Serum (AFP) in 100's or 1000's of ng/ml.
Embryonal Carcinoma	Large epithelioid cells; pleomorphic vesicular nuclei with >1 macronucleolus; dense amphophilic cytoplasm; any one pattern (solid, glandular, papillary)	***CD30***, Cytokeratin AE1/AE3, OCT3/4	Serum LDH, Serum hCG
Choriocarcinoma	Biphasic pattern containing cytotrophoblasts and syncytiotrophoblasts	***hCG, hPL***, inhibin, GATA3, GDF3	Serum hCG > 1000 mIU/ml

Abbreviations: hCG- human chorionic gonadotropin; hPL-human placental lactogen; AFP- Alfa fetoprotein; LDH- Lactate Dehydrogenase; PLAP- Placental Alkaline Phosphatase; ULN-Upper Limit Normal

In the case of bilateral testicular tumors in an elderly patient with generalized lymphadenopathy, the most common diagnosis that comes to mind first is a testicular NHL. Primary testicular lymphomas represent 5% of all testicular malignancies and present with a painless unilateral/ bilateral testicular mass. Secondary involvement of the testis is more common than primary testicular lymphoma.[8] The most common entity among Testicular NHLs is DLBCL.

The second diagnosis that is considered in this age is a Spermatocytic tumor, which is a rare testicular tumor. However, this tumor has an indolent course and rarely metastasizes, hence it was not considered as a differential in the present case.

Metastases from other cancers, such as urothelial, prostate, lung, and renal carcinoma that can present as a testicular mass should be evaluated as well.

Diagnosing MGCTs is easy because of the typical histopathological features, and specific tumor and Immunohistochemical markers for each type, provided they are considered in the differential diagnosis[6,10] (**Table 1**).

This case underscores an atypical presentation of metachronous bilateral MGCT in an elderly patient predominantly composed of Yolk Sac and Seminomatous components, with widespread dissemination, misleading us initially to a diagnosis of testicular NHL. However, a comprehensive diagnostic workup panel of FNAC, Immunocytochemistry, Tumor markers, CECT, and histopathology from the previous right orchidectomy all helped in arriving at the right diagnosis.

4. Conclusion

This case highlights the diagnostic challenges in elderly patients with testicular tumors. Although testicular GCTs are rare in such patients, they should nevertheless be included in the differential diagnosis when dealing with aggressive testicular masses. The overlap in clinical and radiological features between testicular GCTs and other malignancies, such as NHL, can be quite confusing. However, a high index of clinical suspicion along with use of ancillary tests like Tumor markers, FNAC, and Immunocytochemistry/ Immunohistochemistry can help to clinch this grave entity, which should not be misdiagnosed at any cost as it carries a very dismal prognosis and high mortality.

5. Source of Funding

None.

6. Conflict of Interest

None.

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