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ISOLATED TESTICULAR LYMPHOMA : AN UNUSUAL PRESENTATION

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ABSTRACT

Testicular lymphoma is a rare and aggressive form of extranodal non-Hodgkin lymphoma, predominantly affecting elderly males. Unlike more common testicular malignancies, primary testicular lymphoma (PTL) exhibits distinct clinical behavior and poses diagnostic and therapeutic challenges. Here, we present the case of a 75-year-old male with a painless, progressively enlarging right scrotal swelling, ultimately diagnosed as diffuse large B-cell lymphoma (DLBCL) of the testis. Clinical evaluation, imaging, and histopathology confirmed the diagnosis. Immunohistochemical profiling demonstrated positivity for CD45, CD19, and CD20 with a high Ki-67 index, confirming the B-cell phenotype. The patient underwent radical orchiectomy followed by histological evaluation. This case highlights the importance of differentiating PTL from other testicular tumors for appropriate management and prognostication. We also review the existing literature on PTL, emphasizing its pathological spectrum, immunophenotype, treatment strategies, and prognosis.

Keywords: Testicular lymphoma, Non-Hodgkin lymphoma, Diffuse large B-cell lymphoma, Immunohistochemistry, Orchiectomy, Extranodal lymphoma.

INTRODUCTION

Primary testicular lymphoma (PTL) represents a rare, extranodal manifestation of non-Hodgkin lymphoma (NHL), accounting for less than 5% of all testicular malignancies and only 1–2% of all NHLs.[1] It primarily affects men over the age of 60 and is typically characterized by aggressive clinical behavior, a high relapse rate, and poor overall prognosis.[2-4] Unlike germ cell tumors of the testis, PTL lacks

elevated tumor markers and presents diagnostic challenges due to its clinical and histological overlap with other testicular neoplasms and inflammatory conditions. Among the histological subtypes, diffuse large B-cell lymphoma (DLBCL) is the most common, comprising approximately 80–90% of PTL cases.[5] These lymphomas exhibit a propensity for widespread dissemination, particularly to the central nervous system (CNS), contralateral testis, and skin, even after initial treatment.[6-8] Hence, early diagnosis and comprehensive staging are critical in optimizing outcomes. Histopathological evaluation supported by immunohistochemistry (IHC) is crucial for accurate diagnosis. While hematoxylin and eosin (H&E) staining reveals a monomorphic lymphoid infiltrate, IHC helps confirm the B-cell origin and rules out mimickers such as seminoma or orchitis.[9-11] Management typically involves a combination of radical orchiectomy, systemic chemotherapy (often R-CHOP), radiotherapy, and CNS prophylaxis.[12] In this report, we present an unusual case of isolated testicular DLBCL in a 75-year-old male. We also conduct a comprehensive review of the literature to delineate current diagnostic protocols, treatment guidelines, and prognostic indicators in PTL.

REVIEW OF LITERATURE

Epidemiology and Incidence: Testicular lymphoma is an uncommon, constituting only about 1–5% of all testicular neoplasms and approximately 1–2% of all non-Hodgkin lymphomas.[1] It is the most prevalent testicular malignancy in men over the age of 60.[2] In a population-based study using SEER data involving 1,169 cases, the majority were DLBCL subtype with median age at diagnosis around 70 years.[5]

Pathogenesis and Risk Factors : The exact pathogenesis remains poorly understood. Hypotheses include immune privilege status of the testis, lack of lymphatic drainage, and hormonal factors facilitating lymphomagenesis. Chronic inflammation or infections may also play contributory roles. Testicular immune surveillance differs from systemic immunity, allowing for sanctuary-like conditions that may facilitate neoplastic transformation.[7]

Histopathological Subtypes : Histologically, DLBCL dominates the spectrum of PTL. Other less common variants include follicular lymphoma, Burkitt lymphoma, and T-cell lymphomas.[8] DLBCL typically demonstrates a diffuse intertubular infiltration of large atypical lymphoid cells, often obliterating normal testicular architecture. IHC markers such as CD20, CD45, and BCL6 support B-cell lineage identification.[10]

Clinical Features and Differential Diagnosis : Patients commonly present with painless scrotal swelling, often unilateral, though bilateral cases are reported in 6–10% of presentations.[10] The differential diagnosis includes seminoma, embryonal carcinoma, spermatocytic tumor, granulomatous orchitis, and chronic viral orchitis. Imaging via ultrasonography may show hypoechoic lesions with increased vascularity, but lacks specificity.[6,9]

Immunohistochemistry and Diagnostic Role : IHC is an indispensable in establishing the diagnosis of PTL. PTL cells are typically positive for pan B-cell markers such as CD20, CD19, CD79a, and CD45. Negative staining for cytokeratin,

PLAP, and EMA helps exclude germ cell tumors.[9,11] Ki-67 labeling index often exceeds 80% in aggressive variants, underscoring their high proliferative capacity.[12]

Treatment Modalities : The management of PTL is multifaceted. Radical orchiectomy remains the first step, providing diagnostic tissue and eliminating a potential sanctuary site due to the blood-testis barrier. Adjuvant therapy typically includes R-CHOP chemotherapy, prophylactic scrotal irradiation, and CNS-directed therapy using intrathecal methotrexate or cytarabine.[4,12]

Prognosis Despite treatment advances, prognosis remains guarded, especially in advanced-stage or relapsed disease. Five-year overall survival varies between 50–70% but drops significantly with CNS or contralateral testicular involvement.[3,6] Risk stratification using International Prognostic Index (IPI) and histological grading guides treatment intensity.

CASE PRESENTATION

A 75-year-old male presented to the outpatient clinic with a chief complaint of progressive right-sided scrotal swelling for the past three months. The swelling was associated with a dull, dragging discomfort localized to the right hemiscrotum but was not accompanied by acute pain, fever, urinary symptoms, trauma, or systemic signs like weight loss or night sweats.

On general physical examination, the patient was afebrile with stable vitals. There was no evidence of pallor, icterus, clubbing, cyanosis, or lymphadenopathy. Abdominal examination did not reveal hepatosplenomegaly or any palpable masses. Local examination of the scrotum showed an enlarged, firm-to-hard, non-tender mass involving the right testis. The mass was discrete from the left testis and extended superiorly towards the epididymis. There was no transillumination, and the overlying skin appeared intact without any ulceration or discoloration. The left testis and epididymis were unremarkable.

Routine hematological parameters including complete blood count, erythrocyte sedimentation rate, renal and liver function tests were within normal limits. Urinalysis showed no abnormality. Serum tumor markers—alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (β-hCG), and lactate dehydrogenase (LDH)—were all within the reference range.

High-resolution ultrasonography (USG) of the scrotum revealed an enlarged right testis measuring approximately 6 cm in maximal dimension, with heterogeneous echotexture and increased internal vascularity. The right epididymis and spermatic cord were also bulky but showed no discrete masses. No calcifications or hydrocele were noted. The left testis appeared normal. Abdominal ultrasound and contrast-enhanced CT (if performed) would be expected to rule out retroperitoneal lymphadenopathy or visceral involvement, although no lymphadenopathy was identified clinically or radiologically in this case.

Based on the clinical and radiological findings, the patient was taken up for right radical orchiectomy under general anesthesia. The orchiectomy specimen measured 6 × 5.5 × 3.5 cm, with a spermatic cord segment of 6 × 2 cm. The epididymis and

spermatic cord appeared grossly uninvolved. The external surface showed mild congestion. On cut section, a well-circumscribed, tan-white homogenous mass was seen replacing almost the entire testicular parenchyma. Foci of necrosis and hemorrhage were present. The epididymis, tunica albuginea, tunica vaginalis, and spermatic cord appeared grossly uninvolved.

Microscopically, the testicular parenchyma was completely replaced by a dense, diffuse infiltrate of neoplastic lymphoid cells. These cells were monomorphic with large nuclei, irregular nuclear contours, fine chromatin, and prominent nucleoli. The neoplastic cells invaded the intertubular spaces, widely separating the seminiferous tubules, many of which showed hyalinization and spermatogenic arrest. There was no infiltration into the tunica albuginea, epididymis, or spermatic cord.(Fig 1 : A,B,C)

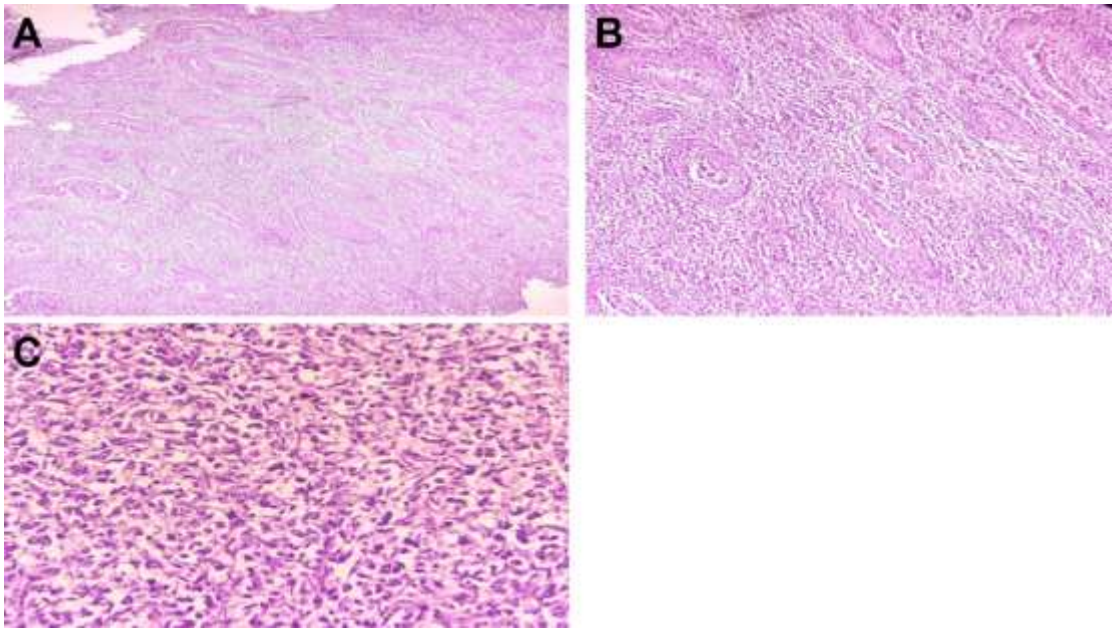

Fig 1 : A) A monomorphic population of neoplastic lymphoid cells diffusely infiltrating testicular parenchyma.(H & E; 40X) B) The neoplastic lymphoid cells diffusely infiltrating into the tissue spaces, producing a wide separation of intact seminiferous tubules.(H & E; 100X) C) Tumor cells demonstrated enlarged nuclei with irregular nuclear membranes and conspicuous nucleoli.(H & E; 400X)

Immunohistochemical staining revealed strong membranous positivity for CD45, CD19, and CD20, consistent with a B-cell phenotype.(Figure 2 : A,B,C). The tumor cells were negative for CD3 (T-cell marker), pancytokeratin, and epithelial membrane antigen (EMA), excluding germ cell tumors and epithelial malignancies. The Ki-67 proliferation index was high (~90%), indicating a high-grade neoplasm. Based on histological and immunophenotypic features, a final diagnosis of diffuse large B-cell lymphoma (DLBCL) of the testis was made.

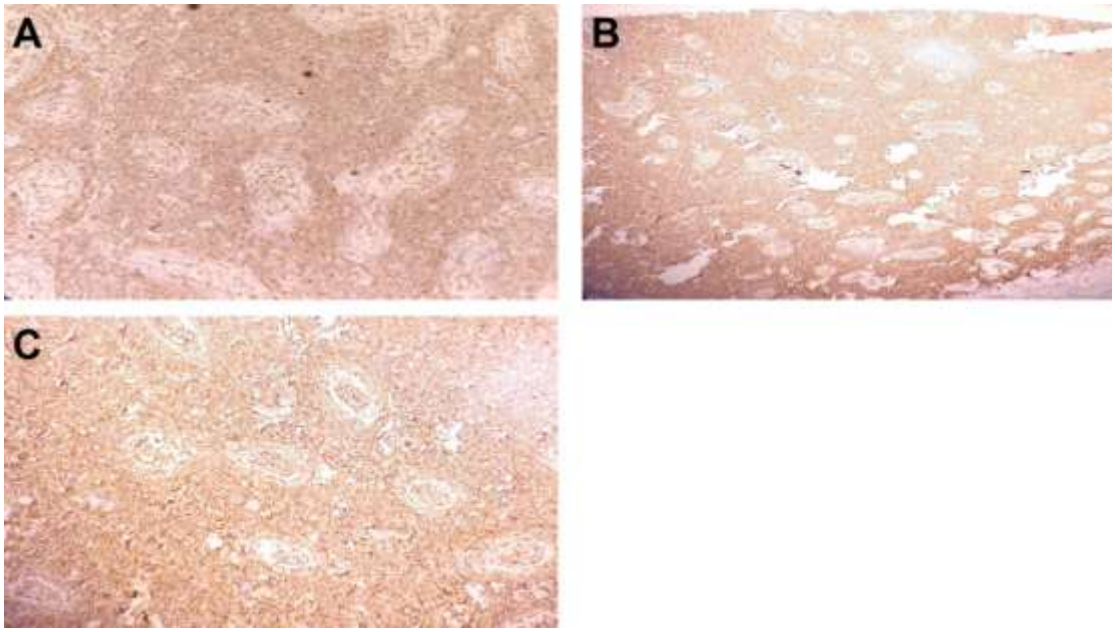

Fig 2 : Immunostaining revealed that the tumor cells exhibited diffuse, intense reactivity for A) CD 45; B) CD 20; C) CD 19. (IHC; 100X)

RESULTS

The histological and immunohistochemical evaluation clearly established the diagnosis of primary testicular lymphoma of DLBCL type. The critical diagnostic markers were: CD45, CD19, CD20 positivity and CD3, EMA, cytokeratin negativity. Ki-67 Index was approximately 90%. No evidence of systemic disease was found on clinical, radiological, or laboratory examination. There was no involvement of lymph nodes or distant organs at presentation. Serum tumor markers for testicular germ cell tumors were normal.

DISCUSSION

Primary testicular lymphoma is a rare but important differential diagnosis of testicular masses in elderly males. DLBCL, the most common subtype, is characterized by its aggressive nature and high propensity for relapse, particularly in extranodal sites such as the CNS, contralateral testis, and skin.[3,6,8]

PTL typically presents as a painless unilateral scrotal mass, similar to germ cell tumors, but differs in age of onset, imaging characteristics, and tumor markers. While seminomas and non-seminomatous germ cell tumors occur in younger males and elevate AFP or β-hCG, PTL presents in elderly males and is associated with normal tumor markers.[1,4,9] Histologically, PTL must be differentiated from seminoma, embryonal carcinoma, and inflammatory conditions like viral or granulomatous orchitis. The diffuse intertubular growth pattern and monomorphic large B-cells are hallmarks of DLBCL. Immunohistochemistry is essential to confirm B-cell lineage and exclude germ cell origin. Our case showed typical DLBCL features with strong positivity for CD45, CD19, and CD20.[10,11]

The optimal management of PTL involves multimodal therapy. Radical orchiectomy serves as both a diagnostic and therapeutic intervention, removing a site protected by the blood-testis barrier.[7] Systemic therapy typically consists of R-CHOP, which includes rituximab, a CD20 monoclonal antibody. Intrathecal methotrexate is often used as CNS prophylaxis, given the high CNS relapse risk.[4,12)] Scrotal radiotherapy may be used to reduce relapse in the contralateral testis. In our case, the patient underwent orchiectomy and was planned for systemic R-CHOP chemotherapy with CNS prophylaxis and contralateral testis radiotherapy as per current guidelines.

Despite aggressive treatment, the prognosis of PTL remains poor relative to nodal DLBCL. Key prognostic indicators include age >60 years, advanced stage, high LDH, poor performance status, and involvement of multiple extranodal sites. Five-year survival for localized disease may exceed 70% with appropriate multimodal therapy, but drops sharply with relapse.[2,3,5] This patient, presenting with localized disease and good performance status, is expected to respond favorably to combined therapy. Long-term follow-up with periodic imaging and CNS monitoring is essential.

CONCLUSION

Primary testicular lymphoma, though rare, should be considered in elderly males presenting with a unilateral testicular mass. Diffuse large B-cell lymphoma is the most common histological subtype and requires accurate diagnosis through histopathological and immunohistochemical analysis. The aggressive nature of this malignancy mandates a comprehensive therapeutic strategy including orchiectomy, R-CHOP chemotherapy, CNS prophylaxis, and radiotherapy. Early detection and multidisciplinary management are crucial for improving patient outcomes.

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