

Case Report Article

Primary testicular lymphoma in undescended testis of a middle-age man: a case report

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Abstract

Background: Primary testicular lymphoma (PTL) is an uncommon and aggressive form of extra-nodal non-Hodgkin lymphoma (NHL), accounting for <5.0% of testicular malignancies and 1.0% to 2.0% of NHL cases with a median age at diagnosis of 66 to 68 years. PTL accounts for 1–9% of testicular malignancies and 1–2% of NHLs. There are a handful of described lymphomas in the literature affecting normally positioned testis of aged men, yet none were reported in a cryptorchid middle-aged man. PTL is an extremely aggressive malignancy with poor progression-free survival and overall survival.

Case presentation: A 47-year-old man presented to the urology clinic complaining of multiple painless swellings in the neck and groins. He also complains of back pain, drenching night sweats, a swollen right lower limb, constipation, anorexia, weight loss, and occasional vomiting. The illness's duration is 2 months. He had a right inguinal testis. Histology examination of the excised testis and lymph nodes revealed an advanced "diffuse large beta-cell lymphoma" in both. The patient was referred for oncology care.

Conclusion: It is an extremely rare case of diffuse large B-cell lymphoma (DLBCL) in the undescended testis of a middle-aged man. To the best of our knowledge, this is the first published case of its kind about the tumor's type, testis anomaly, and patient's age.

Keywords: Primary Testicular Lymphoma, Diffuse Large B-Cell Lymphoma, Testis, Saudi Arabia.

Background

Primary testicular lymphoma (PTL) is a rare entity with an annual incidence that ranges between 0.09 and 0.26 per 100,000 person-years. Moreover, it is the most common malignant testicular neoplasm in men over 60, which accounts for approximately 1–9% of all testicular tumors and 1–2% of all non-Hodgkin's lymphomas. Similar studies reported that the median age at diagnosis of PTL is 67 [1-3]. The most common clinical symptom of PTL is unilateral, painless testicular swelling. Nevertheless, bilateral testicular swelling is seen in around 35% of patients [3]. PTL is both the most common testicular malignancy in men aged over 60 years and the most common bilateral testicular neoplasm [4]. Anecdotal reports that associate PTL development with trauma, chronic orchitis, cryptorchidism, or filariasis exist, but no case-control studies have confirmed their etiologic significance. Diffuse large B-cell lymphoma (DLBCL) is the most common histotype in primary

forms, accounting for >85% of all PTL cases. It is bilateral in 35.0% of cases [5]. It is an aggressive form of extra-nodal non-Hodgkin lymphoma (NHL), accounting for <5.0% of testicular malignancies and 1% to 2% of NHL cases. It diffusely infiltrates and engulfs the architecture of the involved tissue [6]. It begins in the testis and often spreads to the contralateral testis as well as to the central nervous system in 10% of cases. It usually carries a poor prognosis [7,8]. Other aggressive types include Burkitt's lymphoma, which is prevalent with secondary testicular involvement [4]. The most common clinical presentation is a unilateral painless scrotal swelling, sometimes with sharp scrotal pain or a hydrocele. Systemic B symptoms are present in 25.0–41.0% of patients with advanced stages. Less frequently, abdominal pain and ascites can be seen in patients with involvement of the retroperitoneal lymph nodes. PTL has a propensity to disseminate to other extra-nodal organs, including the contralateral testis, CNS, skin, Waldeyer's ring, lung, pleura, and soft tissue [4]. The Surveillance, Epidemiology, and End Results (SEER) database included 1,169 patients diagnosed with PTL between 1973 and 2013. The median age of patients was 70 years old. The most prevalent tumor histological subtype was DLBCL (970/1,169,

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82.9%), followed by follicular lymphoma (21/1,169, 1.80%; Table II) and Burkitt's lymphoma (15/1,169, 1.28%). T-cell lymphomas, including mature T-cell lymphoma, anaplastic large cell lymphoma, NK/T-cell lymphoma, and precursor T-cell lymphoblastic lymphoma, accounted for only a small number of cases (15/1,169, 1.3%) [9]. Cryptorchidism is associated with a four-fold increase in the risk of a testicular germ cell tumor (TGCT) (10). The most common type of TGCT in cryptorchid testes is seminoma [11]. The diagnosis of PT-DLBCL depends on examining the histology, i.e., microscopic anatomy, of biopsy samples taken from the tumors. Most of these tumors are large, e.g., 6 centimeters, and show medium-to large-sized lymphoid tumor B-cells diffusely infiltrating and effacing the architecture of the involved tissue [12]. T-DLBCL has a unique biology with distinct genetic characteristics and clinical presentation, and the increasing knowledge on the tumor microenvironment of T-DLBCL highlights the significance of host immunity and immune escape in this rare lymphoma, which presents in an immune-privileged site of the testis [13]. Other forms of PTL include testicular mantle cell lymphoma, extra-nodal marginal zone B cell lymphoma, extra-nodal NK/T-cell lymphoma, nasal type, peripheral T-cell lymphoma, activin receptor-like kinase-1-negative anaplastic large cell lymphoma, and pediatric-type follicular lymphoma [5]. Some European investigators have combined PT-DLBCL and most of the latter lymphomas into a lymphoma group termed "non-Hodgkin's primitive lymphoma of the testes" [14,15]. Serum Lactate dehydrogenase (LDH) has diagnostic and prognostic values in many body cancers, including NHL. It reflects the tumor bulk, as its elevation in the serum denotes tissue destruction caused by tumor growth [16].

Case presentation

A 47-year-old man presented to the Urology clinic at King Abdulaziz Hospital in Makkah, Saudi Arabia, complaining of multiple painless swellings in the neck and groin areas. He also complained of back pain, drenching night sweats, a swollen right lower limb, constipation, anorexia, weight loss, and occasional vomiting. No neuroglial manifestations. The duration of the illness was 2 months. He has no past medical or surgical history of importance. No history of trauma, infection, or filariasis. He is a father of four, not a smoker, and holds a menial job. Clinically, he is overweight and of average body build. Physically, the right testis is palpated in the right inguinal area. There is multiple, firm, painless enlarged lymph nodes at the neck, femoral, and inguinal areas. His right lower limb has non-pitting edema. Laboratory tests showed normal complete blood count (CBC), blood sugar, and renal functions. Uric acid is very high at 873(mg/dL). Lactate dehydrogenase (LDH) is, likewise, very high 2152 (units/L). Serology screening, including HIV, is negative. Ultrasonographic examination of the scrotum revealed a normal-sized left testis with average echotexture and vascularity. Empty right scrotal sac. A Doppler examination of the right leg showed no evidence of recent deep venous thrombosis (DVT). Multiple enlarged right inguinal lymph nodes with a globular shape and coarse texture. Diffuse right lower limb subcutaneous edema. Computed Tomography (CT) scan of the chest, abdomen, and pelvis discovered sizable mediastinal lymph nodes LNs mainly at the retrocaval group, measuring up to 2.5cm in greatest diameter. Bilateral axillary,

supraclavicular, and deep cervical enlarged LNs. Scattered mosaic attenuation within both lungs, though no sizable masses or cavitations. No significant pleural or pericardial effusion. Extensive enlarged abdominal LNs mainly at para-aortic 2.5cm (figure 1), internal and external iliac groups; the largest being 2.5cm. Multiple enlarged obturator groups bilaterally exist; the largest measures 9 x 5cm. Both inguinal (largest 5 x 3cm) with extensive necrosis (figure 2), right pelvic (5.5 x 5.5cm). The liver is of normal size with average tissue density. It shows no focal or enhancing lesions. "The gallbladder, intra- and extra-hepatic biliary radicles, the pancreas, adrenals, kidneys, and spleen are normal." No ascites. Intact major abdominal vasculature. Marantic Resonance Image (MRI + c) of the abdomen unraveled multiple bilateral bulky masses of LNs at the inguinal and iliac groups; the largest measures 9 x 5.9cm. It shows normal left testis (figure 3). The bladder is squeezed cephalad (figure 4). The patient was scheduled for right inguinal orchiectomy and LN sampling, where inguinal and cervical LNs were extirpated. Histopathology later revealed complete infiltration of normal tissue by large atypical B lymphoid cells with prominent nucleoli denoting diffuse large beta-cell lymphoma in the submitted LNs (figure 5a, 5b). The excised right testis and nodes were entirely replaced by lymphoma architecture (figure 6). The tissues were positive for CD20 and CD79a. They were negative for cytokeratin and PLAP. The patient was referred for oncology care. Based on the standard An Arbor staging system for PTL, it is stage IV-B.

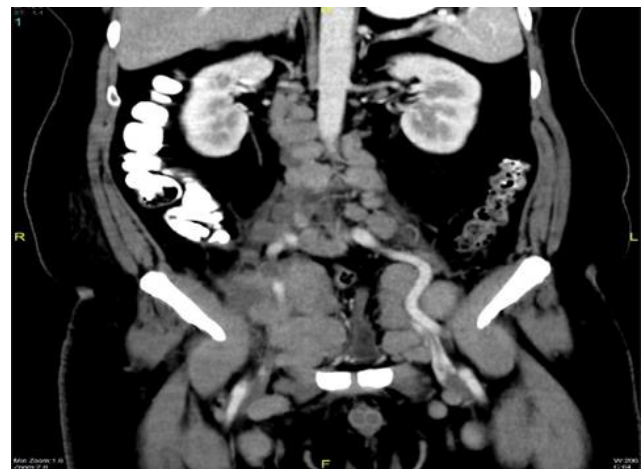


Figure 1: CT c+ multiple enlarged para-aortic nodes

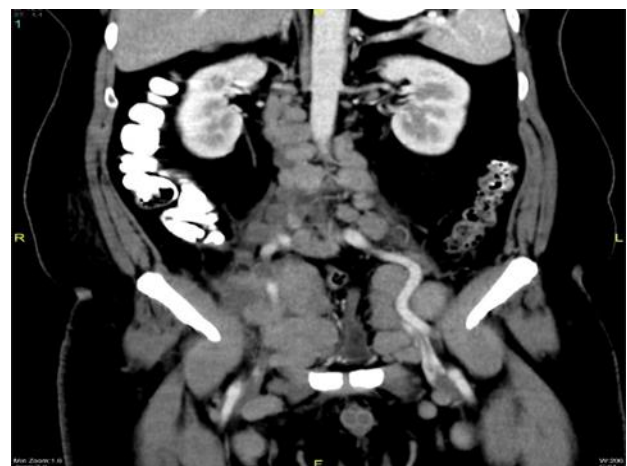


Figure 2: CT c+ bilateral enlarged inguinal nodes with necrosis

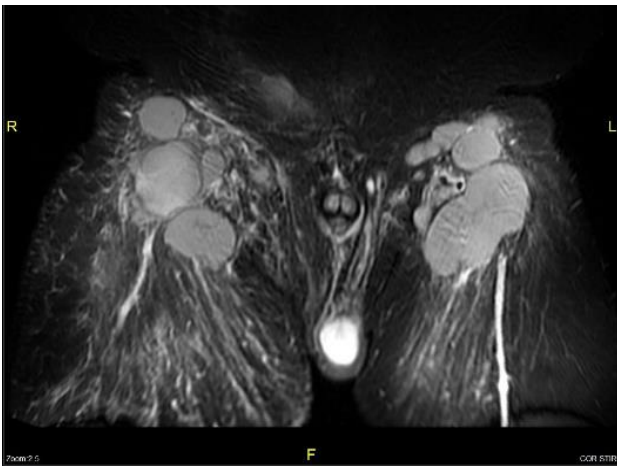


Figure 3: Coronal STIR: bilateral enlarged inguinal nodes with normal testis

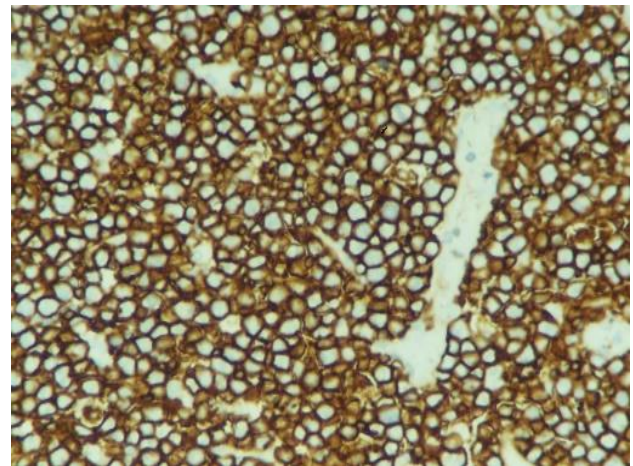


Figure 6: Right testicular tissue replaced by tumor cells exhibiting positive CD20

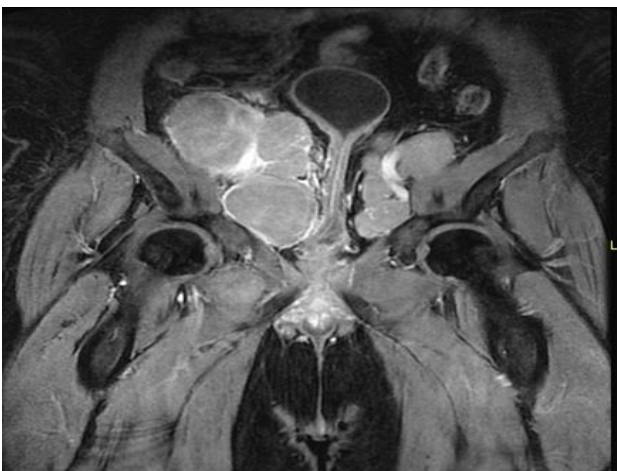


Figure 4: Coronal STIR: the bladder appears squeezed up by the massive pelvic nodes

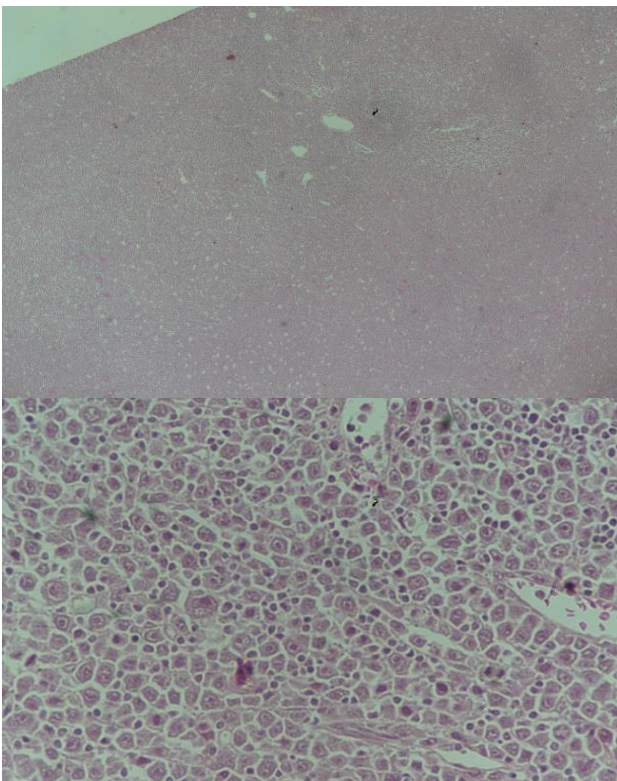


Figure 5 (a & b): Complete infiltration of cervical lymph node tissue by large atypical B lymphoid cells with prominent nucleoli

Discussion

The only primary lymphoma in undescended testis case in the literature we came across is a case report published in 2018 by Donghua He, entitled "Anaplastic large cell lymphoma in the undescended testis of a patient with 46, XY disorder of sex development" [17]. The elevated serum uric acid is well explained by "tumor lysis syndrome". LDH has diagnostic and prognostic values in many body cancers, including NHL. It reflects the tumor bulk, as its elevation in the serum denotes tissue destruction caused by tumor growth [16]. Due to the rareness of the disease, no randomized clinical trials have been conducted, and the currently recognized standard of care is based on retrospective analyses and a few phase II trials. In recent years, the tumor microenvironment (TME) and tumor-related immunity have been the focus of many tumor biology studies, and the emergence of targeted therapies and checkpoint inhibitors has significantly modulated the field of cancer therapies. T-DLBCL is presented in an immune-privileged site of the testis, and the roles of NF- κ B pathway signaling, 9p24.1 aberrations, and tumor-infiltrating immune cells, especially immune checkpoint expressing lymphocytes and macrophages, seem to be unique compared to other lymphoma entities. Preliminary data on the use of immune checkpoint inhibitors in the treatment of T-DLBCL are promising, and more studies are ongoing [13].

Conclusion

We report an extremely rare case of DLBCL in the undescended testis of a middle-aged man. To the best of our knowledge, this is the first published case of its kind about the tumor's type, testis anomaly, and patient's age.

Abbreviation

PTL: Primary Testicular Lymphoma; NHL: Non-Hodgkin Lymphoma; DLBCL: Diffuse Large B-Cell Lymphoma; CNS: Central Nervous System; SEER: The Surveillance, Epidemiology, and End Results; TGCT: Testicular Germ Cell Tumor; LDH: Serum Lactate Dehydrogenase; DVT: Deep Venous Thrombosis; CT: Computed Tomography; LNs: Lymph Nodes; MRI: Magnetic Resonance Image; Complete Blood Count (CBC): Lactate dehydrogenase (LDH)

Declaration

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Availability of data and materials

Data will be available by emailing atifkatib@gmail.com

Authors' contributions

All authors were equally participated in the design, reviewing, and editing of the manuscript in its final form. All authors read and approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki. Ethical permission was granted by the Urology clinic at King Abdulaziz Hospital in Makkah, Saudi Arabia [2023].

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

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