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Case report

Diffuse Large B-cell Lymphoma of Testis: a Case Report and Current Literature Review

Yavuz Guler[1], Burak Ucpinar[2], Akif Erbin[2]

[1]*Department of Urology, Safa Hospital, Istanbul, Turkey*
[2]*Department of Urology, Haseki Training and Research Hospital, Istanbul, Turkey*

Corresponding author: Akif Erbin, Department of Urology, Haseki Traning and Research Hospital, Fatih, 34096 Istanbul, Turkey; E-mail: akiferbin@hotmail.com; Tel.: +905065431062

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Abstract

Introduction: Testicular cancers detected in older males are mostly testicular lymphomas. Primary testicular lymphoma (PTL) is a rare, clinically aggressive form of extranodal lymphoma. In population-based studies, the incidence of PTL is 0.09-0.26/100.000. The vast majority of PTL are diffuse large B-cell lymphoma (DLBCL).

Case presentation: We present a case of PTL diagnosed in a 68-year-old male patient and also, we discuss the incidence, clinical presentation, prognostic factors and management of this rare pathology in the light of current literature. Histopathological and immunohistochemical exams of the patient confirmed the diagnosis of DLBCL after radical orchiectomy. According to the internal prognostic index (IPI), patients' IPI score was evaluated as 5 and according to Ann Arbor staging, patients' stage was interpreted as grade 3E. Cyclophosphamide, vincristine, etoposide, and prednisolone chemotherapy was planned for the patient and until now, the patient received his first chemotherapy regimen.

Discussion: Primary testicular lymphoma should be kept in mind for every patient who admits with a testicular mass, especially in advanced age. Misinterpreatation of the clinical findings can delay the definitive diagnosis. Primary testicular lymphoma should be managed with a multi-disciplinary team including urologists, medical and radiation oncologists.

Keywords:

diffuse large B-cell, lymphoma, testis

BACKGROUND

Non-Hodgkin lymphoma (NHL) constitute 1-4% of all extranodal lymphomas and 1-7% of testicular cancers. Testicular NHL differ from germ cell and stromal testicular tumors by their frequent bilateral testis involvement (8-38%), bilateral metasynchronized testis involvement (35%) and synchronous involvement (3%).[1] In population-based studies, the incidence of primary testicular lymphoma (PTL) is 0.09-0.26/100000.[2] Testicular cancers detected in elderly males are mostly testicular lymphomas. The vast majority of PTLs are diffuse large B-cell lymphomas (DLBCL).[3,4] Even though the disease has poor prognosis, early diagnosis and effective management is crucial. The disease is managed with multiple treatment modalities including surgery, chemotherapy and radiotherapy. We aimed to present a case of primary DLBCL of testis with current literature review.

CASE REPORT

Written informed consent was obtained from the patient to report this case study. A 68-year-old male patient had a

complaint of stiffness and pain in the left testicle for the last 6 months. Before being referred to our clinic, he was treated with various antibiotics, considering it to be chronic orchitis. The values were calculated as Hgb: 9.6 g/dL, Hct: 29.2%, Wbc: 5.91 mm3, LDH: 350 IU/L. There were no other abnormalities in the laboratory tests such as liver function tests, renal function tests, coagulation parameters and tumor markers (alpha-fetoprotein, beta-hCG). Also, serum antigens for immuno-deficiency virus (HIV) and serum antibodies against HIV were negative. Scrotal gray scale and Doppler ultrasonography revealed a 6.5×4.5 cm hypoechoic mass, which was indistinguishable from testicular tissue, and the mass showed intense blood flow. Abdomino-pelvic and thoracic magnetic resonance imaging (MRI) were performed for staging; multiple enlarged lymph nodes were detected in the infradiaphragmatic area, mainly around the bilateral iliac vessels. However, no other tumoral tissue was identified in the extranodal regions outside the testes.

Radical orchiectomy was performed to reach a definitive diagnosis and initiate the appropriate treatment. Pathology report revealed testicular capsule, epididymis, lymphovascular area and spermatic cord invasion by the tumor, however, no invasion was detected in hilar soft tissue and perineural area. Surgical borders were reported as negative. Immunohistochemical staining results indicated strong CD 20 and focal CD 3 (membrane markers for B-lymphocytes) positivity in tumor cells. Ki 67 (nuclear proliferation marker) was strongly positive in about 80% of tumors cells, bcl-6 (nuclear marker of germinal center lymphocytes) and CD 10 were negative in tumor cells. Multiple myeloma oncogene 1 (MUM1) was detected to be weakly positive ***(Fig. 1****). According to the World Health organization diagnosis criteria and using Hans algorithm, the diagnosis was DLBCL of testis with germinal center phenotype.*

According to the internal prognostic index (IPI), patients' IPI score was evaluated as 5 and according to Ann Arbor staging, patients' stage was interpreted as grade 3E. The patient was referred to the oncology department after the orchiectomy. Cyclophosphamide, vincristine, etoposide, and prednisolone (CHOP) chemotherapy was planned for the patient and until now, the patient received his first chemotherapy regimen.

DISCUSSION

Primary testicular lymphoma can either be primary, or can present as testicular involvement of a different site of origin. Autopsy studies revealed the increased likelihood of metastasis from nodal or extranodal areas to testis (secondary testicular lymphoma). Microscopic testicular invasion was detected in about 20% of patients who died due to dissem-

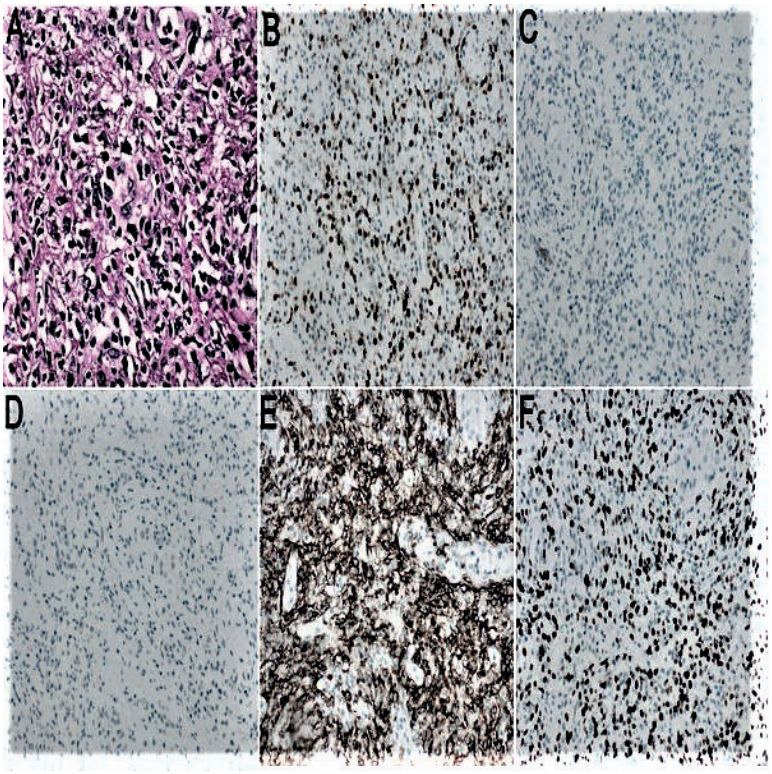

Figure 1. a-f: The lymphatic cellular infiltration and proliferation in testis, monomorphic, medium and large round cells with nuclear pleomorphisim, H&E (×40) (**A**), MUM1 (×20): weak positive (**B**), CD10 (×20): negative (**C**), BCL6 (×20): negative (**D**), CD20 (×20): strong positive (**E**), F-Ki67 (×20): 80% positive, it shows high proliferation rate of lymphoma cells (**F**).

inated NHL. In our case, the detected testicular lymphoma might have been the primary site of lymphoma. However, testicular involvement of an abdominal lymphoma is also a reasonable clinical scenario. But not knowing the exact origin of the tumor does not affect the management of stage 3E disease. Patients with only testicular involvement without systemic involvement are less commonly encountered. There have been, however, reports of testicular lymphomas associated with regional manifestations that does not present with systemic involvement (e.g, lymphoma of the skin or lymphoma of the heart).[5]

Our patient presented with a painless, firm, big testicular mass, which was indistinguishable from the affected testicular tissue. In the literature, the average tumor diameter at first admission is reported to be between 6 and 8 cm and 40% of the patients also present with hydrocele. Lymphoma-specific systemic symptoms are not common at baseline, but if present, are a strong indicator of systemic disease and are present in 25-41% of patients with advanced stage.[6]

It is well-known that testicular lymphoma is more common among patients over 60 years of age, and rarely encountered in younger patients.[7] Secondary testicular lymphoma is more common in patients under 60 years of age and bilateral testicular involvement is more common. Bertalotto et al. reported that 75% of 43 patients with testicular lymphoma were over the age of 60 at the time of diagnosis.[3]

The etiological and predisposing factors of the PTLs are not well understood. However, no relation between lymphoma and trauma, chronic orchitis or undescended testis was found.[3] Although specific risk factors for PTL are limited, HIV infection has been identified as a factor for aggressive NHL.[8] In HIV-infected patients, lymphoma occurs more extensively in extranodal sites such as testis. HIV-positive patients develop lymphoma at a younger age and immunoblastic, plasmablastic and Burrkit-like histology is more common with a mean survival limited to 6 months. However, the initiation of combined anti-viral therapy has been reported to improve the outcome of DLBCL treatment in these patients.[6,8]

In ultrasonographic examination, hypoplasia, diffuse enlargement, and increased echogenicity of the testis and loss of hypervascularity, or a striped pattern of the entire testis might be observed in neoplastic infiltrative diseases such as plasmacytoma, leukemia and lymphoma. However, these feature can be observed in inflammatory diseases such as chronic granulomatous orchitis and other inflammatory processes as well. Thus, in the absence of clinical signs and symptoms of inflammation, correct interpretation of the findings might be challenging. Eventually, in these cases, a biopsy is often necessary and orchidectomy stands at a crucial place in the diagnosis.

When testicular lymphoma is diagnosed, an appropriate treatment strategy should be prepared with a multi-disciplinary team that includes a urologist, a pathologist and an oncologist. Prognosis is usually poor and disease-free survival is short. Although the standards of treatment for germ cell and stromal testicular tumors are well known, there is a debate in the testis lymphoma treatment. Biopsy to confirm the diagnosis, followed by systemic chemotherapy consisting of cyclophosphamide, doxorubicin, vincristine, and prednisolone is a treatment option. Regardless of the stage of the disease, relapse in extranodal regions and central nervous system (CNS) commonly occurs in patients who only receive orchiectomy as treatment.[6] Because tumor relapses are common in the CNS, the CNS prophylaxis must be done with intrathecal chemotherapy.[9] In our case, the disease was stage 3 at the time of diagnosis and chemotherapy was inevitable. Also, since the risk of relapse to the counter-testis is high, counter-testis radiotherapy is strongly indicated in standard treatment.[10-12] De Zhou et al. reported that patients treated with contralateral testis radiotherapy had no relapse but there was a relapse in 4/14 of patients who did not receive treatment.[13]

CONCLUSION

Testicular lymphoma is a rarely encountered pathology which should be considered for every patient who is admitted with a testicular mass, especially if they happen to be in advanced age. Misinterpreatation of the clinical findings as orchitis could delay the definitive diagnosis. When testicular lymphoma is diagnosed, an appropriate treatment strategy should be prepared with a multi-disciplinary team including urologists, medical and radiation oncologists.

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Диффузная В-крупноклеточная лимфома яичка: клинический случай и обзор современной литературы

Явуз Гюлер[1], Бурак Учпинар[2], Акиф Ербин[2]

[1]*Отделение урологии, Больница Сафа, Стамбул, Турция*
[2]*Отделение урологии, Учебно-исследовательская больница Хасеки, Стамбул, Турция*

Адрес для корреспонденции: Акиф Ербин, Отделение урологии, Учебно-исследовательская больница Хасеки, Фатих, 34096 Стамбул, Турция; E-mail: akiferbin@hotmail.com; Тел .: +905065431062

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Абстракт

Введение: Рак яичка, обнаруженный у пожилых мужчин, - это в основном лимфома яичка. Первичная тестикулярная лимфома (ПТЛ) является редкой, клинически агрессивной формой экстранодальной лимфомы. В популяционных исследованиях частота ПТЛ составляет 0,09-0,26 / 100 000. Большинство ПТЛ представляют собой диффузные В-крупноклеточные лимфомы (ДБККЛ).

Презентация случая: Мы представляем случай ПТЛ, диагностированный у 68-летнего пациента мужского пола, а также обсуждаем частоту, клиническую картину, прогностические факторы и лечение этой редкой патологии в свете современной медицинской литературы. Гистопатологические и иммуногистохимические исследования пациентов подтверждают диагноз ДБККЛ после радикальной орхиэктомии. Согласно Международному прогнозному индексу (IPI), показатель IPI пациента составляет 5, а согласно шкале Энн-Арбора стадия пациента определяется как 3E. Для пациента была запланирована химиотерапия циклофосфамидом, винкристином, этопозидом и преднизолоном, и к этому времени он прошёл первый курс химиотерапии.

Обсуждение: Предполагаемая первичная лимфома яичка должен рассматриваться в отношении каждого пациента поступившего с увеличенной массой яичка, особенно среди пожилых людей. Неправильная интерпретация клинических результатов может задержать окончательный диагноз. Первичная лимфома яичка должна подвергаться лечению с участием мультидисциплинарной группы врачей, включающей урологов, медицинских и радиологических онкологов.

Ключевые слова

диффузная крупная В-клетка, лимфома, яичко