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Case Report

Primary Testicular Diffuse Large B-cell Lymphoma Presenting in a Young Adult

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Abstract

Primary testicular lymphoma is a rare type of extranodal non-Hodgkin lymphoma (NHL), its positive diagnosis is based on histopathological findings. Treatment modalities consist of surgical excision, chemotherapy, and radiation therapy but the accurate procedures are not standardized. The authors report a new case of primary testicular lymphoma, and we discuss its diagnostic and therapeutic aspects. Sperm cryopreservation was carried out. The patient was started on chemotherapy with cyclophosphamide, hydroxydaunorubicin, oncovin,and prednisone (CHOP) regime.

Keywords: Primary testicular lymphoma; diffuse large B-cell lymphoma; testis; orchiectomy.

INTRODUCTION

Primary testicular lymphoma was first reported by Malassez and curling in 1866, It is a rare testicular neoplasm that mainly affects elderly patients, with an annual incidence of 0.26 cases per 100,000 person-years. Additionally, orchiectomy followed by chemotherapy is traditionally the recommended treatment for patients with PTL.

There are neither any well-documented etiological or predisposing factors nor any significant associations existing between histories of trauma, chronic orchitis, or cryptorchidism and subsequent development of TNHL.

This localization is characterized by increased aggressiveness and a high risk of relapse, even after 10–15 years of onset, especially in the contralateral testicle.

We report here the case of a 25-year-old young man with primary testicular DLBCL. He underwent a radical right orchiectomy for diagnostic and therapeutic purposes.

Histopathological and immunohistochemical examinations confirmed the diagnosis of diffuse large B-cell lymphoma, and the stage was IIB. According to the International Prognostic Index (IPI) score, the patient was classified as low risk. He received a combination of treatments including surgery, central nervous system prophylaxis, and radiation therapy. The outcome was very good and the patient achieved complete remission.

Through this case study, we discuss and describe its diagnostic and therapeutic challenge.

CASE PRESENTATION

A 25-year-old male young patient, with a past medical history of pulmonary tuberculosis at 22-year-old, presented to the urology department with three years history of slowly, progressive, and painless right testicular swelling, without the context of trauma, fever, or other associated symptoms.

In physical examination, the right testis was enlarged, painless, with stony consistency and quite tense, with a normal spermatic cord. The left scrotal skin and right testis were normal. There was no palpable abdominal mass or organomegaly, with no lymph node masses were palpable in the inguinal or Supraclavicular areas. The patient was in good general health, and the remainder of the clinical examination was normal.

Color Doppler ultrasonography of the scrotum showed an enlarged heterogeneous right testis, with diffuse hypoechoic areas, and increased vascularity.

Preoperative serum tumor markers including alpha-fetoprotein (αFP), human chorionic gonadotropin (hCG), and lactate dehydrogenase (LDH) levels were normal. The other laboratory tests were normal. Right radical inguinal orchiectomy under spinal anesthesia was performed. It measured 66x60x40 mm and had an attached spermatic cord of 7 cm. (Fig.1).

Histopathology revealed the replacement of testicular parenchyma by a diffuse, monomorphic, neoplastic proliferation, consisting of large discohesive sheets of cells of lymphocyte type, marked with nuclear pleomorphism (Fig. 2), with large necrotic tumor foci estimated at 50%, and the tumor was limited to the testicular parenchyma without the involvement of tunica albuginea, tunica vaginalis, epididymis, or spermaticcord.

Immunohistochemical (IHC) examination (Fig. 3) revealed CD20 (membrane markers for B-lymphocytes) strongly positive and diffuse in tumor cells. Ki-67 (nuclear proliferation marker) was strongly positive in about 85% of tumor cells. Bcl-6 (a nuclear marker of germinal center lymphocytes), CD10, CD30, CD 117, and PLAP were negative in tumor cells.

These features rendered the diagnosis of diffuse large B-cell lymphoma (DLBCL) of the testis with non- germinal center type, according to the World Health Organization (WHO) classification of lymphoid neoplasms.

To accurately assess the disease extension, positron emission tomography/computed tomography (PET/CT) scan, CT scan of the neck, thorax, abdomen, and pelvis, bone marrow biopsy, examination of the oronasopharynx, and gastroscopy with biopsy, were performed. None of these tests revealed any evidence of extratesticular location of lymphoma or lymph nodes.

The diagnosis of stage I primary testicular large B-cell lymphoma of germinal center B-cell-like phenotype was made. The patient was subsequently referred to medical oncology and radiation oncology departments with the purpose of adjuvant chemotherapy and radiotherapy.

At 5 years of follow-up, the patient was in excellent health, control imaging showed no evidence of recurrence.

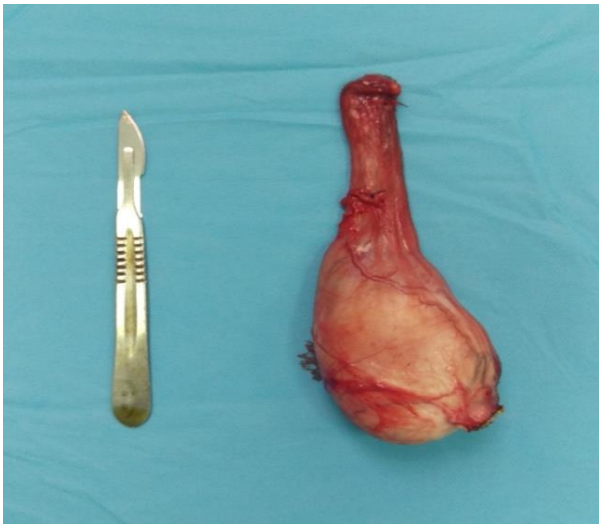

Fig-1: Right radical inguinal orchidectomy

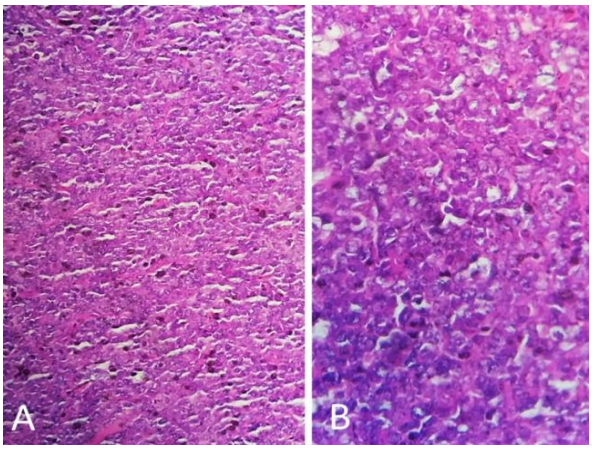

Fig-2: Photomicrograph showing a proliferation of diffuse architecture (A) made of centroblastic and immunoblastic malignant cells with numerous mitosis figures (Hematoxylin eosin X40)

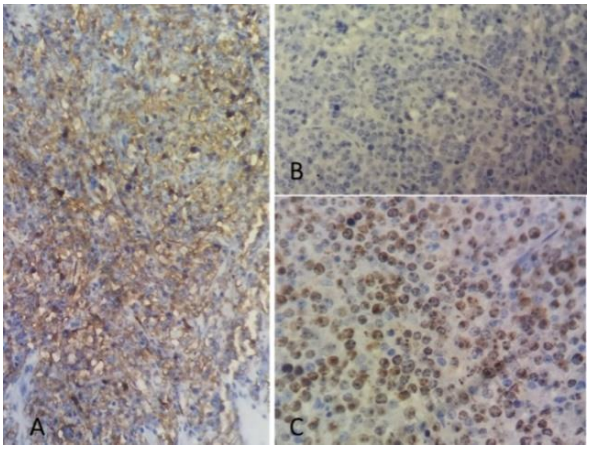

Fig-3: In the immunohistochemical study, tumor cells express CD20 with membrane labeling (A) and do not express DC10 (B). The Ki67 is estimated at 85%

DISCUSSION

Primary testicular lymphoma (PTL) is a rare location of extranodal non-Hodgkin lymphoma (NHL), accounting for 1%to 2% of all cases of NHL, and representing 1%to 5% of all primary testicular tumors [1, 2]. Diffuse large B-cell lymphoma (DLBCL) is the most dominant histological subtype, and it is seen in about 80%-90% of cases of testicular lymphoma [1, 2], it mainly affects the elderly men aged over 60 years. However, according to recent publications, there is an increasing number of younger patients [1, 2]. This localization is characterized by increased aggressiveness and a high risk of relapse, even after 10–15 years of onset, especially in the contralateral testicle (5–35%), and at patients who have not received radiotherapy on the contralateral testicle, with a risk of central nervous system (CNS) relapse, at five years 20% and at 10 years 35%.

Its occurrence can be isolated or associated with other neoplasia or associated with immunodeficiency status such as immunosuppressive treatment, human immunodeficiency virus (HIV) infection, or tuberculosis infection. The patient was staged IIB at diagnosis; approximately 20% of patients with primitive testicular lymphoma were stabilized in stage II at diagnosis, our patient is still young (25 years) with slowly progressing local symptoms and testicular masses with normal testicular markers. Our patient has a history of pulmonary tuberculosis, which corresponds with the onset of testicular symptom.

The clinical presentation includes unilateral painless testicular swelling and systemic B symptoms in patients with advanced-stage disease. However bilateral involvement can be noticed in up to 10% of the cases [3]. Granulomatous orchitis, plasmacytoma, pseudolymphoma, and rhabdomyosarcoma are the main differential diagnosis. Primary testicular lymphoma can infiltrate the epididymis, spermatic cord, with the potential to spread to extranodal sites, such as the central nervous system (CNS) (up to 30%), soft tissues, and Waldeyer's ring (5%), skin (up to 35%), eyes, pleura and lung, the involvement of these sites may occur either simultaneously or happened later in the evolution of the disease [1, 3, 4].

Imaging techniques play a very important role in the initial diagnosis, staging of patients, and follow-up examination. Ultrasonography (US) is the most common imaging technique used to diagnose testicular masses. PTLs are observed in the form of hypoechoic focal or diffuse testicular lesions, with increased vascularity; however, this feature is not specific to PTL. CT or magnetic resonance imaging (MRI) can also contribute to the diagnosis by evaluating the structure of the testis and epididymis.PET/CT is recommended for evaluating the initial staging, follow-up, assessment of relapse, and treatment response.

In our case, testicular involvement was isolated, without any other organ involvement. The radical orchiectomy is the first stage in the management of PTL, both for diagnostic and therapeutic purposes, but should not be considered as the sole treatment of PTLeven in stage I patients to achieve favorable outcomes, and to avoid distant relapse, as indicated by several studies[3, 5].

The use of multimodal therapy based on orchiectomy followed by chemotherapy(R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone), radiotherapy on the contralateral testicle (25–30 Gy in 1.5–2 Gy fractions), and CNS prophylaxis is associated with an improvement in the 5-yearsurvival rate from 30 to 86.6% [3-5].

The most important prognostic factors include older age, advanced stage, high International Prognostic Index (IPI) scores, elevated lactate dehydrogenase (LDH), B symptoms, and orchiectomy alone which are associated with a poor prognosis and with high mortality rates [5].

Our patient was diagnosed with PTL at an early stage, his IPI score was low risk, and his good prognosis for 2 years of follow-up did not show any recurrence.

The prognosis for TNHL is generally poor, with a high incidence of recurrence and progressive systemic lymphomatous involvement.

In our case, a systemic chemotherapy protocol comprising the combination of rituximab, cyclophosphamide, doxorubicin, and vincristine and an intrathecal methotrexate therapy was implemented to decrease the risk of relapse in the central nervous system. Evolution was favorable; the patient is in complete remission two and a half years after the end of the therapeutic protocol.

Additionally, radiotherapy was conducted on the contralateral testis, the paraaortic and right iliac lymph nodes, and no relapse was observed at the end of a 6-month follow-up.

The International Extranodal Lymphoma Study Group (IELSG) prognostic score for Cytology may prove to be a helpful investigation, particularly when facing diagnostic dilemmas in patients who present with normal testicular tumor markers and with testicular swelling, and especially in young patients. Therefore, these patients should have both short- and long-term follow-up.

CONCLUSION

Primary testicular lymphoma is a rare disease with a poor prognosis. The rare incidence of the disease, its development, and its tumoral behavior

different from germinal cancer have made it difficult to determine the therapeutic modalities to be applied after orchiectomy, Therefore, primary malignant lymphoma of the testis should be considered as the manifestation of systemic disease in the testis. The contralateral testis and relapse in the central nervous system should always be taken into consideration. Lymphoma should be kept in mind for patients who present with a mass in the testis, and the urologist, pathologist, and oncologist should take joint action.

Despite the complex therapeutic protocol, the prognosis in these locations remains reserved. Future prospective studies, some of them already underway, will provide additional information on the most effective therapeutic approach with a significant impact on survival.

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