Primary testicular diffuse large B-cell lymphoma: A case report

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1. Introduction

Primary testicular lymphoma (PTL) is a group of uncommon neoplasms, with the subtypes of diffuse large B-cell lymphoma (DLBCL), follicular lymphoma and Burkitt’s lymphoma [1,2]. In general, primary testicular DLBCL, the frequent subtype among all, arises in old age (i.e., >60 years) [3–5]. The typical clinical signs of testicular DLBCL include testicular swelling, B-symptoms and elevated lactate dehydrogenase (LDH) levels [6]. In general, testicular DLBCL tumors are classified based on Cotswold modification of Ann Arbor staging system, where crucial disease parameters like tumor size, lymphadenopathy and regions of lymph node involvement are considered towards the assessment of overall clinical stage of the disease [7]. Primary testicular DLBCL has been reported to exhibit aggressive clinical behavior, poor prognosis and high tendency to disseminate to the central nervous system (CNS) and thereby related to high morbidity and mortality rates [3,8]. The hybrid 2-[fluorine-18] fluoro-2-deoxy-d-glucose (FDG) positron emission tomography/computed tomography (PET/CT) demonstrated two para-aortic FDG avid lymph nodes on the left side at the level of L2 vertebra. Presently, the patient has been planned for doxorubicin-based chemotherapy (i.e., cyclophosphamide, doxorubicin, vincristine and prednisone; CHOP) along with intrathecal Methotrexate (MTX), which would presumably improve the prognosis. Our study would expand the pool of this uncommon tumor towards its better understanding.

Herein, we present a case of 47 year old male diagnosed with primary testicular DLBCL. Specifically, the patient and underwent unilateral (left) radical orchiectomy. Histopathological examination revealed extensive involvement and replacement of testicular parenchyma by a tumor composed of large discohesive sheets of cells with pleomorphic, hyperchromatic nuclei and prominent nucleoli. Immunohistochemical (IHC) staining showed reactivity for LCA & Pan B (CD20) and negativity for OCT 3/4, SALL4 and Inhibin. Moreover, Pan T (CD3) highlighted reactive T-cells. These features rendered the diagnosis of DLBCL of testis. The hybrid 2-[fluorine-18] fluoro-2-deoxy-d-glucose (FDG) positron emission tomography/computed tomography (PET/CT) demonstrated two para-aortic FDG avid lymph nodes on the left side at the level of L2 vertebra. Presently, the patient has been planned for doxorubicin-based chemotherapy (i.e., cyclophosphamide, doxorubicin, vincristine and prednisone; CHOP) along with intrathecal Methotrexate (MTX), which would presumably improve the prognosis. Our study would expand the pool of this uncommon tumor towards its better understanding.

2. Case report

A 47 years old male presented with three month history of left testicular swelling. No B-symptoms were present. The patients underwent unilateral (left) orchiectomy. Histopathology revealed extensive involvement and replacement of testicular parenchyma by a tumor composed of large discohesive sheets of cells with pleomorphic, hyperchromatic nuclei and prominent nucleoli. Necrotic foci were also identified. Immunohistochemical (IHC) staining showed the following reactivity pattern in tumor cells: positivity for LCA & Pan B (CD20) and negativity for OCT 3/4, SALL4 and Inhibin. Moreover, Pan T (CD3) highlighted reactive T-cells. All these features rendered the diagnosis of DLBCL according to WHO classification of lymphoid neoplasms (see Fig. 1 and Table 1).

To accurately assess the disease extension and evaluate the stage, FDG PET/CT was performed which demonstrated two para-aortic FDG avid lymph nodes on the left side at the level of L2 ver-
The range of maximum standardized uptake value (SUVmax) was up to 9.79 and size of 1.1 x 1.5 cm along the left external iliac vessel. FDG avid lymph nodes were also seen with SUVmax ranges up to 5.65 and subcentimeter in size. Faint FDG uptake was seen along the surgical tract, possibly because of post-surgical changes. Soft tissue density lesion was seen in the upper part of the scrotal sac with SUV ranging up to 5.98 and subcentimeter in size.

The Eastern Cooperative Oncology Group (ECOG) performance status for the patient was zero, serum lactate dehydrogenase (LDH) was elevated (303 U/L) and international prognostic index (IPI) score was zero, signifying the low risk of the disease. Consequently, the clinical stage of the disease was Stage IIAE.

3. Discussion

Primary testicular DLBCL is a rare neoplasm with typical manifestation in the older age. This study documents the first case of primary testicular DLBCL from Pakistan, as part of the centralized registry program for uncommon tumors project, a recent but fast spreading project focused at the comprehensive study (and database) of rare tumors in Pakistan [13–15]. Primary testicular DLBCL are usually related to high morbidity and mortality rates. The clinical presentation of primary testicular DLBCL includes swelling of testis, B-symptoms (i.e., fever, night sweats and weight loss) and elevated LDH levels [4]. Typically, these tumors are characterized by a high risk to disseminate to the CNS, thereby warranting routine CNS prophylaxis with chemo- or radio-therapy [3,8].

Imaging of tumor metabolism with FDG PET/CT for the initial staging, follow up, treatment response monitoring and assessment of disease relapse in lymphomas has become a valuable molecular technique [9–12]. Indeed, PET has been recommended for evaluating the initial staging of patients presented with DLBCL [16], as carried out in this study. Specifically, two para-aortic FDG avid lymph nodes exhibiting SUVmax of up to 9.79 and size of 1.1 x 1.5 cm were seen, which rendered the clinical stage to IIAE. Moreover, the intensity of FDG uptake, and consequently SUVmax values, in lymphoma patients is a multifactorial process, comprising of histologic type, grade, tumor proliferative index, upregulation of glucose metabolism, the presence of hypoxia, etc. [16]. For instances, several studies have shown that high-grade lymphomas (e.g., DLBCL) are more FDG avid (i.e., threefold higher SUV) than are low-grade lymphomas [16,17].

Our patient presented with three months history of left testis swelling, and underwent unilateral (left) radical orchiectomy for both diagnostic and therapeutic purposes [6,18,19]. Indeed, radical orchiectomy appears the primary intervention to achieve favorable outcomes of the treatment [18]. However, orchiectomy alone should not be considered as the sole treatment of DLBCL, as indicated by several studies. Specifically, patients treated with orchiectomy alone would mostly experience disease relapse within two years; 5–35% in the contralateral testis [20]. Additionally, relapses to distant extranodal sites, particularly to CNS, also remains a major therapeutic challenge [3,8]. In this context, we have planned doxorubicin-based chemotherapy for our patient. In particular, six courses of cyclophosphamide (750 mg/m²), doxorubicin (50 mg/m²), vincristine (1.4 mg/m²) and prednisone (100 mg/m²) (CHOP) along with intrathecal Methotrexate (MTX; 12 mg) have been planned on day one with three weeks interval, which would presumably improve the prognosis [21]. Importantly, the patient is non-affording for rituximab.

4. Conclusion

We presented an uncommon but aggressive case of primary testicular diffuse large-B cell lymphoma (DLBCL), whose diagnostic work-up was carried out with surgery and FDG PET/CT. Specifically, histopathology findings from the tissue samples obtained from unilateral (left) radical orchiectomy rendered DLBCL of testis.
Thereafter, PET/CT demonstrated two FDG avid lymph nodes in the para-aortic region. Presently, the patient has been planned for doxorubicin-based chemotherapy (i.e., cyclophosphamide, doxorubicin, vincristine and prednisone: CHOP) along with intrathecal Methoxate (MTX), which would presumably improve the prognosis. Our study demonstrated that DLBCL of testis is a rare disease where PET/CT plays an important role towards the assessment of local or distal spread of the disease.

Fig. 2. Illustrative FDG PET/CT image demonstrating two para-aortic FDG avid lymph nodes on the left side at the level of L2 vertebra, as indicated by the yellow arrow.