Primary testicular lymphoma: Two case reports and review of the literature

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Introduction

Primary testicular lymphoma (PTL) is an extranodal lymphoma in which primary origin is testis, and it accounts only 1-2% of all non-Hodgkin lymphomas (NHL) and 1-9% of all testis tumors (1, 2). Most of the patients are above 60 years (3) and PTL is the most commonly seen neoplasm in this age group (4).

Most common clinical symptom is unilateral and rapid onset painless swelling of the testis (2). On physical examination, whole testis is palpated as a hard mass according to the volume of the mass or tumor. If there is no hydrocele, painless, rapidly growing mass without fluctuation anticipates it in elderly patient. It is known as the most commonly seen bilateral testis tumor (5).

Initial investigation of a patient with testicular mass should include tumor markers. The tests which should be requested are beta human chorionic gonadotrophin (HCG), alpha-fetoprotein (AFP), gamma-glutamyl transferase (GGT) and lactate dehydrogenase (LDH). In PTL patients the results of those tests are mostly normal and the markers are negative. In a subgroup of patients, LDH levels may show slight increase. In rare lymphoma types AFP and HCG may also increase (6). An increased sedimentation rate may be present.

Scrotal ultrasonography (USG), does not give specific findings but can give leading findings about the mass (7). In most of the patients, hypoechoic heterogenity is observed in accordance with the dimensions of the tumor (8). Besides, accompanying reactive hydrocele is found in 40% of the patients (2). When examining and staging a metastatic disease, special investigations like cerebrospinal fluid examination (CSF), bone biopsy, skin biopsy, computed tomography (CT) or positron emission tomography (PET) are requested.

Lymphomas are originated by B cells in 90%. At the beginning of the 20th century, Hodgkin lymphoma (HL), one of the B cell originated lymphoma, was distinguished from non-Hodgkin lymphoma with the recognition of Reed-Sternberg cells (9). World Health Organization (WHO), classifies the HL into 2 separate biologic and clinical antity as nodular lymphocyte predominant HL and classical HL. For classical HL four subtype has been mentioned as nodular sclerosing, lymphocyte rich, lymphocyte depleted and mixed cellularity subtype (10). In this classification, NHL is divided into four subtypes as precursor B-cell, mature B-cell, precursor T-cell and mature T-cell.

In International Working Formulation (IWF) as reflecting biological aggressiveness, NHL is divided into low, middle and high grade; the border within these categories are artificial. Low grade lymphomas are characterized by small dimensional cell with round or jagged nucleus and low mitosis rate; middle/high grade HL are characterized by large dimensional cell, prominent nucleolus and high grade mitotic index (11). Diffuse large B-cell lymphoma (DLBCL) accounts 80-90% of all primary adult testis tumors (12).

From both clinical and pathological perspective, seminomas, embryonal carcinoma, granulamatous or viral orchitis should also be considered.

Discussion

PTL mostly presented as testicular mass in elderly men. Approximately 25% of the patients had fever (> 38 C), night sweeting, weight loss (more than 10% in last six months). The symptomatic patients were classified according to Ann Arbor grading as B. The patients without any symptom are classified in A subtype and the patients with symptoms in group B. For example, both of our patients did not have those symptoms and were classified as EIEA and EIVA. At the time of diagnosis, the central nervous system (CNS) is involved in 10%. Initial treatment is radical inguinal orchiectomy. Testicular NHL patients should be referred to hematology and oncology centers for staging and follow up. Most of the patients have localized tumor to the testis (Stage 1 or 2) (13). In a series these rates were 60% for stage I and 30% for stage II (14). In a second study 7 patients out of 12 (58%) were stage I and II (Ann Arbor) and the remaining five patients (42)% were stage III and IV (15).

No conflict of interest declared.

In a third study with 27 patients, 24 patients were reported in early stage (Stage I:17, Stage II:7) (16). We classified our patients as stage I and stage IV.

Painless enlargement of the testis is the most commonly seen symptom as seen in other testis tumors (15, 17, 18). Presenting signs of our patients were different. In our first case painless swelling, in the second one weakness, fatigue and back pain were the initial symptoms followed by recognition of the swelling at the testis.

Fever, night sweating and weight loss are rarely seen and they are accompanied with the aggressive form of the lymphoma (16). In our two patients we do not encounter these symptoms although they are described in 25-40% of patients (19).

On physical examination, mostly non-sensitive, hard mass indistinguishable from testis was identified. Scrotal ultrasonography (USG) is very helpful in the diagnosis. Normal testis tissue texture is homogeneous hyperechoic whereas lymphoma involvement is hypoechoic. At USG, lobulated structures with defined borders are visible. Granulomatous orchitis, pseudolymphoma, plasmacytoma and rhabdomyosarcoma are some of the other pathologies that mimic the testicular lymphoma. In some reports, previous trauma, chronic orchitis, undescended testis and filiariasis of the spermatic cord are considered as predisposing risk factors (7). There was none of these predisposing factor in our cases.

In the patients with AIDS, primary testis lymphoma is reported as an initial sign of the disease. These patients are generally seen in earlier ages; their lymphoma mostly have aggressive histological appearance and is related with worse prognosis (20). Lymphoma may invade locally epididymis, spermatic cord and scrotum skin. At the time of diagnosis or during disease process extranodal metastasis may occur. Most frequently central nervous system (CNS), Waldeyer ring, skin and lung may be involved and more rarely prostate, kidney, liver, bone marrow, pleura and bone. High stage tumors tend to invade the extranodal sites like CNS, skin, Waldeyer ring and lungs. Stage and histologic grades are the most important factors that determine the prognosis (21, 22). The reported series showed that B cell type is dominant and major lymphoma subtype is DLBCL22. Pathologic diagnoses of our patients were B cell lymphoma with DLBCL subtype.

Primary testicular lymphoma is more frequently seen in elderly and it is a potential life threatening disease. In early stages (I and II) chemotheraphy and profilactic scrotal or iliac and/or paraaortic lymph node radiotreatment is done as theraphy after orchiectomy. When all stages are considered 5 year survival rate is 12% (13). One of our patients was stage IV and after 6 doses of chemotheraphy following the orchiectomy there was regression both in bone involvement and intraabdominal lymph nodes.

There was no CNS involvement and relapse during the treatment or in follow up. We did not apply intrathecal treatment.

In conclusion, as PTL is a rare disease, there is lack of data that can guide the treatment. However with the aid of retrospective data evaluation, better prognosis was obtained for nodal lymphoma. Despite the improvements in local and systemic disease central nervous system (CNS) relapse remains the worst complication.. Strategies that may decrease the risk of PTL patients will end up with better prognosis.

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