Primary testicular lymphoma with cardiac involvement in an immunocompetent patient: case report and a concise review of literature

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Abstract

Primary testicular lymphoma (PTL) is a rare testicular tumor representing less than 9% of all testicular cancers. PTL usually tends to spread to or relapse at nodal structures or extranodal sites such as contralateral testes, central nervous system, skin, lung, pleura, Waldeyer’s ring and soft tissues. We present a case of PTL with huge left atrial mass, an extremely unusual site of involvement. Early disease usually carries a good prognosis, whereas advanced stage carries an extremely poor prognosis. Herein, we report the complete remission to date in a patient with advanced stage PTL with huge left atrial mass, treated with systemic rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone and intrathecal methotrexate. A brief review of literature focusing on various aspects of management of primary testicular lymphoma and lymphomatous involvement of heart is also discussed.

Introduction

Primary testicular lymphoma (PTL) is a rare disease representing 1-2% of all non-Hodgkin lymphomas and less than 9% of all testicular cancers.1,2 Unlike other testicular cancers, PTL occurs mainly in patients aged over 50 and in fact 85% of all PTLs are diagnosed in patients over the age of 60.3 Most patients present with localized disease (stage I or II).4 However, PTL has a tendency to disseminate at other extra-nodal sites such as contralateral testes, central nervous system, skin, lung, pleura, Waldeyer’s ring and soft tissues.5 Involvement of Waldeyer’s ring is enigmatic. This may be because of a common embryonic origin, since both the testis and the oropharynx and nasopharynx are derived from the endoderm.6 Involvement of these sites may occur either concurrently at presentation or subsequently at relapse.

Lymphomatous involvement of heart is a rare phenomenon and has been documented in only 10-25% of autopsy cases.7 Ante-mortem diagnosis is often challenging, as signs and symptoms are very subtle and non-specific.8 However, presence of a cardiac tumor can be potentially life threatening owing to its location.

We present a rare case of PTL with left atrial mass in an immunocompetent male, which responded to chemotherapy resulting in complete remission. To the best of our knowledge, this is the first reported case of ante-mortem diagnosis of PTL with cardiac involvement in an immunocompetent male.

Case Report

A 67 year old male presented to our hospital with painless enlargement of left testicle, lower abdominal pain, urinary frequency, fever and a 9 kg weight loss over 2 months. His medical history was significant for dyslipidemia and hypertension. There were no solid or hematological cancers in his family history. Physical examination was significant for a firm, enlarged left testicle and suprapubic mass measuring about 3 cm. The remainder of the physical exam was unremarkable. Initial laboratory data revealed mild anemia with hemoglobin of 10.2 g/dL, platelet count of 1.19×10^9/L, and a lactate dehydrogenase (LDH) of 369 U/L. Given the concerns for a malignancy, he underwent computed tomography (CT) scan of chest, abdomen and pelvis. Imaging revealed a nodular mass above the urinary bladder measuring 8.6×4 cm and surprisingly a left atrial mass measuring 5.7×2.9 cm. A 2D echocardiogram showed a very large mobile mass measuring 78 mm in the left atrium prolapsing through mitral valve and creating a degree of functional mitral stenosis.

A CT guided biopsy performed on the most accessible site-suprapubic mass, revealed a diffuse large B cell lymphoma (Figure 1). Flow cytometric analysis revealed a kappa light chain restricted B-cell population that was positive for CD19. It showed weak expression of CD20 and revealed a usual male chromosome karyotype.

For staging purposes, a bone marrow biopsy and lumbar puncture was performed which showed no lymphomatous involvement. Positron emission tomography–CT (PET-CT) showed hypermetabolic activity in suprapubic area, left atrium and left testes (Figure 2). A diagnosis of stage IV testicular lymphoma was made, given the presence of testicular mass, locoregional nodal involvement (suprapubic mass) and distant extranodal site involvement (infracardiac mass).

His international prognostic index score was calculated to 4 (age greater than 60, high LDH, more than 1 extranodal site involvement, Ann Arbor stage IV and an ECOG performance status of 1). During the hospital stay, the patient had multiple episodes of symptomatic hypotension, thought to be secondary to infracardiac mass. Given the symptomatic nature of the disease, patient was started on chemotherapy on an urgent basis. He was commenced on systemic rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) and prophylactic intrathecal methotrexate. A repeat PET-CT done after 2 cycles showed near complete metabolic response to treatment (Figure 3). He completed a total of 6 cycles of R-CHOP and 4 cycles of prophylactic intrathecal methotrexate. An echocardiogram at the end of the treatment revealed complete resolution of the left atrial mass.

Discussion

The incidence of PTL is rising. When compared to nodal DLBCL, testicular DLBCL patients have a better overall prognosis, but are at higher risk of late disease-related deaths.9

Diagnosis and staging of primary testicular lymphoma

As in all scenarios with any suspected tumor in the testes, the primary option remains surgery, i.e., inguinal orchietomy for diagnosis and treatment. Orchietomy removes the tumor located in a sanctuary site with good local control, and provides important information on grade and pathology subtype.10 Histologically, 80-90% of primary testicular lymphomas are diffuse large-cell type with B-cell immunophenotype.1 Complete initial staging workup is the same as for all other non-Hodgkin’s lymphomas. It includes a complete
physical examination, complete hematological and biochemical exams, total-body computerized tomography, and bone marrow aspirate and biopsy. Cerebrospinal fluid examination for malignant cells is recommended in view of the high incidence of central nervous system relapse. PET-CT has been widely used in initial lymphoma staging, but few data are available on primary testicular lymphoma.13

**Treatment of primary testicular lymphoma**

Given the rarity of the tumor, there have been no standardized treatment regimens. Most trials are retrospective analyses from single institutions or by international collaborative groups.5,14 To date there has been only one prospective trial in PTL, which addresses safety and efficacy of a combined treatment strategy.13 Treatment of PTL depends on stage at time of diagnosis and differs for early disease (stage I, II) as opposed to advanced disease (stage III, IV).

For early disease, there seems to be a consensus on using standard orchiectomy, followed by anthracycline based regimen and locoregional use of radiation.14-16 Literature regarding use of rituximab is conflicting. Gundrum et al., used Surveillance, Epidemiology and End Results (SEER) database and concluded that introduction of rituximab in clinical practice did not improve early outcomes in testicular DLBCL. However, Coiffier et al., in a randomized study showed improved outcomes with R-CHOP regimen as compared to CHOP alone for DLBCL.17 Vitolo et al., in a recent and only prospective trial on PTL showed R-CHOP, intrathecal methotrexate and testicular radiotherapy to be associated with good outcomes in patients in early stage PTL.15 The prophylactic use of intrathecal chemotherapy remains controversial, given that most of CNS relapse occurs in parenchymal tissue than in leptomeninges and patients who received intrathecal therapy still experienced CNS relapses.15-18

For advanced disease, there seems to be no consensus regarding treatment regimen in literature. Some authors suggest that it should be treated as advanced DLBCL. However, one must be careful in extrapolating DLBCL data for advanced PTL given very different disease clinical features, patterns of relapses and prognosis implying different tumor biology.16,19 A recent study by Mazloom et al., suggested advanced stage as one of the poor prognostic factors for PTL.20 This warrants more investigation and possible consensus treatment regimen of this rare but aggressive tumor.

**Cardiac lymphoma**

Lymphomatous involvement of heart is a rare phenomenon and is commonly observed in immunocompromised patients such as HIV/AIDS or following bone marrow or solid organ transplantation.21-22 Systemic chemotherapy appears to be effective, albeit available literature is purely retrospective in nature.23-22 Radiation therapy poses a risk of cardiomyopathy, radiation pericarditis, coronary artery disease.23 Complete cardiac lymphoma resection by surgery is very difficult. Surgery should be reserved primarily for diagnostic purposes in cases where less invasive procedures are inconclusive.23 However, a curative surgical approach is discouraged.24 Surgical resection of tumor may be considered only on a case by case basis.25 For the case in discussion, surgical approach was considered but not pursued, as the patient responded very promptly to systemic chemotherapy.

This case report illustrates a rare presentation of advanced stage PTL with cardiac involvement. It was presumed that the malignancy was of testicular origin with cardiac involvement and not the other way around because distant metastases of primary cardiac lymphoma have never been reported in the literature. However, distal embolization can occur in primary cardiac lymphoma.26-27 Various autopsy series have shown
that cardiac involvement of disseminated lymphoma is common, with incidence between 9% and 24%. Although no direct tissue diagnosis of cardiac mass was made, it seemed appropriate to assume cardiac mass to be of lymphomatous origin given high uptake on PET scan, concurrent testicular mass and complete response to systemic chemotherapy.

Conclusions

In summary, we report the complete remission to date in a patient with advanced stage PTL with cardiac involvement following systemic R-CHOP and intrathecal methotrexate. We also highlight the paucity of data and need for future directions in advanced stage PTL as well as cardiac lymphoma.

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