Leukemia and Lymphoma

Testicular relapse of primary central nervous system lymphoma

To cite this Article: Rajappa, Senthil J., Uppin, Shantiveer G. and Digumarti, Raghunadharao, "Testicular relapse of primary central nervous system lymphoma", Leukemia and Lymphoma, 48:5, 1023 - 1025

To link to this article: DOI: 10.1080/10428190701200042
URL: http://dx.doi.org/10.1080/10428190701200042
LETTER TO THE EDITOR

Testicular relapse of primary central nervous system lymphoma

SENTHIL J. RAJAPPA1, SHANTIVEER G. UPPIN2, & RAGHUNADHARAO DIGUMARTI1

1Department of Medical Oncology and 2Department of Pathology, Nizam’s Institute of Medical Sciences, Punjagutta, Hyderabad, India

Received 22 December 2006; accepted 5 January 2007

Primary central nervous system lymphoma (PCNSL) is a rare form of extra-nodal non-Hodgkin’s lymphoma (NHL), which involves the brain, spinal cord, meninges, and eye [1]. The mean age of patients with PCNSL is 60 years. It is usually a diffuse large B-cell lymphoma (DLBCL). Multiagent chemotherapy with methotrexate with or without radiotherapy is the treatment of choice. Most patients experience a relapse or progression of their tumor. Systemic relapse is rare [2,3]. We report a case of PCNSL who had a testicular and local relapse.

A 48-year-old man presented with headache, vomiting, and generalized clonic tonic seizures of 15 days in December 2003. The clinical exam was unremarkable except for papilledema of the right eye. He was evaluated with a contrast-enhanced magnetic resonance imaging (MRI), which showed a solitary lesion in the right fronto-parietal area [Figure 1(a)]. He underwent a near total excision of the mass. The histopathology and immunohistochemistry revealed a diagnosis of diffuse large B-cell non-Hodgkin’s lymphoma [Figure 1(b)]. Serology for human immunodeficiency virus (HIV) was negative. The staging work-up including a contrast enhanced computed tomography (CT) scan of the chest and abdomen, bone marrow biopsy, and an ultrasound of the testes were normal. The slit lamp examination of the eyes and cerebrospinal fluid (CSF) analysis were negative for involvement by lymphoma. A diagnosis of primary central nervous system lymphoma was made. He was treated with high dose methotrexate, intrathecal methotrexate, and steroids followed by radiotherapy and high dose cytosine arabinoside. A post-treatment scan showed complete response. He was on regular follow-up.

He presented three years later with complaints of right testicular swelling of 15 days. Examination revealed a hard right testicular mass with minimal hydrocele. The testicular ultrasound was suggestive of a right testicular tumor. The left testis was normal. The neurological exam was unremarkable. An MRI of the brain showed local recurrence of the tumor [Figure 1(c)]. A restaging revealed no evidence of disease elsewhere. The beta human chorionic gonadotropin (HCG), alfa-feto protein (AFP), and lactate dehydrogenase (LDH) were within normal limits. He underwent a high inguinal orchiectomy. The histopathology and immunohistochemistry showed features of DLBCL similar to the one diagnosed from the brain in 2003 [Figure 1(d)].

PCNSL represents 4% of all primary brain tumors [4]. Although PCNSL in immunocompetant patients is potentially curable, long-term remissions are achieved in only a small fraction of patients. Methotrexate based combined-modality therapy results in a 2-year survival of 43–73% [1]. Most patients invariably relapse in the central nervous system. Systemic relapse of PCNSL is rare and ranges between 5–7% [2,3]. The reported sites of systemic relapse include breast, liver, spleen, orbit, lymph nodes, and subcutaneous tissue. Autopsy series report a 7–8% incidence, most of which are occult during life [5]. There is only one report of a simultaneous local and testicular relapse of PCNSL preceding this [6].

The International PCNSL collaborative group has published standard guidelines for evaluation of patients with PCNSL [7]. At diagnosis, all patients should have a contrast enhanced MRI of the brain, CSF, and ocular slit lamp examination. As
3.9–12.5% [8,9] of patients with PCNSL can have occult extra-neural involvement, the work up should include a contrast enhanced CT scan of the chest, abdomen, and pelvis and a bone marrow biopsy. Although positron emission tomography scan is useful in the staging of lymphomas, its role in evaluation of extra neural disease in PCNSL is yet to be defined [1]. Clinical and ultrasound examination of the testes should be considered for elderly patients with PCNSL [7].

Primary testicular lymphoma is a rare disease and represents 1–2% of all patients with NHL [10]. Both at diagnosis and at relapse, it has the propensity to involve unusual sites like the CNS, lung, pleura, Waldeyer’s ring, and skin [10]. The estimated 5- and 10-year risk of CNS relapses are 19% and 34%, respectively [11]. CNS prophylaxis is recommended for all patients with testicular lymphoma.

Although the clinical scenario of a PCNSL with testicular relapse is most probable, an occult primary testicular lymphoma with central nervous system disease at diagnosis cannot be ruled out. However, the likelihood of this being a testicular primary is highly improbable as the clinical examination and ultrasound of the testis was normal at diagnosis. Moreover, in the absence of local therapy, it is less likely that a testicular focus could have been under control as a result of the chemotherapy administered for treatment of the central nervous system disease 3 years ago.

The exact reason for the increased incidence of extra nodal relapse of testicular lymphomas, especially in the CNS, continues to be elusive [11]. PCNSL and testicular lymphomas have distinct immunologic features. About 61% of testicular and 46% of PCNSLs do not express major histocompatibility type II (MHC II) antigens compared with 5% of nodal lymphomas [12]. Lack of expression of MHC class II proteins alters the ability of tumor cells to express tumor-associated antigens, hence evading immune responses in immune-privileged sites. Other proposed explanations include unique pattern of expression of adhesion molecules resulting in poor adhesion to extra cellular matrix and poor penetration of chemotherapy in both the CNS and testis [13,14]. However, the exact differences in biology between testicular lymphomas and PCNSL remain to be defined.

This the second instance in the literature that a simultaneous relapse of PCNSL locally in the CNS

![Figure 1](https://example.com/figure1.png)

Figure 1. (a) MRI contrast image shows lobulated enhancing lesion with perilesional edema involving the right fronto-parietal area. (b) H&E stain showing diffuse replacement by small round cells with hyperchromatic nuclei and scant cytoplasm (magnification ×100). (c) MRI contrast shows irregular enhancing lesion with peripheral enhancement involving the right para-sagittal fronto-parietal area. (d) H&E stain showing diffuse replacement by small round cells similar to the brain lesion (magnification ×100).
and in the testis is being reported. The outcome for these patients continues to be dismal. Hopefully, ongoing research to determine the differences in biology between the various lymphomas will lead to better treatment protocols and improved outcomes.

References