

An Atypical Ocular Presentation of Multifocal Extranodal Non Hodgkin's Lymphoma: A Case Report

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Abstract

Non-Hodgkin's lymphoma (NHL) is a diverse group of neoplasms both in their natural history and response to treatment. NHL mostly arises in the lymph nodes and is known as nodal-NHL (N-NHL) but can arise in other tissues where it is known as extranodal NHL (EN-NHL). The exact definition of extranodal NHL is debatable. Here, we present an unusual case of EN-NHL presenting at an advanced stage with synchronous involvement of eye and larynx due to late diagnosis resulting from unusual presentation.

Keywords: Non Hodgkin's lymphoma; Multifocal; Extra nodal; T-cell lymphoma; Ocular adenexa

Introduction

Non-Hodgkin's lymphoma (NHL) is a diverse group of neoplasms both in their natural history and response to treatment. NHL mostly arise in the lymph nodes termed as nodal NHL (N-NHL), but approximately 25-40% arise in tissues other than the lymph node, and therefore termed extra nodal lymphomas (EN-NHL) [1]. The definition of EN-NHL is controversial especially in patients where both nodal and extra nodal sites are involved [2]. Some series on primary EN-NHL have included patients with only localized disease while studies with liberal criteria included patients with disseminated disease. The common extranodal sites involved are gastrointestinal tract, upper aerodigestive tract, bones, and spine while unusual sites with involvement less than 3% are breast, central nervous system, testis, lung and skin [3]. Here we report a case of EN-NHL presenting at an advanced stage with synchronous involvement of right ocular adnexa and larynx due to late diagnosis resulting from unusual presentation.

Case Report

A twenty three years old male presented with foreign body sensation in right eye with increased lacrimation, progressive shortness of breath, pain during swallowing solids, weight loss, hoarseness of voice, and intermittent restlessness with palpitation. There was no history of night sweats, cough, fever, hemoptysis or injury to conjunctiva. On ocular examination, a diffuse salmon pink colored swelling was seen inferio-medially to limbus. Vision, intraocular pressure, fundal findings and pupillary reactions were within normal limits bilaterally. Ocular movements were full and symmetrical in both eyes. On further examination, a large smooth rounded mass was seen in left supraglottic larynx. No lymph nodes were palpable in neck. Computed tomography scan of face and neck showed soft tissue growth with smooth margins in supraglottis. Computed tomography scan of thorax, abdomen and pelvis revealed right pleural effusion with multiple soft tissue densities within the pleural fluid. There was loss of volume in right lower lobe and areas of atelectasis in the middle lobe. A heterogenous soft tissue mass was seen anteriorly at the interface of right lung and the pericardial surface extending into the retrosternal soft tissue fat within the mediastinum causing the displacement of heart to the left and posteriorly. Smaller satellite lesions were seen at the periphery of the mass within the anterior mediastinum. Mild pericardial effusion was present. Left lung showed small, nodular and atelectatic lesions at the base adjacent to diaphragmatic surface. There was no pleural effusion on left

side (Figure 1). Findings in abdomen and pelvis were normal except for the presence of few subcentimeter nodes in retroperitoneum and mesentery. Histopathological examination of excisional biopsy from laryngeal lesion (Figure 2) and incisional biopsy from ocular lesion was suggestive of high grade Non-Hodgkin's lymphoma (Figure 5). The immunohistochemistry of the specimen showed that the tumor cells were immunopositive for CD3 and immunonegative for CD20, CD15 and CD30 which was consistent with T-cell NHL. Bilateral bone marrow biopsy showed lymphoid hyperplasia. Lumbar puncture was done to rule out central nervous system involvement which turned out to be negative. His complete blood counts as well as the routine laboratory chemistries were normal. Serum lactic dehydrogenase was 570U/L (normal value 230-460 U/L). Polymerase chain reaction was negative for Epstein - Barr virus (EBV) and Human herpes virus-6 (HHV-6). A diagnosis of stage IV T-cell NHL was made. According to International prognostic index, the patient was among high risk group with a score of four. Keeping in consideration multifocal presentation of disease, patient was given cyclophosphamide, doxorubicin, vincristine



Figure 1: Contrast enhanced computed tomography of thorax showing right sided pleural effusion, anterior mediastinal mass with left and posterior displacement of heart.

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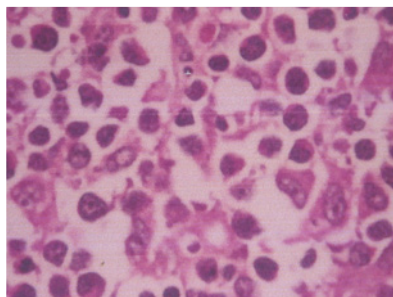


Figure 2: Photomicrograph of histopathological analysis of excisional biopsy specimen from larynx showing large atypical lymphoid cells with nuclei having prominent nucleoli suggestive of NHL. H&E stain, 100 X magnification.

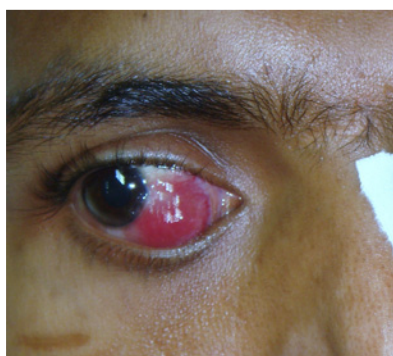


Figure 3: Ocular lesion at presentation showing a diffuse salmon pink colored swelling seen infero-medially to limbus about 13.5 x 13 mm in size.



Figure 4: Ocular lesion after two cycles of combined regimen CHOP chemotherapy.

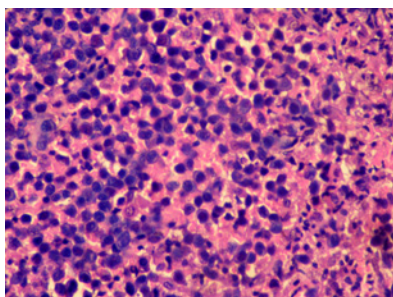


Figure 5: Photomicrograph of histopathological analysis of biopsy specimen from conjunctival lesion showing predominantly monomorphic atypical lymphoid cells with inconspicuous nucleoli. H&E stain, 40X magnification.

and prednisolone (CHOP) based chemotherapy. Initial response to the treatment was excellent. The size of conjunctival swelling present inferomedially to limbus in right eye (Figure 3) was significantly

reduced after two cycles of chemotherapy (Figure 4). Patient had subjective improvement in symptoms. Despite good initial response to chemotherapy, patient's general condition deteriorated after fourth cycle with hematological toxicities and liver function derangement. He was administered four cycles of chemotherapy but was not found fit for fifth chemotherapy. In spite of best supportive care, patient was not fit for next chemotherapy and there was increase in pleural and pericardial effusion with time. He succumbed to his disease six months after his diagnosis due to cardio-pulmonary arrest.

Discussion

NHL with primary laryngeal presentation is very rare. Few cases have been reported with localized laryngeal lymphoma [3,4]. The symptoms usually include dysphonia and progressive airway obstruction requiring tracheostomy. Laryngeal NHLs are usually of B-cell lineage. The patient reported here had high grade lymphoma of T-cell lineage. In a solitary laryngeal lymphoma, radiation therapy may be the sole therapeutic modality necessary to achieve an excellent prognosis. As far as ocular involvement of NHL is concerned it has been reported that not more than 1% of patients with NHL have evidence of orbital involvement including adnexae, extra-ocular muscles, eyelids, and/or the lacrimal glands [5]. Ocular NHL can be essential primary intraocular NHL, intraocular NHL with central nervous system involvement or as a manifestation of systemic NHL. NHL in eye can manifest as conjunctival mass, orbital mass, choroidal infiltration with secondary uveitis and infiltrative optic neuropathy. Conjunctiva involved by malignant lymphoid tumors can be mucosa associated lymphoid tissue type (MALT-type) or non-MALT type. Ocular inflammation is a common finding and presents a diagnostic challenge to clinicians. Differential diagnosis of the most common and important conjunctival lesions includes episcleritis, pterygium, pingecula, papilloma, kaposi's sarcoma, limbal dermoid, dermolipoma, lymphangioma, granuloma, amelanotic melanoma, amyloid, NHL eyelid and carcinoma. International Prognostic Index is used to assess prognosis of patients of NHL. Score is calculated as total of points where one point is assigned for each of the following risk factors: Age greater than 60 years; Stage III or IV disease; Elevated serum LDH; ECOG (Eastern Cooperative Oncology Group)/ Zubrod performance status of 2, 3, or 4; More than 1 extranodal site. The sum of the points allotted correlates with the following risk groups:

Low risk (0-1 points) - 5-year survival of 73%

Low-intermediate risk (2 points) - 5-year survival of 51%

High-intermediate risk (3 points) - 5-year survival of 43%

High risk (4-5 points) - 5-year survival of 26%

Patients with poor prognosis should be considered candidates for novel strategies. Treatment options for ocular NHL include radiotherapy, chemotherapy, excisional biopsy and cryotherapy. Intralesional use of interferon alpha has been attempted [6]. Immunotherapy includes anti-CD20 antibody, even with chemotherapy, and radio immunotherapy for patients with CD20 positive NHL. Conjunctival ocular adnexal lymphoma with nodal involvement has been shown to be associated with a worse prognosis. High-grade ocular adnexal lymphoma have significantly higher incidence of stage IV disease, higher LDH levels, and greater IPI or performance status scores compared with those with low-grade disease. For clinical application, however, prognostic factors as defined by the IPI must be combined with histologic classification for appropriate clinical decisions. Polymerase chain reaction (PCR) was negative for EBV and HHV-6. The result could be due to the fact that

the sensitivity of PCR is reduced 10 to 100-folds in routinely processed material as compared with fresh tissue [7]. Multifocal presentation and CD20 negative status of this patient made him a candidate for chemotherapy without immunotherapy. Despite excellent response in disease with chemotherapies, his general condition deteriorated and patient was not fit for further chemotherapy. He succumbed to his disease after four cycles of chemotherapy. Previous studies have shown that recurrence free survival rate for patients with localized low grade malignancy and disseminated intermediate grade NHL is better for EN-NHL than N-NHL but patients with disseminated high grade EN-NHL had the worst prognosis [8].

Conclusion

With increasing incidence of EN-NHL worldwide, it's important for clinicians to be aware and keep unusual sites of presentation in mind for timely diagnosis and treatment. Any delay in diagnosis has important implications on the morbidity and mortality of the condition especially in high grade lymphomas.

References

1. Zucca E, Roggero E, Bertoni F, Cavalli F (1997) Primary extranodal Non-Hodgkin's lymphomas, part 1: Gastrointestinal. *Ann Oncol* 8: 727-737.
2. Krol AD, le Cessie S, Snijder S, Kluin-Nelemans JC, Kluin PM, et al. (2003) Primary extranodal Non-Hodgkin's lymphoma (NHL): the impact of alternative definitions tested in the Comprehensive Cancer Centre West population-based NHL registry. *Ann Oncol* 14: 131-139.
3. Lal A, Bhurgri Y, Vaziri I, Rizvi NB, Sadaf A, et al. (2008) Extranodal Non-Hodgkin's lymphomas- a retrospective review of clinic-pathologic features and outcomes in comparison with nodal Non-Hodgkin's lymphoma. *Asian Pac J Cancer Prev* 9: 453-458.
4. Chen TK (1984) Localized laryngeal lymphoma. *J Surg Oncol* 26: 208-209.
5. Diebold J, Audouin J, Viry B, Ghandour C, Betti P, et al. (1990) Primary lymphoplasmacytic lymphoma of the larynx : a rare localization of MALT-type lymphoma. *Ann Otol Rhinol Laryngol* 99: 577-580.
6. Ishikawa D, Nakayama I, Azumi A, Inoue M (1999) A case of orbital lymphoproliferative lesion diagnosed as malignant lymphoma after recurring 11 years later. *Nippon Ganka Gakkai Zasshi* 103: 821-825.
7. Reid AH, Cunningham RE, Frizzera G, O'Leary TJ (1993) bcl-2 rearrangement in Hodgkin's disease. Results of polymerase chain reaction, flow cytometry, and sequencing on formalin-fixed, paraffin-embedded tissue. *Am J Pathol* 142: 395-402.
8. Blasi MA, Gherlinzoni F, Calvisi G, Sasso P, Tani M, Cellini M, et al. (2001) Local chemotherapy with interferon-alpha for conjunctival mucosa-associated lymphoid tissue lymphoma: a preliminary report. *Ophthalmology* 108: 559-562.