

Paranasal Sinus Lymphoma Presenting as an Orbital Mass

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Abstract

The paranasal sinuses are rare sites for origination of primary Non-Hodgkin's lymphoma (NHL). Most often, primary paranasal lymphomas are diffuse large B-cell lymphomas (DLBCL) associated with a poor prognosis. This paper describes an uncommon case of ethmoid sinus lymphoma with lateral displacement of the left orbit and involvement of the nasal vault, skull base, and frontal sinuses. Excisional biopsy and flow cytometry findings favored the diagnosis of DLBCL, non-germinal center type. Moreover, CT showed an epigastric mass and enlarged lymph nodes along the left iliac chain and spleen. Radiation therapy was immediately started and the patient achieved significant symptomatic relief after four treatments. Accurate diagnosis of extranodal NHL lymphomas through a thorough history, physical exam, imaging, and immunopathology is necessary to initiate prompt treatment of this rare, aggressive disease.

Keywords: Non-Hodgkin's lymphoma; Diffuse large B-cell; Extranodal; Ethmoid sinus; R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)

Introduction

Primary sinonasal lymphomas are rare manifestations of extranodal Non-Hodgkin lymphomas (NHL) and constitute only 2% of all primary extranodal NHL [1]. Moreover, diffuse large B-cell lymphoma (DLBCL) is the most prevalent subtype of NHL in the paranasal sinuses and is associated with poor prognosis [2]. Paranasal lymphoma can be challenging to diagnose as symptoms are often non-specific and have variable presentation. The subsequent delay in treatment may affect prognosis, thus timely diagnosis and initiation of therapy are of utmost importance. In this report we describe an unusual case of primary paranasal DLBCL with local invasion to surrounding tissues.

Case Report

A 52-year-old male was initially evaluated for gradual enlargement of a left face mass of one-year duration. He presented to the emergency department with complaints of pain and swelling of left side of his face, eventually the mass covered his left face and forced his left eye closed. The patient reported a one-month history of anosmia and hypogeusia, but denied associated nasal symptoms and weight loss. Physical exam revealed a large mass with erythematous periorbital swelling. The patient was admitted and evaluated by an ear, nose, and throat specialist. Maxillofacial computed tomography (CT) (Figure 1) and magnetic resonance imaging (MRI) (Figure 2) of the brain revealed an invasive 7 × 8 × 4.3 cm mass displacing the left orbit laterally and penetrating the medial right orbit. The left optic nerve and all left extraocular muscles appeared stretched. The nasal vault, skull base, and bilateral frontal sinuses were involved but the central nervous system was spared. A biopsy was performed via left endoscopic partial ethmoidectomy that showed large, atypical lymphocytes with mitotic figures (Figure 3). Additionally, flow cytometry revealed CD20 positive CD10 negative cells and BCL-2 was positive with variable BCL-6 positivity (Figure 4). These findings were consistent with malignant Non-Hodgkin's large B cell lymphoma, non-germinal center type.

A computerized tomography (CT) scan of the chest, abdomen, and pelvis revealed a 4.6 × 3 cm soft tissue mass situated against the greater curvature of the stomach, several enlarged lymph nodes along the left iliac chain and left groin, and multiple perisplenic nodes up to 12 mm

diameter. A positron emission tomography-computed tomography (PET/CT) showed metastatic involving the left orbit, maxillary sinus, and maxilla. Radiation therapy was initiated immediately. Clinical improvement was noted after four doses of radiotherapy to the orbital region. Upon completion of the course, the patient had regained vision and no palpable disease remained. The patient was subsequently evaluated by medical oncology for systemic chemotherapy with R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone).

Discussion

In Western countries, the most common type of Non-Hodgkin's lymphoma is diffuse large B-cell lymphoma (DLBCL) with 25-33% having a primary extranodal origin [2]. Lymphomas of the nasal cavity and paranasal sinuses, however, are uncommon and only constitute approximately 1% of NHL cases in North America [3]. DLBCL claims male predominance, and incidence varies both with ethnicity and increased age [4]. Pathogenesis is complex, and can occur de novo from a mature B cell or arise from transformation of other low grade B cell lymphomas. DLBCL is a heterogeneous group of tumors that typically completely efface normal lymph node architecture with enlarged, atypical lymphoid cells [5]. Diagnosis can be made using excisional tissue biopsy, and pathologically by morphology and immunophenotyping. DLBCL most often express the pan B cell markers CD19, CD20, and CD45. BCL-2, BCL-6, CD10, and MUM1/IRF4 are also commonly expressed antigens [6].

The maxillary sinuses are the most frequently involved site for sinonasal lymphomas and ethmoid sinus involvement is much less

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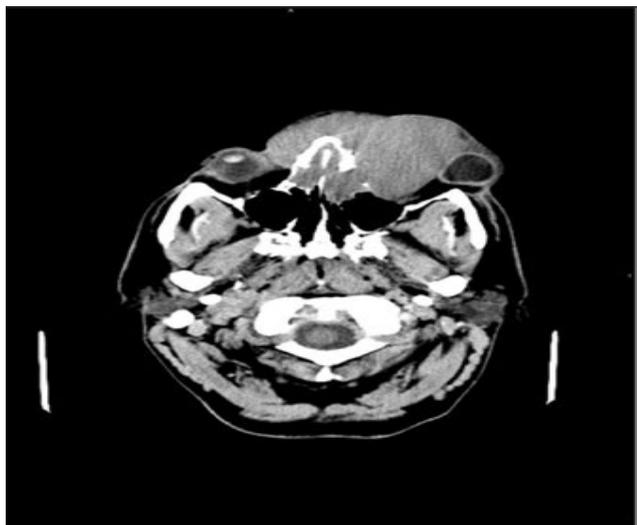


Figure 1: Maxillofacial CT without contrast. Large destructive soft tissue mass centered in region of the left anterior ethmoid air cells where it fills the ethmoid and both frontal sinuses. The mass markedly deforms and displaces the left globe anterolaterally.

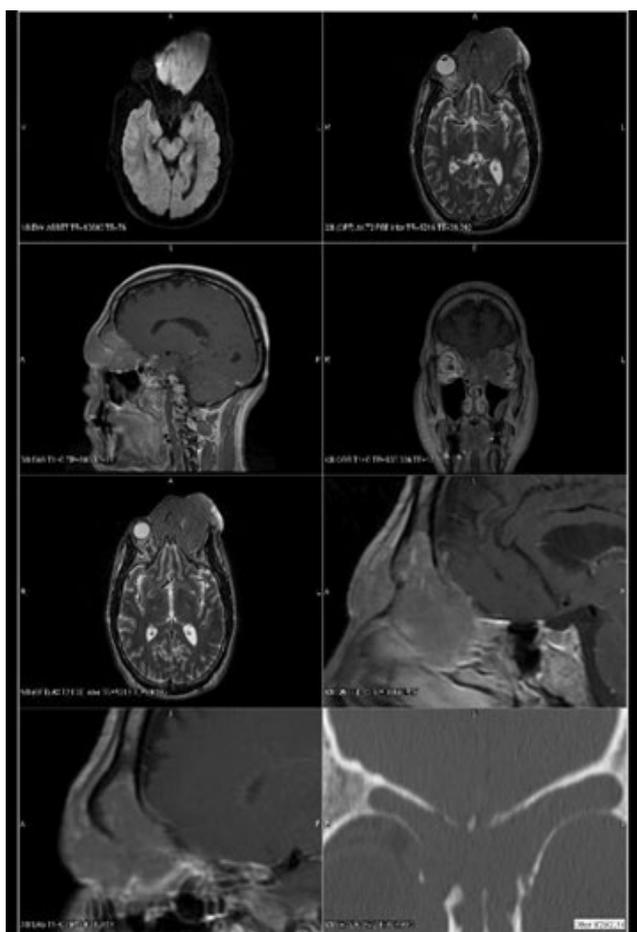


Figure 2: Maxillofacial CT without contrast. Large destructive soft tissue mass centered in region of the left anterior ethmoid air cells where it fills the ethmoid and both frontal sinuses. The mass markedly deforms and displaces the left globe anterolaterally.

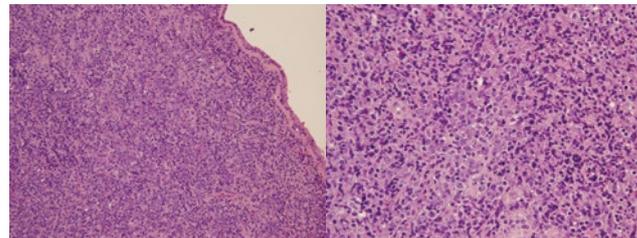


Figure 3: A) H&E staining at 10X shows respiratory epithelium with sheets of irregular lymphocytes with mitotic figures and destruction of normal architecture consistent with lymphoma. B) H&E staining at 40X shows large, irregular lymphocytes with abundant cytoplasm and multiple, prominent nucleoli. Various mitotic figures present.

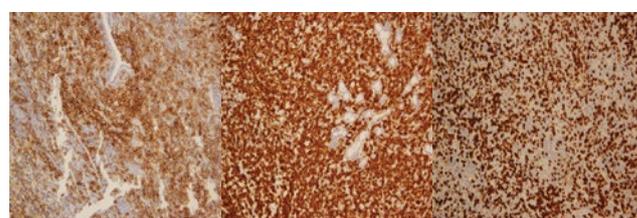


Figure 4: A) CD20+ staining of abnormal lymphocytes supports B cell origin. B) BCL-2+ staining with predominance of B cells consistent with a B-cell lymphoma. C) CD3+ cells show normal morphology consistent with T cells. No neoplastic cells stained positive supporting B-cell involvement.

common [7]. Symptoms of paranasal sinus lymphoma can be non-specific and variable, making diagnosis difficult. Common complaints include pain, persistent rhinosinusitis, nasal obstruction, facial edema, B symptoms, or unintended weight loss [8]. This disease is often associated with a poor prognosis due to its aggressive nature and the increased likelihood of invasion and spread into the CNS [3]. There is some evidence that CNS chemoprophylaxis may also improve 5-year outcomes and, thus, could be considered if the risk of CNS invasion is an immediate concern [3].

The International Prognostic Index and its derivations constitute the major prognostic tools for DLBCL. The following factors significantly correlate with a decreased overall survival: age >60, serum lactate dehydrogenase >normal, ECOG performance status ≥ 2 , Clinical stage III or IV, and number of involved extranodal disease sites >1. Furthermore, Lopez-Guillermo et al. found that in multivariate analysis, IPI, bulky disease, and serum $\beta 2m$ were most important factors for predicting overall survival, irrespective of primary site of lymphoma [2].

Treatment involves a combined modality approach often involving surgery, multi-agent systemic chemotherapy, and localized radiation therapy. Additionally, allopurinol and rasburicase should be given to patients undergoing chemotherapy to prevent Tumor Lysis Syndrome [9]. The current standard of care is the combination of rituximab with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy. The addition of rituximab, a monoclonal antibody, to the standard CHOP regimen has significantly improved overall outcome [10]. R-CHOP altered the IPI prognostic value and several studies were done to re-evaluate the new treatment modality. In 2010, Hui et al. found that there was no difference in outcome between patients with primary extranodal and nodal DLBCL, but for those treated with R-CHOP, the existence of extranodal disease remained prognostic regardless of primary presentation [11]. Though one might then assume a primary paranasal location would not alter prognosis,

the variable presentation and late diagnosis are the leading detriments affecting patient survival. Indeed, multiple secondary extranodal involvement was discovered on the patient's PET/CT. Overall, the 5-year survival rate for patients is approximately 50% [4,12].

Conclusion

Paranasal sinus lymphoma is a rare malignancy that is challenging to diagnose. It should be included on any differential involving a mass of the nasal or sinus tract and treatment should be started as soon as possible after definitive diagnosis has been made. A multidisciplinary team approach is crucial for effective therapy and treatment for this aggressive malignancy.

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