Primary non-Hodgkin’s lymphoma of the frontal sinus: Case report and review of the literature

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Abstract
Non-Hodgkin’s lymphoma of the sinonasal tract is an uncommon lesion, representing 1.5 to 15% of all lymphomas. Most cases of primary non-Hodgkin’s lymphoma of the sinonasal tract occur in the maxillary sinus, ethmoid sinus, and nasal cavity; its occurrence in the frontal sinus is extremely rare. We report a case of primary type B non-Hodgkin’s lymphoma of the frontal sinus in a 43-year-old man. The patient complained of frontal headaches that had not improved with analgesic drugs, and he presented with a frontal bulge that involved the left upper eyelid; the bulge had progressively enlarged over a 3-month period. A biopsy of the mass identified the type B non-Hodgkin’s lymphoma. Immunohistochemical study not only confirmed the histologic type of the tumor, it also provided some important information about the primary tumor site.

Advances in immunohistochemistry have shown that type B non-Hodgkin’s lymphoma is more common in North American and European patients, whereas subtype T is more common in Asians and in some Latin American countries, particularly Peru and Guatemala (up to 88% of all cases). It is still unclear whether this difference is linked exclusively to geographic variables or to differences in the specific characteristics of the nasal cavities in various populations; tumors of the nasal cavities are more common in Asia, as are tumors of T lineage.

In terms of sinonasal localization, NHLs preferentially attack the maxillary sinuses, ethmoid sinuses, and nasal cavity; primary involvement of the frontal sinus is rare. NHLs frequently occur in patients with acquired immunodeficiency syndrome (AIDS), but involvement of the paranasal sinuses in these patients is rare; the most common sites are the central nervous system, gastrointestinal tract, and bone marrow.

In this article, we report a case of primary type B NHL of the frontal sinus in a patient with AIDS. We discuss the clinical, diagnostic, therapeutic, and prognostic factors related to the management of this type of patient.

Case report
In September 1999, we evaluated a 43-year-old man from São Paulo who had been diagnosed with human immunodeficiency virus (HIV) infection in 1986. He was being treated at an AIDS clinic with saquinavir, ritonavir, and stavudine; his CD4 count was 65 cells/mm³. He also had a 5-year history of diabetes, which was being controlled with an oral hypoglycemic.

One month prior to presentation, the patient began to experience frontal headaches that did not respond to common analgesics. The headaches were accompanied by the presence of a progressive, hard, 15-cm, left frontal bulging that involved the left upper eyelid. A few weeks later, a serosanguineous secretion began to drain from the nasal...
fossae; he was treated with amoxicillin for 10 days but did not improve. He was then referred to our service.

On examination, the patient exhibited the left frontal orbital bulging and eyelid closure (figure 1). The orbital involvement had caused proptosis and chemosis. There was no sign of fluctuation, but there was light local hyperemia.

Anterior rhinoscopy did not detect any tissue mass in the nasal cavity. However, computed tomography (CT) of the paranasal sinuses revealed that a tumor had filled the left frontal sinus, eroded the roof of the orbit and the floor of the left anterior fossa, and invaded the eye, ethmoid sinus, and left anterior fossa (figure 2). A biopsy specimen was obtained via a Lynch incision. Examination of the specimen revealed that it was a histologically high-grade, diffuse NHL with large B cells. Immunohistochemistry demonstrated positivity for leukocyte-common antigen (LCA), CD20, and CD45RO without atypical lymphocytes, and negativity for CD15 and CD30.

The patient was scheduled for chemotherapy and a bone marrow biopsy for staging. However, before these measures could be undertaken, he developed clinical complications and died in October 1999.

Discussion

Disease characteristics. Most type B NHLs are of intermediate histologic grade and are characterized by large cells or a mixture of large and small cells. In addition to confirming the lineage of NHL, immunohistochemistry allows pathologists to draw inferences regarding the

Figure 1. On presentation, frontal (A) and lateral (B) views show the left frontal orbital bulging with eyelid closure.

Figure 2. Coronal (A) and axial (B) CTs show that the tumor has filled the left frontal sinus, eroded the roof of the orbit and the floor of the left anterior fossa, and invaded the eye, ethmoid sinus, and left anterior fossa.
tumor’s site of origin. Tumors that originate in the nasal fossae exhibit the immunophenotypic characteristics of type T tumors, and those that originate in the paranasal sinuses exhibit the characteristics of type B tumors. In our patient, the finding of LCA and CD20 positivity was compatible with a B lineage and with origin in the paranasal sinuses. Of interest, most of these tumors are negative for T-lineage markers such as CD45RO,2,3,6 but our patient was CD45RO-positive. Studies have shown that CD45RO can be positive in the presence of normal or malignant T cells, and they are therefore not highly specific for a determination of tumor lineage.9

Lymphomas generally occur in patients in the seventh or eighth decade of life; there is no clear predilection for either sex.1,7,10,11 Cuadra-Garcia et al studied 33 patients with large-cell B lymphoma whose age and sex distribution matched this profile (mean age: 63 yr; no predilection for either sex).10 However, 2 of these patients were HIV-positive, and both were younger than 50 years, as was our patient.

Most studies of sinonasal NHL have shown that the maxillary sinus is the most common site of origin,2,6,11,12 followed by the nasal fossae and the ethmoid sinuses.2 Primary involvement of the frontal sinus is rare; most cases of frontal sinus involvement are secondary to extension from other sinuses. Even so, most cases of sinonasal NHL involve more than one sinus, which means that determination of the primary site can be somewhat arbitrary.2,10 According to Sofferman and Cummings2 and later Nakamura et al,2 a tumor confined exclusively to the ethmoid sinus is extremely rare. Involvement of the ethmoid sinus is related to tumoral extension from adjacent sinuses (primarily the maxillary and frontal sinuses).

Nasal obstruction is the most common symptom of sinonasal NHL.1,2,6,7,11-13 Edema, facial bulging, epistaxis, a nasal mass, headache, rhinorrhea, proptosis, paralysis of the cranial nerves, and cavernous sinus syndrome can also occur. According to a study by Lefebvre et al, low-grade tumors tend to form masses in the involved nasal cavity or paranasal sinus and cause nasal obstruction, whereas high-grade tumors cause more aggressive symptoms, such as facial edema, epistaxis, and facial pain.12

Type B lymphomas are usually associated with bone destruction, particularly in the orbital region, where they frequently cause proptosis. Type T lymphomas rarely cause such symptoms. Although NHLs can infiltrate various sinuses in the face, involvement of the ganglia is uncommon. Extension into the orbit, nasopharynx, or sella turcica may cause symptoms in cranial nerve pairs. Bone erosions are quite common. High-grade B tumors very often destroy periorbital soft tissue and bone tissue,2 as occurred in our patient. However, bone destruction by a lymphoma is generally not as aggressive as that caused by a spinous cell carcinoma because the periosteum is preserved.12 Multiple-sinus involvement is also believed to be associated with bone permeation, often without destruction of bone divisions. Tomographically, the condition manifests as a mass that has invaded adjacent soft tissues but has left cortical bone intact.

**Diagnosis.** The diagnosis of sinonasal NHL is based on a detailed clinical history and a complete physical examination. In terms of imaging examinations, CT of the paranasal sinuses is the best means of identifying the tumor site and extension into the sinuses and orbit. Magnetic resonance imaging is also quite useful for diagnosing NHLs, especially because it can distinguish between a tumor lesion and mucosal edema or secretions retained in the paranasal sinuses. Mucosal secretions enhance well on T1-weighted imaging, whereas tumors such as lymphomas exhibit moderate enhancement on T2-weighted imaging.

Biopsy analysis can confirm the diagnosis and help determine the tumor’s lineage. Staging is achieved by chest and abdomen CT, bone gallium scintigraphy, and a bone marrow biopsy.

**Tumor classification.** Three systems have been used to classify paranasal sinus lymphomas: the Ann Arbor classification,14 the international histologic classification,15 and the revised European-American lymphoma (REAL) classification16; the Ann Arbor system is the most widely used (table 1).

Most sinonasal NHLs present as stage I tumors, although the incidence of higher-stage tumors is significant.1,7,11 Our patient died before we were able to complete the staging process.

**Treatment.** Treatment is controversial with regard to the best combination of treatments for these patients.

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<th>Table 1. Ann Arbor classification of lymphomas14</th>
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Several decades ago, these lymphomas were treated with local radiotherapy only, and short-term results were fairly good. However, those patients experienced a high incidence of local and distant recurrence. The addition of chemotherapy has lowered the rates of local recurrence and metastasis and improved survival. 

Likewise, studies have shown that patients treated exclusively with chemotherapy have a higher risk of local recurrence. Studies have also shown that surgical exeresis has not resulted in a good therapeutic response. Recent studies have suggested that radiotherapy combined with chemotherapy yields the best 5-year survival rates and the lowest recurrence rates for all stages of disease.

Nevertheless, combined therapy is associated with concerns about local treatment failure (which is more common with T lymphomas) and metastases to the central nervous system.

**Prognosis.** Various prognostic factors have been reported (table 2). Reported survival rates vary widely; these variations are attributable in part to the relative rarity of paranasal NHL.

Shima et al studied 14 patients with NHL of the sinonasal tract and reported a 5-year survival rate of 85% for tumors of the paranasal sinuses (maxillary and ethmoid) and a 5-year rate of 25% for tumors of the nasal cavity. Patients with B-lineage tumors had a 5-year survival rate of 61%, compared with only 12% for patients with T-lineage tumors. These authors found no statistically significant differences in survival between patients with stage I and stage II disease and between patients who underwent different types of treatment.

In a series of 20 patients with sinonasal NHL, Kojima et al found that patients whose tumor involved only the paranasal sinuses had a higher 5-year survival rate than did patients with involvement of both the nasal cavity and paranasal sinuses.

In other studies, Frierson et al studied 11 patients with sinonasal NHL and reported that 6 died between 1 and 43 months after diagnosis; 3 of these patients presented with stage III or IV disease. Nakamura et al evaluated 24 patients with stage I or II disease and reported a 5-year survival rate of 64% for patients with tumors of the nasal cavity and 75% for those with tumors of the paranasal sinuses. Kuten et al conducted a follow-up of 7 patients with stage IE disease and reported a 10-year survival rate of 86% and only 1 recurrence.

Finally, in a study of 18 patients with stage I extralymphatic (IE) disease, Tran et al reported that 12 had no sign of recurrence after a 71-month follow-up; among the other 6 patients, 2 were alive with recurrence and 4 had died.

The case we describe here illustrates the importance of early clinical suspicion and early diagnosis, which can result in a better prognosis.

**References**


