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T-Cell Non-Hodgkin's Lymphoma of the Maxillary Sinus: Diagnostic Challenges in the Sinonasal Tract

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ABSTRACT

Non-Hodgkin's lymphoma (NHL) of the sinonasal tract is an exceptionally rare malignancy that poses a significant diagnostic challenge. Differentiating NHL from inflammatory polyps or other non-malignant lesions can be difficult, making accurate diagnosis challenging for ENT surgeons and pathologists. Consequently, it is crucial to perform multiple deep biopsies and ensure adequate sampling in patients with a clinical presentation suggestive of malignancy.

This case report discusses a 55-year-old male who presented with nasal congestion, blood-stained nasal discharge, and facial swelling that had persisted for approximately two months. Initially treated for rhinosinusitis without improvement from local hospitals, a biopsy performed from our centre confirmed the diagnosis of T-cell type of non-Hodgkin's lymphoma.

Keywords: Non-Hodgkin's Lymphoma, Sinonasal Tract, Maxillary Sinus

*See End Note for complete author details

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INTRODUCTION

Lymphomas are malignant neoplasms of the lymphoreticular system and are distinctly classified into Hodgkin's and non-Hodgkin's lymphoma(NHL).[1] NHL of the sinonasal region is rare and comprises about 0.2%-2% of cases.[2] Non-Hodgkin's lymphoma constitutes 60% of all lymphomas, but the involvement of the nasal cavity and the paranasal sinuses is highly unlikely.[1] Differentiating NHL from destructive non-neoplastic lesions and other malignant neoplasms can be challenging.[2]

CASE REPORT

A 55-year-old male with a history of diabetes and hypertension presented with a two-month history of left nasal blockage, accompanied by blood-stained nasal discharge on the left side for one month, and swelling beneath the left eye for the past two weeks. The symptoms were also associated with headache and left-sided facial pain. The patient noted a progressive increase in the size of the swelling, which was accompanied by pain in the affected area.

On examination, the swelling was of the size of 4x3 cm, on the left nasofacial fold extending superomedially up to the left medial canthus, tender, hard in consistency, non-fluctuant, and fixed **(Figure 1).** The skin over the swelling appeared tense and non-pinchable and didn't show discoloration. Extraocular movements and visual acuity were normal. There was obliteration of the left nasofacial fold, and the inferior orbital margin was irregular on palpation. Anterior rhinoscopy revealed blood-stained nasal discharge with a pinkish polypoidal, non-tender, firm mass in the left nasal cavity, which didn't bleed on probing.

Diagnostic nasal endoscopy showed a pinkish polypoidal mass in the left nasal cavity, which was touching the floor and extending almost up to the anterior end of the left inferior turbinate, possibly arising from the left middle meatus, mucopurulent

Figure 1. Left nasofacial swelling with orbital margin irregularity

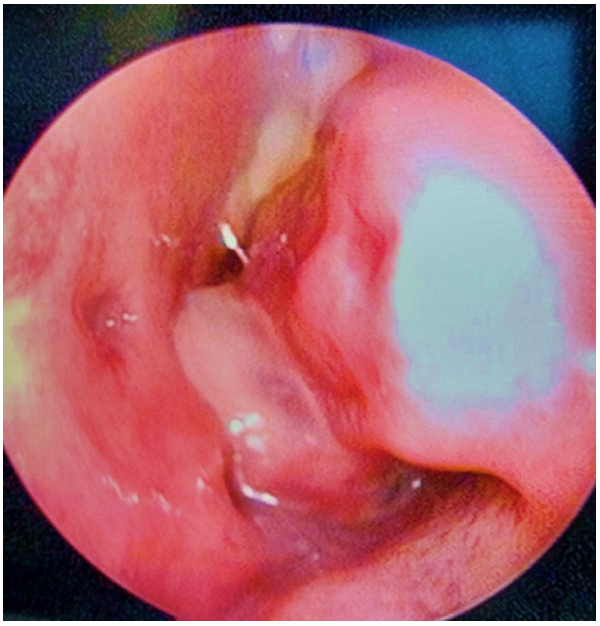

Figure 2. Diagnostic nasal endoscopy

nasal discharge, and lateral nasal wall bulge **(Figure 2).** Contrast-enhanced CT scan of nose and paranasal sinuses showed left maxillary sinus opacification with isodense soft tissue, extension to the premaxillary soft tissue and retroantral region. There was also erosion of the uncinate process, part of the nasal septum, and anterior and posterior walls of the left maxillary sinus. The inferior orbital margin was also seen eroded, with the lesion extending into the orbit **(Figure 3).**

A routine workup and a biopsy were performed on the mass. An immunological workup was done to rule out granulomatous diseases, which were reported negative. Histopathology report confirmed the diagnosis of non-Hodgkin's lymphoma of the sinonasal tract, T-cell type, with CD3 positivity. Immunohistochemical stains for CD20, CD56, HMB-45, and S100 were negative. There were areas of necrosis, hemorrhage, and some neoplastic cells exhibiting angiocentricity. A metastatic workup, including PET-CT, was performed, which showed no evidence of metastasis, and hence, the Ann Arbor stage came to be "Stage I E" (localized sinonasal disease). The patient is undergoing chemotherapy, i.e., CHOP regimen (cyclophosphamide, doxorubicin,

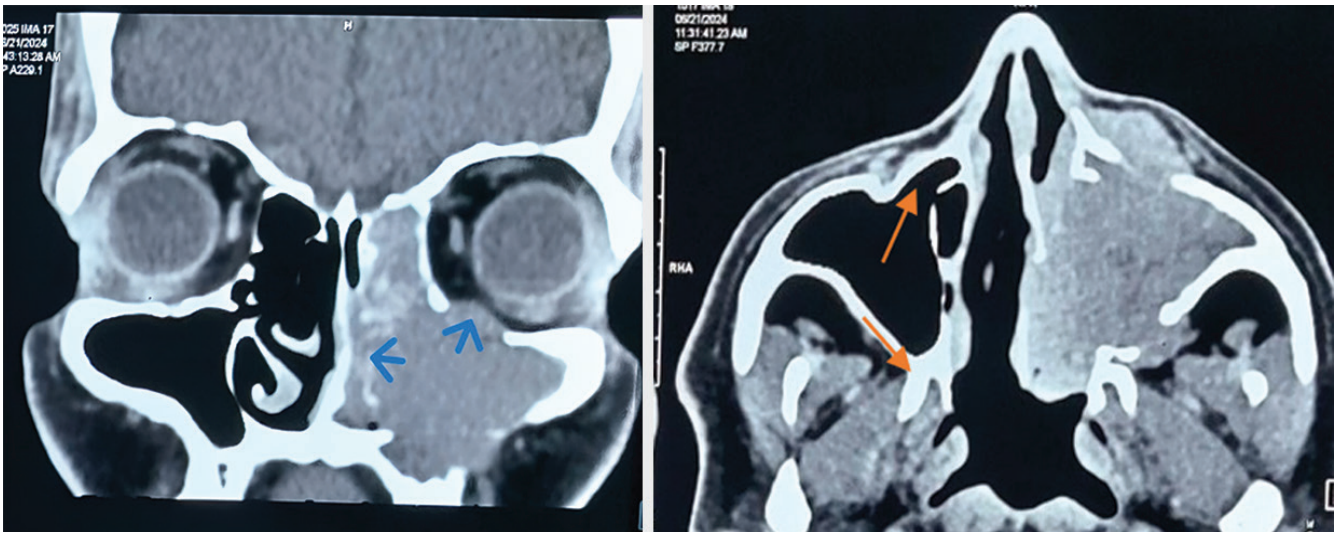

Figure 3 a & b: CECT nose and PNS showing maxillary sinus erosion and orbital extension

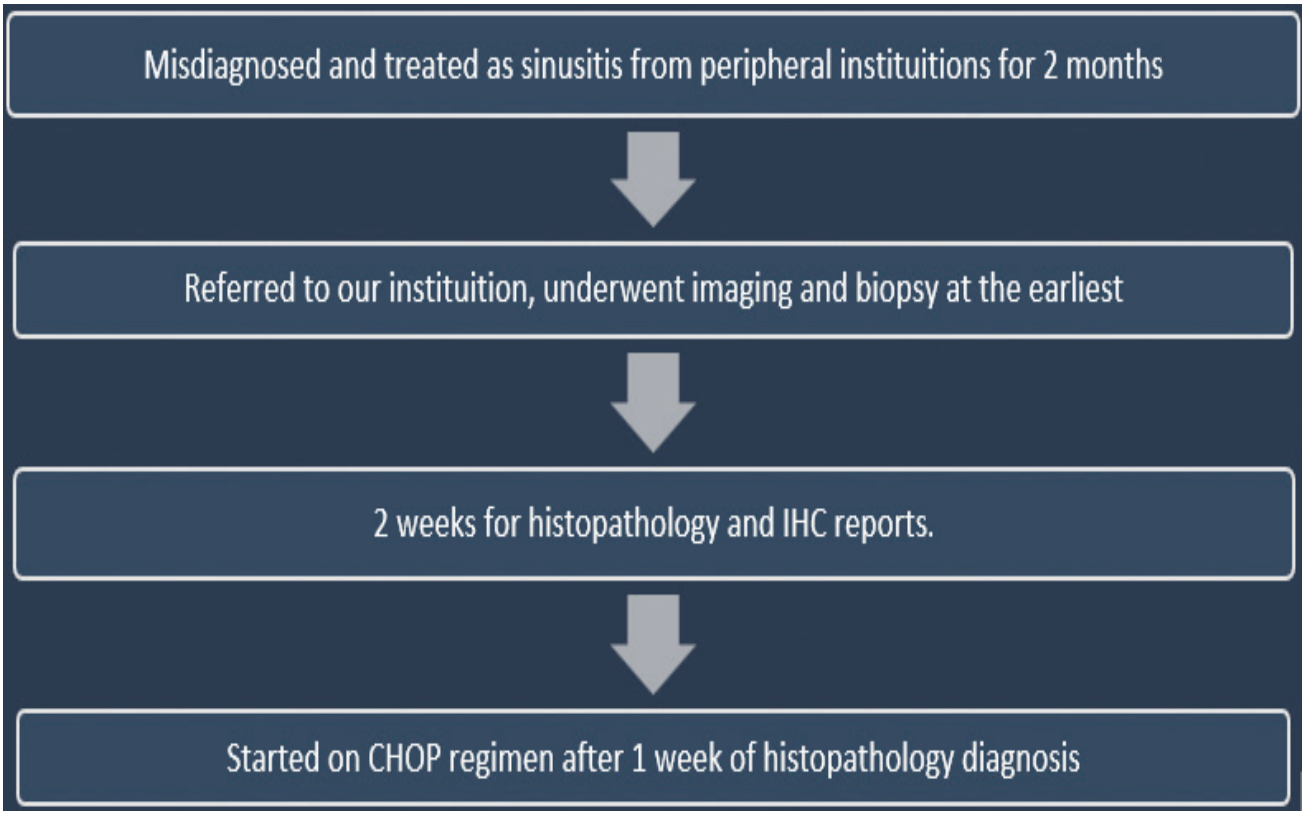

Table 1. Diagnostic timeline of the patient

vincristine, and prednisolone), scheduled for 6 cycles, followed by radiotherapy after reassessment, in the radiation oncology department **(Table 1).**

DISCUSSION

NHL encompasses a diverse range of lymphoid malignancies, each with unique histopathologic, immunologic, cytogenetic, and clinical characteristics.[3]

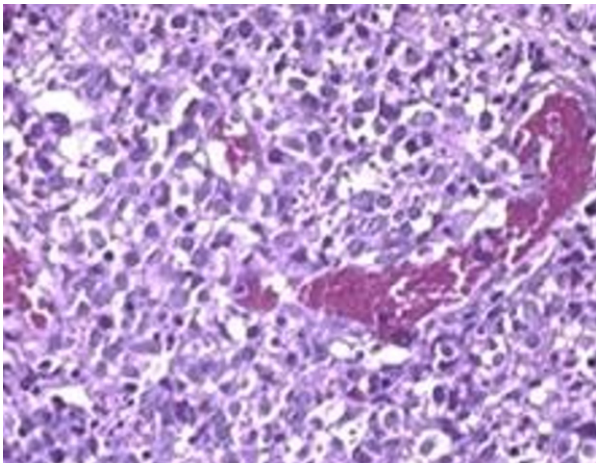

Figure 4. Histopathology – high power

- Histopathological features: NHL varies in cell size, shape, and arrangement. They are classified into diffuse large B-cell lymphoma (DLBCL), T-cell neoplasms, follicular lymphoma, mantle cell lymphoma, etc.
- Cytogenetic features: Various subtypes of NHL express various surface markers. For example, B-cell lymphomas typically express CD19, CD20, and other B-cell markers, while T-cell lymphomas have distinct T-cellmarkers like CD3.
- Molecular Features: Chromosomal translocations (e.g., t (14;18) in follicular lymphoma), mutations, and changes in gene expression determines the classification.

Non-Hodgkin lymphoma of the sinonasal tract – T type generally shows a male preponderance with a male-to-female ratio of 1.35:1, and the majority of cases are found in the 6th to 8th decades.[4] The clinical presentations also vary according to the histologic type. The low-grade lymphomas usually are indolent and present with obstructive symptoms, whereas the high-grade lymphomas present with aggressive symptoms like facial swelling, ulcerations, cranial

Table 2. Markers for T cell lymphoma

Subtype of markers	Markers
T-cell lineage markers	CD3, CD2, CD5, CD7
Additional T-cell subset markers	CD4 and CD8 TIA-1, Granzyme B, Perforin CD30 ALK
T-cell receptor (TCR) markers	βF1 TCRγ
Activation/proliferation markers	Ki-67 (proliferation index) CD25, CD69, HLA-DR (activation markers)
Markers to rule out T cell lymphoma	CD19, CD20, CD56 (markers of B cells)

nerve involvement, and rapid systemic dissemination with disseminated intravascular coagulation.[4]

The T cell variant of the non-Hodgkin's lymphoma is associated with nasal septal destruction, whereas the B cell type is usually associated with soft tissue and osseous involvement. Nodal dissemination is observed in the cervical and axillary lymph nodes. Histopathological variants of the NHLs in the sinonasal tract are diffuse large B-cell lymphoma (58.3%), followed by angiocentric lymphoma (16.67%), lymphoplasmacytoid lymphoma (8.33%), follicle center lymphoma: provisional cytologic grade III (8.33%), and adult T cell lymphoma (8.33%).[1] Histopathology shows angiocentricity with vascular damage and destruction, necrosis, and cytotoxicity.

Compared to nodal lymphomas, diagnosing sinonasal tract lymphomas is particularly challenging due to the presence of areas of necrosis, hemorrhage, and inflammation.[5] It is currently understood that multiple biopsies are often necessary for the identification of the pathology, and usually, there will be misleading reports because of the small biopsy size and technical difficulties in identifying the atypical cells.

T-cell lymphomas seen in the nasal and paranasal sinus areas are associated with Epstein-Barr virus (EBV) infection in the Asian population, but not so in the Caucasian population. Pathogenesis of EBV associated lymphomas show a complex interplay between different patterns of viral gene expression and cellular genetic changes in the host. EBV-encoded protein and non-coding RNA (ncRNA) activate various signal transduction pathways, including NF-κB, phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT), Janus kinase/signal transducer and activator of transcription (JAK/STAT), and lead to the development of lymphoma. In certain Asian populations, HLA-A11 is more prevalent, and HLA-A11 is associated with EBNA-4 mutation, which interferes with the recognition of EBV by cytotoxic T cells.[6]

Extranodal nasal-type T-cell lymphomas were seen involving sites like the larynx, skin, uvula, lacrimal gland, etc. Patients with nasal and paranasal involvement have a better prognosis compared to patients with systemic disease. Extranodal NK/T-cell lymphomas (ENKL) are a rare type of non-Hodgkin's lymphoma with a poor prognosis. This was earlier known as angiocentric lymphoma. Nasal type shows local destruction with necrotizing lesions in the central aspect of the face, particularly in the nasal/paranasal area. They represent about 75% of all nasal lymphomas. Nasal T cell lymphomas in Asians follow an aggressive course, and death occurs due to local relapse and systemic spread.

CT shows lymphomatous masses as iso or hyperintense and with bony destruction and remodelling, while on MRI, it is isointense on T1 and hypointense on T2 with enhancement on gadolinium contrast and diffusion restriction images.[2] The most effective treatment plan involves multidrug chemotherapy (CHOP regimen with cyclophosphamide, hydroxydaunorubicin/doxorubicin, vincristine/oncovin, and prednisolone) for 3 to 6 cycles followed by field radiotherapy. Doses are consolidated 30 Gy after complete response to chemotherapy and 40 Gy for residual (partial response) or uncertain response.[7] In the early stages of the disease, the 5-year overall survival rate ranges from 55% to 90%, while in advanced stages, it drops to less than 40%.[7]

The differential diagnosis for T-cell lymphoma of the nasal cavity includes infectious, autoimmune, and other neoplastic entities. Chronic invasive fungal infections, such as mucormycosis and aspergillosis, and autoimmune conditions like Wegener's granulomatosis may also present with necrotizing lesions. Neoplasms such as sinonasal undifferentiated carcinoma, squamous cell carcinoma, or olfactory neuroblastoma should also be considered. Histopathological examination, immunophenotyping (CD3+, CD56+, cytotoxic markers), and EBV-encoded RNA (EBER) in situ hybridization are key in confirming the diagnosis.

CONCLUSION

Non-Hodgkin lymphoma (NHL) of the sinonasal tract, particularly the T-cell type, is a rare entity, accounting for less than 5% of all neoplasms in this region. The clinical presentation can vary depending on the disease variant, and symptoms may appear at early or late stages. Differentiating NHL from other pathologies, such as inflammatory polyps or benign lesions, can be challenging. This underscores the importance of obtaining multiple biopsies and ensuring adequate tissue sampling in patients with a suspicious clinical presentation. Due to frequent misinterpretation, patients may present later with advanced disease, which is associated with a poorer prognosis.

LIMITATION

EBV–PCR/ISH could not be performed due to technical constraints.

END NOTES

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