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Case Report

Primary Non-Hodgkin's Malignant Lymphoma of the Sinonasal Tract

Authors
Bist SS, Assistant Professor,
Saurabh Varshney, Professor & Head,
Rakesh Kumar Singh, Associate Professor,
Sanjeev Bhagat, Assistant Professor,
Nitin Gupta, Assistant Professor,
Department of ENT, Himalayan Institute of Medical Sciences, HIHT University, Jolly Grant, Doiwala, Dehradun Uttarakhand, India -248140

Address For Correspondence
Dr. S.S. Bist,
Assistant Professor (E.N.T),
Himalayan Institute of Medical Sciences,
HIHT University, Jolly Grant, Doiwala,
Dehradun, Uttarakhand - 248140
E-mail: sampanbist@yahoo.com

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Abstract:
Primary non-Hodgkin's lymphomas (NHL) of the sinonasal tract are rather uncommon entities. Morphologically and radiographically, sinonasal lymphomas are difficult to distinguish from other malignant neoplasms or non- neoplastic processes. They have a variable presentation from fulminant destructive manifestations to chronic indolent type of disease and may mimic as carcinomas and invasive fungal infection respectively. We report a case of primary NHL involving sinonasal tract in elderly female, which was clinically and radiologically mimicking as sinonasal malignany and was proven as NHL on histological examination and confirmed by immunohistochemistry. A high index of suspicion, appropriate histopathological examination and immunohistochemistry is necessary to differentiate sinonasal lymphomas from other possibilities. Failure to do so may miss the diagnosis and delay appropriate treatment.
Key Words: Sinonasal lymphoma, Non Hodgkins lymphoma, Immunohistochemistry

Introduction:

Lymphomas represent a group of malignant neoplasms of lympho-reticular origin which are subdivided into Hodgkin's and Non-Hodgkin's lymphomas (NHL).[1] Approximately 3 to 5% of malignant neoplasms are lymphomas, and 60% of these are NHL.[2] NHL predominates in all areas of the body including the head and neck. Both types originate most commonly within a lymph node. Extra nodal involvement does occur and is more common for NHL. Primary NHL arising in the head and neck area accounts for 10% of all NHL and 30% of extra nodal NHL.[3] According to REAL (Revised European-American Lymphoma) classification 1994, NHL is a heterogeneous group of diseases with peculiar, morphological, phenotypic and molecular features (B-cell, T-cell and putative natural killer (NK)-cell neoplasm's).[4] Unlike other classifications, the REAL classification does not distinguish these tumors as being high or low grade, since it is recognized that each entity has its own characteristic pattern of behavior.[5] Common primary extra nodal sites of lymphomas include liver, soft tissue, dura, bone, stomach, intestine, bone marrow and others. The nasal cavities and paranasal sinuses are rarely affected by primary NHL. Geographic factors play a role in the frequency and histological subtype of NHL of the sinonasal tract. In western populations, sinonasal NHL approximates 0.2% to 1.6% of all NHL, which is B-cell subtype predominant, more common in elderly, and primary located in the paranasal sinuses.[2] In Asian countries, the incidence is higher, about 2.6 to 6.7% of all NHL and the T-cell subtype is the predominant form. In contrast with those in the western world, these lymphomas are more common at younger ages, primarily located in the nasal cavity, and strongly associated with the Epstein –Barr virus.[6] An early diagnosis of primary NHL of the sinonasal tract is unusual because such a lesion develops in an anatomic space and expands toward the sinus or nasal cavity, usually causing no symptoms at the early stages. Only after reaching a considerable size and involving adjacent anatomic structures do the presenting symptoms appear and they may masquerade as other nasal or head and neck diseases. NHL of the sinonasal tract is an important cause of destructive lesions of the nose and midface; their course progresses slowly but relentlessly. A systematic attempt to determine the histological and immunological category of the lymphoma is necessary, since new modalities of treatment are now available that are neoplasm specific. We hereby present a case of primary sinonasal NHL and will be discussing the significance of appropriate histopathological and immunohistochemical analysis for confirmation of diagnosis before starting the treatment.

Case Report:

A 68-years-old female presented with complaint of left nasal obstruction and purulent nasal discharge for 8 months along with swelling around left lower eyelid since 2 months. The patient was referred to our hospital as a suspected case of sinonasal malignancy. Patient had a history of headache, mild epistaxis and purulent postnasal discharge. The patient had no history of double vision, loss of consciousness and neurological deficit. Anterior rhinoscopic examination revealed smooth vascular mass filling the left nasal cavity completely and widening the anterior nares. On probing it was sensitive, firm and bleeds on touch. The patient had oedema of lower eye lid with palpebral hyperemia but no proptosis or restricted eye movements were noted. A diagnostic nasal endoscopy (Fig.1) did not reveal any additional findings and endoscope could not be negotiated on the left side beyond the swelling. Rest of the ENT and systemic examination were normal.

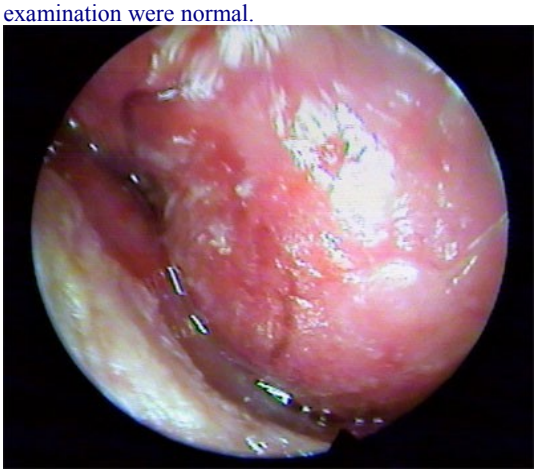

Figure 1: Nasal endoscopy showing smooth pinkish mass completely filling the left nasal cavity

Contrast enhancement computed tomography (CECT) revealed a mildly enhancing soft-tissue density lesion with interspersed hyperdensity filling the left nasal cavity, maxillary antrum, ethmoid and choana. There was a widening of maxillary hiatus with focal areas of erosion of roof of maxillary antrum and medial orbital wall with minimal extracoanal extension into left orbit (Fig.2). CECT report was suggestive of long standing antrochoanal polyposis with fungal component or malignancy.

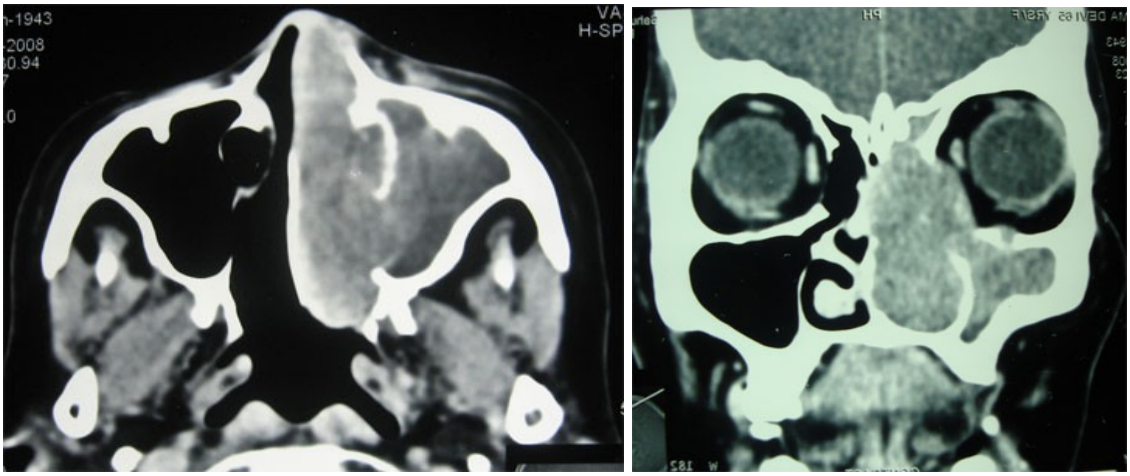

Figure 2: CT scan (Axial & Coronal) shows an enhancing soft-tissue mass occupying the left nasal cavity along with maxillary and ethmoid sinuses.

Clinico-radiologically a provisional diagnosis of carcinoma was made. The patient had previously undergone fine needle aspiration cytology of the lesion elsewhere and was suggestive of malignant lesion. For the confirmation of the diagnosis, biopsy under local anaesthesia from appropriate site was done. Histological analysis revealed a highly cellular tumor with dense sheets of compactly arranged cells with scanty cytoplasm and hyperchromatic nuclei suggestive of a malignant lymphoma or poorly differentiated carcinoma and immunohistochemisty was advised to confirm the diagnosis. Immunohistochemistry revealed that the specimen was strongly positive for the leukocyte common antigen CD45, which is diagnostic of B cell NHL. As staging investigations revealed no other focus, a primary Non –Hodgkin's malignant lymphoma of the sinonasal tract was diagnosed and was staged as IE after a complete systemic workup. The patient was subsequently planned for chemoradiation. The patient underwent 6 cycles of CHOP regimen (cyclophosphamide, adriamycin, vincristine and prednisone) and after completion of chemotherapy CT scan showed significant regression of the tumor mass (Fig.3a). Patient was subsequently followed by involved field radiotherapy (40 Gy) without significant side effects, which resulted in full regression of tumor. On follow-up at 1 year there is no evidence of recurrence on nasal endoscopy (Fig.3b). The patient is still under regular follow up.

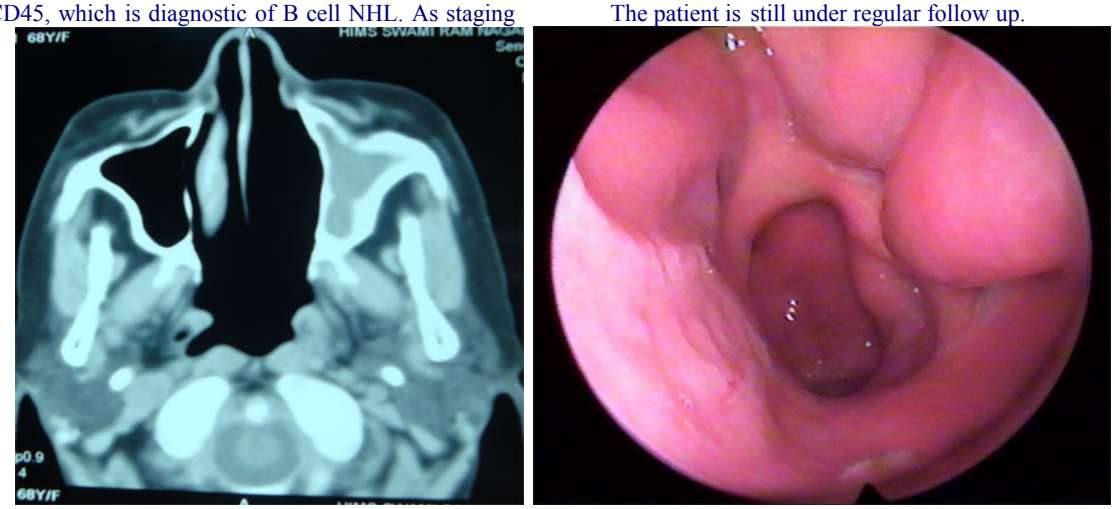

Figure 3: (a) CT scan (Axial) after completion of chemotherapy shows significant regression of the tumor mass. (b) 1 year after completion of chemoradiation endoscopy shows complete regression of the tumor mass. Figure 3: (a) CT scan (Axial) after completion of chemotherapy shows significant regression of the tumor mass. (b) 1 year after completion of chemoradiation endoscopy shows complete regression of the tumor mass.

Discussion:

Lymphomas of the sinonasal tract are known to represent a heterogeneous group of neoplasms.[7] The disease has been given several names, including midline granuloma syndrome, lethal midline granuloma, polymorphic reticulosis and midline destructive granuloma. These terms are no longer acceptable, as most, if not all, of these lesions have been proven to be lymphomas. The classification of these lymphomas continues to defy the efforts of lymphoma experts. The inclusion of all sinonasal lymphomas into one category has been attempted before. A consensus meeting of lymphoma experts from around the world attempting to define lymphomas of the sinonasal tract con-

cluded that these tumors have very characteristic morphological, immunophenotypic and molecular characteristics. Studies have indicated a predominance of T-cell lymphoma in the nasal cavity, while most paranasal lymphomas are B-cell type.[3] Nasal T cell lymphomas usually spread from their site of origin in the nasal cavity and invade adjacent structures via palatine necrosis. T cell lymphomas are characterized by progressive ulceration and necrosis, which are not typical of B cell lymphomas.[7] They are also characterized by their angiotropism or angiocentricity, as tumor cells infiltrate and destroy blood vessel walls and cause variable degrees of geographic necrosis.[8] Numerous studies have shown that patients with T and NK cell lymphomas of the sinonasal area have a high incidence of Epstein-Barr virus (EBV) infection.[8] It is unclear what role EBV plays in the origin of sinonasal lymphomas, but one possible explanation involves clonal proliferation in response to viral stimulation. Sinonasal B cell lymphomas primarily involve the maxillary and ethmoid sinuses, and they extend locally to involve the orbit, cheek, and anterior cranial fossa. They do not usually manifest angioinvasion and so vascular necrosis does not occur.[7] In our patient, however, the tumor appeared to have originated in the nasal cavity and then spread to the paranasal sinuses. Sinonasal lymphoma can occur over a wide range of ages, peaking in the sixth decade, with male predominance. Sinonasal lymphomas are usually submucosal and on gross appearance differ from squamous cell carcinomas, which are usually ulcerative. The most common presenting symptoms of sinonasal lymphomas are nasal obstruction, discharge, epistaxis, headache and unilateral facial, cheek, or nasal swelling.[1] Patients may also show signs of infiltration, such as proptosis, diplopia, blurred vision and cranial nerve palsies secondary to orbital or skull base extension. Dissemination is infrequent, but when it does occur, it typically involves other extranodal sites. Obtaining a histological diagnosis is difficult; in some cases several biopsies are required because of the severe local inflammatory infiltrate and the presence of large areas of necrosis that impaired visualization of neoplastic cells. Because malignant lymphomas are associated with surface crusting, widespread necrosis, and inflammation, they were once considered to be inflammatory lesions. It was not until the introduction of immunohistochemistry that most of these lesions were found to be malignant lymphomas. Based on immunohistochemistry, the three phenotypes of malignant lymphomas are T cell, natural killer (NK) cell and B cell. These lymphoid cells stained positively for CD2, CD45RO, and CD43 (a T cell markers) and for CD45 and CD79a (a B cell marker). In addition, many proliferating T cells have been shown to express an additional marker (CD56), which suggests an NK cell origin; these tumors are classified as T/NK cell lymphomas , but they lack other NK cell markers, such as CD16 and CD57.[7,8]

Radiological imaging is vital in many aspects, including assessment of tumor extension, bony destruction and choice of the best biopsy site and route and finally for staging purposes. Although CT scan is the best technique to demonstrate fine bony detail and should be considered the gold standard investigation, MRI can adequately assess most areas of bony destruction and has additional advantages in distinguishing a tumor from mucosal thickening or retained sinus secretions. The CT imaging features of sinonasal lymphomas are nonspecific. Common findings are bone destruction and invasion of adjacent sinonasal cavities and orbits. The tumors are usually noncalcified and demonstrated variable contrast enhancement. Because of the rarity of the disease, there has been no consensus as to optimal management for primary sinonasal lymphomas. NHLs are frequently treated with, and respond to, a combination of chemotherapy and radiotherapy. A review of several reports suggests that the best treatment outcomes are obtained with the CHOP regimen, given at three-week intervals for six cycles. Chemotherapy is frequently followed by loco-regional radiotherapy at a dose of 30 to 40 Gy. Rituximab is a therapeutic antibody directed against the CD20 surface antigen, which is frequently present in lymphoma cells. Its use in conjunction with CHOP augments a treatment response in lymphomas expressing the CD20 antigen.[9] A large study reported that the use of combined chemotherapy and radiation therapy significantly improved the five-year disease-free survival and overall survival rates.[10] Our patient also received combined chemotherapy and radiation therapy, the sign and symptoms were dramatically improved. Patients with sinonasal lymphomas have a better prognosis than those with nodal and Waldayer's lymphomas of similar histological grades.[8] Favorable prognostic factors include a young age, diagnosis at an early stage of the disease, and an absence of fever, weight loss, and night sweats. A large study done in M.D. Anderson Cancer Center Houston, USA on 70 patients with lymphoma of the nasal cavity and paranasal sinuses reported 5 year survival rate of 52%.[10]

Conclusion:

Lymphomas must always be included in the differential diagnosis of the unilateral sinonasal lesions. Early diagnosis by histological analysis which is confirmed by immunohistochemistry and appropriate staging by CT scan is essential in the management of sinonasal NHL.

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