Original Article

Primary Sinonasal Non-Hodgkin's Lymphoma: Our Experiences at a Tertiary Care Teaching Hospital of Eastern India

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Abstract

Background: Primary sinonasal non-Hodgkin's lymphomas (NHLs) are uncommon malignancies. The lack of specific clinical presentations often causes delayed visit to the clinician and so diagnosis is done in late with advanced stage. **Objective:** The objective of the study was to study the primary sinonasal NHL with respect to clinical presentations, management, and outcome. **Materials and Methods:** This is a retrospective study conducted in a tertiary care teaching hospital from March 2010 to April 2020. The clinical data of the patients of primary sinonasal NHL were evaluated with respect to the age, sex, clinical presentations, staging, diagnosis, treatment, and outcome. **Results:** The mean age of the participants was 62.45 years with male-to-female ratio of 1.5:1. All the cases of sinonasal NHL involved with paranasal sinuses and nasal cavity. Nasal obstruction was the most common symptom. All were diagnosed with large B-cell lymphoma and treated with combined chemotherapy and radiation. Five patients were died during follow-up period. **Conclusion:** Primary sinonasal NHLs are extremely uncommon clinical entity. The diagnosis is based on the histological examination with immunohistochemical study. Early diagnosis and prompt treatment with chemo-regimen and radiotherapy are essential to achieve an optimum outcome. Early diagnosis and treatment improves the treatment outcome.

Keywords: Nasal obstruction, non-Hodgkin's lymphoma, radiotherapy, sinonasal tract

Introduction

Primary sinonasal lymphomas are extranodal and rarely found in clinical practice. Lymphomas include group of malignant neoplasms arising from the lymphoreticular system which is divided into Hodgkin's disease and non-Hodgkin's lymphoma (NHL). Lymphoma constitutes 3%–5% of all malignancies in the human body, with NHL accounts for approximately 60% of the lymphomas.[1] Although it is malignancy of the lymph nodes, lymphoma may occur in extranodal sites in approximately one-third of the patients.[2] In the head and neck region, majority of the extranodal lymphomas found in Waldeyer's ring such as tonsils, adenoids, lingual tonsils, and tubal tonsils. Other uncommon sites affected are nasal cavity, paranasal sinuses, orbit, thyroid gland, and salivary glands. The sinonasal tract such as nasal cavity and paranasal sinuses are extremely rare locations for origin of the NHL. The site of the sinonasal tract constitutes 0.2%–2% of all the NHL.[3] NHL represents nonepithelial tumor of the sinonasal tract, often localizing in the maxillary sinus and ethmoidal sinuses.[4] Primary sinonasal NHL of West is common in elderly male and found in paranasal sinuses, whereas in far east, it is more in younger age group and seen in nasal cavity.[5] It most often found in the maxillary sinus followed by the ethmoid sinuses and the nasal cavity.[6] NHL arises from the malignant lymphatic cells with different stages of maturation. NHL of the sinonasal tract has been called as monoclonal B-cell neoplasia, polymorphic reticulosis, lethal granuloma, and pseudolymphoma.[7] To minimize the misdiagnosis and inappropriate treatment of the primary sinonasal NHL, we had performed this study by retrospective analysis of the clinical presentations, investigations, and treatment.

Materials and Methods

This retrospective study was on patients who were diagnosed of primary sinonasal NHL between the March 2010 and April

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2020. There were 28 patients enrolled in this study. This study was approved by the Institutional Ethics Committee. This study was based on the clinical observation of patients with primary sinonasal NHL. The detail clinical data of these patients were collected from patient registers. The age range of the participants was from 32 years to 76 years. The clinical symptoms of the participants such as nasal obstructions, nasal bleeding, proptosis, facial swelling, visual disturbances, palatal lesions, unilateral glue ear, and trigeminal neuralgia were documented. Patients of NHL arising at the nasopharynx, oropharynx, and oral cavity extending into the sinonasal tract were excluded from this study. All the included patients had no past history of lymphoma. Clinical presentations, investigations, and treatment were documented in each case. All the patients underwent details otorhinolaryngological examination. Otorhinolaryngological examinations and computed tomography (CT) scan were done to find out the site, extent of the tumor, and assess any bony erosion [Figure 1]. The clinical profile of the patients such as age at the diagnosis, symptomatology of the patients, investigations, and treatment was analyzed. The patients of primary sinonasal NHL have symptoms related to pathology of the sinonasal tract and the tissue from the sinonasal area sent for diagnostic purposes. The participant patients were categorized as per the revised European-American lymphoma classification system.[8] Patients with NHL of the nose and paranasal sinuses irrespective of the age, managed at our hospital included in this study. The diagnosis was done on the basis of the clinical records, definitive histomorphologic features of the NHL [Figure 2], and immunophenotypic analysis [Figure 3]. All the biopsy samples were fresh and studied under photon microscopy for analyzing the tumor architecture. Immunohistochemistry determined phenotype (B or T), antibody expression (CD3, CD5, CD10, CD20, Bcl2, and anti-C-Myc), and proliferation index. The staging of the disease was done by Ann Arbor staging system [Table 1]. All the patients were treated at the hemato-oncology department.

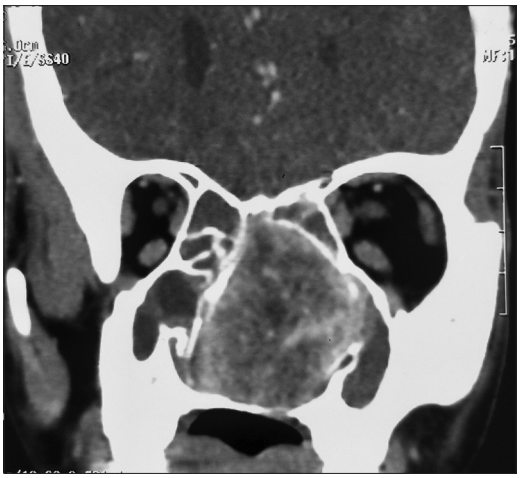

Figure 1: Computed tomography scan of the nose and paranasal sinus with coronal view showing a large sinonasal non-Hodgkin's lymphoma mass with bone erosion

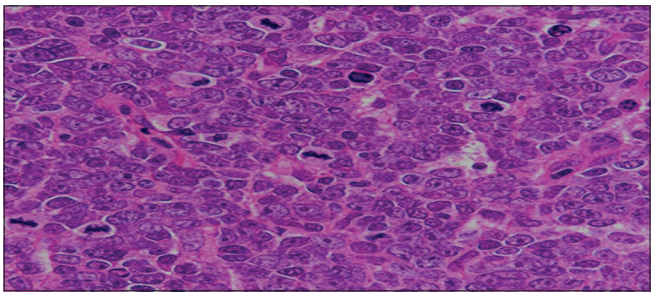

Figure 2: Histopathological picture showing neoplastic cells arranged uniformly with large and round nuclei with little cytoplasm and dispersed coarse to fine nuclear chromatic and inconspicuous nucleoli (H and E, ×400)

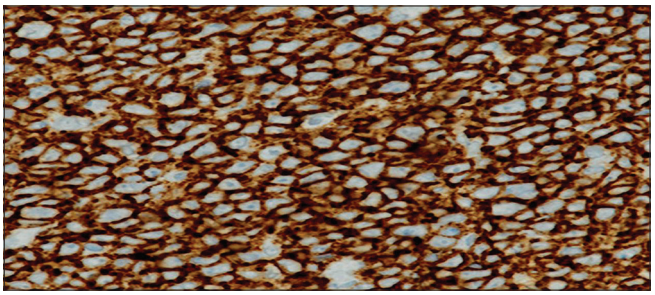

Figure 3: Immunohistochemical staining of tumor cells showing positive for CD20 (×400)

Results

In this retrospective study, 28 patients of primary sinonasal NHL were enrolled. Out of the 28 patients, 17 were male and 11 were female. The male-to-female ratio was 1.5:1. The mean age was 62.45 years (range 32–76 years). Seventeen patients presented with the involvement of the maxillary sinus and 11 patients showed involvement of the nasal cavity, ethmoid sinuses, and sphenoid sinuses. The included patients of primary sinonasal NHL presented with several symptoms mimicking with different sinonasal nonmalignant pathology with common symptoms such as nasal block, nasal mass, and epistaxis. Out of the 28 patients in this study, 23 (82.14%) presented with nasal obstruction, 18 (64.28%) presented with epistaxis, 18 (64.28%) presented with mass in the one side nasal cavity, 16 (57.14%) presented with nasal discharge, 15 (53.57%) presented with swelling, 11 (39.28%) presented with disturbances in vision, 10 (35.71%) presented with diplopia, 8 (28.57%) presented with proptosis, 7 (25%) presented with epiphora, 6 (21.42%) patients presented with headache, 4 (14.28%) patients presented with cranial nerve deficits, and 4 (14.28%) patients presented with serous otitis media as shown in Table 2. Out of the 28 patients, 21 showed more than one symptoms. Other than important and common sinonasal symptoms such as nasal obstruction, epistaxis, and facial swelling, the less specific and important clinical presentations were found in these patients such as proptosis, hearing

Table 1: Ann arbor staging of lymphoma

Stage	Definition
I	Single location of extralymphatic involvement without involvement of lymph nodes
II	Extralymphatic involvement, regional lymph node involvement, and possible additional lymph nodes on same side of the diaphragm
III	Extralymphatic involvement, regional lymph node involvement, lymph nodes on both sides of diaphragm, no involvement of spleen
IV	Involvement of one or more extralymphatic sites or metastasis to liver, bone marrow, lungs, or cerebrospinal fluid
E	Extranodal invasion by contiguity
X	Large tumors (diameter >10 cm)
B	With symptoms such as weight loss, sweats, and fever

Table 2: Clinical presentations of patients with primary sinonasal non-Hodgkin's lymphoma

Symptoms	Number of patients, *n* (%)
Nasal blockage	23 (82.14)
Epistaxis	18 (64.28)
Unilateral nasal mass	18 (64.28)
Rhinorrhea	16 (57.14)
Facial swelling	15 (53.57)
Disturbances in vision	11 (39.28)
Diplopia	10 (35.71)
Proptosis	8 (28.57)
Epiphora	7 (25)
Headache	6 (21.42)
Cranial nerve deficit	4 (14.28)
Unilateral serous otitis media/hearing loss	4 (14.28)

loss, otitis media, granulations in nasal cavity, bulging of the palate, facial swelling, and visual disturbances. CT scans of the nose and paranasal sinuses were done in all the cases. Out of the 28 cases, 17 (60.71%) were seen in maxillary sinus, 5 (17.85%) cases seen in the nasal cavity, 4 (14.28%) cases seen in the ethmoidal sinuses, and 2 (7.14%) cases seen in the sphenoid sinuses. Out of the 28 cases, 9 cases (32.14%) showed bony erosion of the paranasal sinuses. Biopsy report of the sinonasal mass revealed diffuse large B-cell lymphoma in all the cases of the NHL. Ann Arbor staging showed Stage IE: eight cases (28.57%), IIE: 11 cases (39.28%), Stage IIIE: 6 cases (21.42%), and Stage IV: 3 case (10.71%). All the participants were treated with chemotherapy and/or radiation as per local guidelines. The patients were referred to the hemato-oncology department for the tumor staging and chemotherapy. The chemotherapy regimen of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) and radiation of 45–50 Gy at daily fractions of 1.8–2.0 Gy were given. Out of the 28 patients, 22 received chemotherapy followed by radiotherapy, three patients received only radiotherapy, two patients received only chemotherapy, and oldest patient (76-year-old) of this study avoided any form of treatment [Table 3]. The patient follow-up was done at 3 months, 6 months, 1 year, 1.5 years, and 2 years. The median follow-up duration for survival patients was 68 months (range: 21–152 months). Out of the 28 patients, 5 died from the disease, whereas rest of the patients freed from the disease.

Discussion

Although lymphoma is common in lymph nodes, it can also found in extranodal sites of patients.[9] Approximately one-third of extranodal lymphomas are seen in the head and neck region.[10] The common extranodal sites in the head-and-neck region for NHL are in Waldeyer's ring comprising tonsils, adenoids, tubal tonsils, and lingual tonsils.[11] The extranodal lymphoma is rarely found in sinonasal tract.[12] The sinonasal lymphoma constitutes only 0.2%–2% of the head-and-neck lymphomas.[10] The histologic types are mainly non-Hodgkin malignant lymphoma, particularly diffuse large B-cell lymphoma (DLBCL) and natural killer (NK) T-cell lymphoma are common variants.[13] In Caucasian populations, DLBCL is common, whereas NK/T cell lymphoma predominates in South America.[12] The histological pattern of the lymphoma in a study includes 82% DLBCL and 18% NK/T cell lymphoma.[12] NK/T cell lymphoma often affects the nasal cavities, whereas the DLBCL affects the paranasal sinuses.[14] In this study, all the cases were DLBCL which is the most common type of lymphoid malignancy in adults. DLBCL corresponds to a group of lymphoid malignancies consisting of large cells with vesicular nuclei, prominent nucleoli, and basophilic cytoplasm along with high proliferation rate. The etiology for NK/T cell lymphoma is associated with Epstein–Barr virus infection.[15]

The mean age for diagnosis of the sinonasal NHL ranges from 45 to 75 years with male predominance[10] as in this study with male-to-female ratio of 1.5:1 and mean age of 62.45 years which is consistent with previous study. The most common clinical presentations of the primary sinonasal NHL are nasal obstruction, unilateral swelling over the face and cheek, and nasal swelling.[10] Other less common symptoms are blurred vision or diplopia, headache, nasal bleeding, and pain over nose or cheek. Occasionally, patients presenting with symptoms such as nasal congestion and rhinorrhea mimic to the chronic sinusitis. The early diagnosis of the primary sinonasal NHL is usually rare because such lesions arise at the anatomical space and expands in paranasal sinuses or nasal cavity often cause no symptoms at the early period or stage of the disease. After reaching the considerable size, this tumor may present with symptoms and these may masquerade as other clinical findings of the nasal or head-and-neck diseases. This may be the cause for getting relatively advanced stage of the primary sinonasal NHL in population.

Table 3: Treatment options of the sinonasal non-Hodgkin's lymphoma

Treatment options	Number of patients, *n* (%)
Only radiotherapy	3 (10.71)
Chemotherapy followed by radiotherapy	22 (78.57)
Only chemotherapy	2 (7.14)
No active treatment done	1 (3.57)

The diagnostic endoscopic examination of the nasal cavity will assess the tumor size and extension of the mass to nasopharynx or origin either at the paranasal sinuses, nasal cavity, and nasopharynx. The morphological assessment of the lymphoma or its invasion is better assessed by contrast-enhanced CT scan. The imaging or radiographs of the nose and paranasal sinuses show bony erosion of the sinus walls because of the infiltrating pattern of the NHL in the sinuses.[16] In this study, out of the 28 cases, 9 cases showed bony erosion. High-grade B-cell lymphomas often cause destruction of the orbital soft-tissue and bone, whereas the perforation of the nasal septum is usually associated with high-grade type of the T-cell lesions.[16] Radiograph shows a definite mass or less commonly cloudy or opaque paranasal sinus. CT scan is useful and acts as gold standard investigation for evaluating the extent of the destruction and involvement of the paranasal sinuses and orbit. Immunohistochemical study with immune markers such as CD20, CD79a, bcl-6, MUM-2, CD3, CD5, CD10, and cyclic D1 and Ki-67 are used for the confirmation of the diagnosis.[17] An 18F fluorodeoxyglucose positron emission tomography CT reveals localized changes.

The treatment of the sinonasal NHL involves a team of clinicians including otolaryngologists, pathologists, radiologist, and oncologists. After proper evaluation of the patient, staging of the tumor is essential for recommending appropriate treatment. The treatment of primary sinonasal tract NHL is exclusively medical which are chemotherapy and/or external radiotherapy. The exclusive radiotherapy is the choice of the treatment in small tumor of size <5 cm.[10] In case of larger tumors, combination treatment of chemotherapy and radiotherapy are helpful.[14] The previous study documented that addition of chemotherapy significantly improves 5-year freedom from the progression of all the stages of the disease.[18] Previously, patients with NHL were treated with local radiotherapy had a better response, even complete tumor regression, but with high incidence of local recurrence and distant metastasis.[19] However, presently, combination of chemotherapy especially anthracycline-based regimen (i.e., CHOP) and local radiation leads to reduction of recurrence and metastasis, leading to overall improvement in survival without much side effects.[19] The common side effects of CHOP regimen are fatigue, alopecia, taste disturbance, mucositis, stomatitis, and nausea. In four of our patients developed neutropenia which needed transfusion of the blood products (granulocyte transfusion).[20,21] The causes of death in all of five patients are following development of neutropenic sepsis during treatment period.

Primary sinonasal NHLs are extremely rare lesions. The early diagnosis with staging and appropriate treatment are helpful to achieve the optimum outcome, and it is imperative that the clinical and otolaryngologists must be familiar with these clinical presentations and management. Early diagnosis along with high index of suspicion and newer treatment options such as high dose chemotherapy and stem cell transplantation.

Chemotherapy and immunotherapy with rituximab, CHOP (i.e., R-CHOP regimen) are also newer treatment options in sinonasal NHL.[22] The previous study reported that the prognosis of the lymphomas at the sinonasal region is better than the prognosis of the nodal lymphomas of the similar type of histologic grading.[23] One study showed that the 5-year survival of sinonasal NHL is 52% and the 5-year freedom from the progression is 57%.[24] The factors responsible for overall survival are the stage of the tumor and age of the patients. The early diagnosis and treatment are helpful for improvement of the treatment outcomes in patients with NHL Hodgkin's lymphoma of the sinonasal tract.

Conclusion

Primary sinonasal NHL is a rare clinical incidence in day-to-day clinical practice. It should be considered as a differential diagnosis of the sinonasal polyposis or chronic sinusitis. Hence, the clinician or otolaryngologist should keep in the mind the existence of the primary sinonasal NHL to avoid delayed diagnosis and treatment. Delayed diagnosis and treatment will lead to high morbidity and mortality of the patient. Although sinonasal NHL has nonspecific clinical presentations, it is very important to have a high index of suspiciousness to rule out NHL in the sinonasal tract as this disease is a curable lesion.

Study limitation

This study has a relatively small sample size and may limit the outcome of the above interpretation. However, the outcome of this study will surely encourage the future research work in the primary sinonasal NHL.

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Conflicts of interest

There are no conflicts of interest.

References

1. Boring CC, Squires TS, Tong T. Cancer statistics, 1993. CA Cancer J Clin 1993;43:7-26.
2. Budu VA, Tuşaliu M, Decuseară T, Bulescu IA, Popp CG, Panfiloiu A, *et al.* Sinonasal non-Hodgkin's malignant lymphoma – Review of a clinical case. Rom J Morphol Embryol 2017;58:181-5.
3. Cleary KR, Batsakis JG. Sinonasal lymphomas. Ann Otol Rhinol Laryngol 1994;103:911-4.
4. Neves MC, Lessa MM, Voegels RL, Butugan O. Primary non-Hodgkin's lymphoma of the frontal sinus: Case report and review of the literature. Ear Nose Throat J 2005;84:47-51.
5. Cheung MM, Chan JK, Lau WH, Foo W, Chan PT, Ng CS, *et al.* Primary non-Hodgkin's lymphoma of the nose and nasopharynx:

Clinical features, tumor immunophenotype, and treatment outcome in 113 patients. J Clin Oncol 1998;16:70-7.
6. Peng KA, Kita AE, Suh JD, Bhuta SM, Wang MB. Sinonasal lymphoma: Case series and review of the literature. Int Forum Allergy Rhinol 2014;4:670-4.
7. Fajardo-dolci G, Magaña RC, Bautista EL, Huerta D. Sinonasal lymphoma. Otolaryngol Head Neck Surg 1999;121:323-6.
8. Harris NL, Jaffe ES, Stein H, Banks PM, Chan JK, Cleary ML, *et al.* A revised European-American classification of lymphoid neoplasms: A proposal from the International Lymphoma Study Group. Blood 1994;84:1361-92.
9. López-Guillermo A, Colomo L, Jiménez M, Bosch F, Villamor N, Arenillas L, *et al.* Diffuse large B-cell lymphoma: Clinical and biological characterization and outcome according to the nodal or extranodal primary origin. J Clin Oncol 2005;23:2797-804.
10. Quraishi MS, Bessell EM, Clark D, Jones NS, Bradley PJ. Non-Hodgkin's lymphoma of the sinonasal tract. Laryngoscope 2000;110:1489-92.
11. Salplahta D, Comănescu MV, Anghelina F, Ioniţă E, Mogoantă CA, Anghelina L. Non-Hodgkin lymphomas of Waldeyer's ring. Rom J Morphol Embryol 2012;53:1057-60.
12. Kanumuri VV, Khan MN, Vazquez A, Govindaraj S, Baredes S, Eloy JA. Diffuse large B-cell lymphoma of the sinonasal tract: Analysis of survival in 852 cases. Am J Otolaryngol 2014;35:154-8.
13. Huang Y, Jia B, Jiang S, Zhou S, Yang J, Liu P, *et al.* Different clinical characteristics and treatment strategies for patients with localized sinonasal diffuse large B cell lymphoma and extranodal NK/T cell lymphoma. J Hematol Oncol 2017;10:7.
14. Hatta C, Ogasawara H, Okita J, Kubota A, Ishida M, Sakagami M. Non-Hodgkin's malignant lymphoma of the sinonasal tract – Treatment outcome for 53 patients according to REAL classification. Auris Nasus Larynx 2001;28:55-60.
15. Tababi S, Kharrat S, Sellami M, Mamy J, Zainine R, Beltaief N, *et al.* Extranodal NK/T-cell lymphoma, nasal type: report of 15 cases. Eur Ann Otorhinolaryngol Head Neck Dis 2012;129:141-7.
16. Yasumoto M, Taura S, Shibuya H, Honda M. Primary malignant lymphoma of the maxillary sinus: CT and MRI. Neuroradiology 2000;42:285-9.
17. Hans CP, Weisenburger DD, Greiner TC, Gascoyne RD, Delabie J, Ott G, *et al.* Confirmation of the molecular classification of diffuse large B-cell lymphoma by immunohistochemistry using a tissue microarray. Blood 2004;103:275-82.
18. Moin A, Shetty AD. Management of non-hodgkin's lymphoma in maxillofacial region with chemotherapy. ann maxillofac surg 2017;7:312-5.
19. Moganadass VV, Paul M, Marimuthu SG, Kalimuthu S. Primary extranodal non-Hodgkin's lymphoma of maxillary sinus: Rare incident. Eur J Rhinol Allergy 2019;2:61-3.
20. Swain SK, Sahu MC. An unusual presentation of nasofacial NK/T-cell lymphoma – A case report. Egypt J Ear Nose Throat Allied Sci 2017;18:299-302.
21. Burton GV, Atwater S, Borowitz MJ, Huang AT. Extranodal head and neck lymphoma. Prognosis and patterns of recurrence. Arch Otolaryngol Head Neck Surg 1990;116:69-73.
22. Nagafuji H, Yokoi H, Ohara A, Fujiwara M, Takayama N, Saito K. Primary diffuse large B-cell lymphoma of the frontal sinus: A case report and literature review. Radiol Case Rep 2018;13:635-9.
23. Vidal RW, Devaney K, Ferlito A, Rinaldo A, Carbone A. Sinonasal malignant lymphomas: A distinct clinicopathological category. Ann Otol Rhinol Laryngol 1999;108:411-9.
24. Logsdon MD, Ha CS, Kavadi VS, Cabanillas F, Hess MA, Cox JD. Lymphoma of the nasal cavity and paranasal sinuses: Improved outcome and altered prognostic factors with combined modality therapy. Cancer 1997;80:477-88.