

Primary Extranodal B-cell Lymphoma

Mohammed Asif Shaik, Shefali Waghray, Sultan Mohammed Kaleem, Surekha Morrthy, Naheeda Shaheen

ABSTRACT

Non-Hodgkin's lymphoma (NHL) constitutes a diverse group of lymphoid neoplasm that differs in manner of presentation, response to therapy and prognosis. They are less predictable and have a greater prediction to disseminate to extranodal sites. Their incidence has been increased over the last four decades and, head and neck is the second most common region for the extranodal lymphomas after that of gastrointestinal tract. Approximately 2.5% of malignant lymphomas arise in the oral and paraoral region. Generally, the oral manifestations of NHL are secondary to a more widespread involvement throughout the body. The cause of NHL is still unclear. Most of the lymphomas have been shown to be predominant of B-lineage. We present a case of a B-cell lymphoma with nodal and extranodal involvement.

Keywords: Non-Hodgkin's lymphoma, Extranodal lymphoma, B-cell lymphoma.

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INTRODUCTION

Non-Hodgkin's lymphoma belongs to a heterogeneous group of lymphoid neoplasms with a spectrum of behavior ranging from indolent to highly aggressive and potentially fatal neoplasm.¹ Majority of adult non-Hodgkin's lymphomas are of B-cell origin and they have a greater tendency to disseminate into extranodal tissue. The common primary extranodal sites of lymphoma include liver, intestine, bone marrow and soft tissue. The head and neck is the second most common region for extranodal lymphoma after gastrointestinal tract. Among various head and neck sites Waldeyer's ring, which is an area encompassed by the nasopharynx, the tonsil and the base of the tongue are most often involved by non-Hodgkin's lymphoma.² Patients of any age group can be affected. However, most patients are middle to older age with male preponderance. Death in these patients is due to sepsis or due to compression of the vital organs by the enlarged lymph nodes.³

CASE REPORT

A 60-year-old female patient reported to the Department of Oral Medicine and Radiology, Sri Sai College of Dental Surgery, Vikarabad, India with a chief complaint of multiple swellings on the right and left side of the face for 1 year (Fig. 1). Initially the patient noticed a small asymptomatic

swelling on the right side of the face which gradually progressed to present size. Apparently multiple swellings were noticed on the left side of the face which were gradually progressing in size. Subsequently, progressive swellings were noticed on either sides of the neck, in the inguinal and axillary region. Patient gave history of dysphagia, dysphonia and weight loss due to the swellings. Medical and family history was uneventful. On general physical examination multiple bilateral lymph nodes of the cervical region, the axilla and inguinal region were palpable which were soft in consistency, mobile and nontender in nature. Tender hepatosplenomegaly was noticed on examination. Extraoral examination revealed multiple nodular swellings on right and left angle of the mandible. The swellings on the right side of the face were extending superiorly from the tragus of the ear, inferiorly till the parasymphysis region. The swellings on the left side of the face were extending from the auricle till the symphysis region. On intraoral examination a single well-defined mass was noticed on the left side of the palate which was extending anteriorly from the marginal gingiva of the left central incisor posteriorly to the second molar region (Fig. 2). The mucosa over the swelling was ulcerated and the mucosa surrounding the ulcer was inflamed. Based on clinical presentation and general physical examination a provisional diagnosis of malignant lymphoma was given with a differential diagnosis of non-Hodgkin's lymphoma. Patient was referred for further investigations, where complete blood picture was within normal limits. The test for HIV and HBsAg was nonreactive. No abnormalities were detected in liver and renal function test. The ultrasound of abdomen revealed moderate

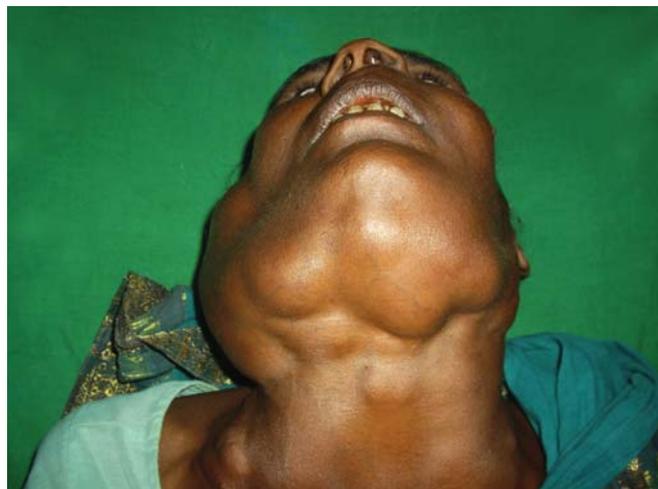


Fig. 1: Multiple swellings noticed on right and left side of the face

splenomegaly, with grade I parenchymal enlargement of kidneys and multiple nonhomogenous hypoechoic involvement of lymph nodes of diaphragm which suggested of generalized lymphadenopathy of the abdomen. The T1-weighted image of MRI revealed enlargement of lymph nodes of the maxillofacial region (Fig. 3). The full tissue biopsy of the cervical lymph nodes revealed pleomorphic proliferation of large cells with scant to moderate cytoplasm which was suggestive of intermediate grade type of non-Hodgkin's lymphoma. The CD20 immunohistochemical stain of the palate revealed diffusely arranged B lymphocytes suggestive of B cell non-Hodgkin's lymphoma (Fig. 4). The patient was referred to the cancer institute where she was first treated with chemotherapy (RCHOP – rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin and prednisolone) eight cycles in each 28 days interval followed by radiation therapy (4000 cGy for 4 weeks, 5 days a week). Unfortunately the patient could not survive due to the rapid dissemination of the disease.



Fig. 2: Single swelling seen on the left side of the palate

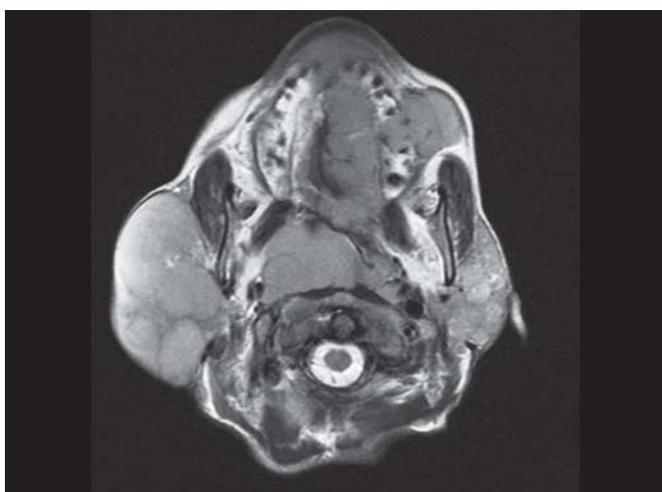


Fig. 3: T1-weighted image of MRI showing enlarged lymph nodes of maxillofacial region

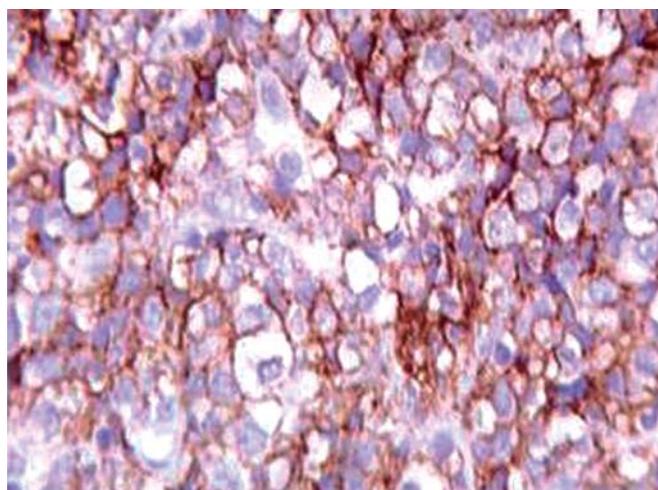


Fig. 4: CD20 immunohistochemical stain of palate showing diffusely arranged B lymphocytes suggestive of B-cell lymphoma

DISCUSSION

A substantial percentage of non-Hodgkin's lymphomas (NHL) arise from tissue other than lymph nodes and even from sites which normally contain no lymphoid tissue. These forms are referred to as primary extranodal lymphomas.⁴ It has recently been demonstrated that NHLs on the whole are showing a rapid increase in incidence which, at least in the USA during the past 20 years, they have been exceeded only by lung cancer among women and malignant melanomas in men.⁵ It is more common in males with a reported incidence of 19.2 cases per 100,000 populations in female.⁶ They can arise in almost every organ. Gastrointestinal involvement represents the most common form of extranodal lymphoma⁷ and the similar findings were observed in the present case. If tonsils and Waldeyer's ring are considered, head and neck localization is the second most frequent site of involvement averaging about one-fifth of all cases.^{6,7} The frequency of occurrence of NHL of the oral cavity and of the maxillofacial region is somewhat complex in this area there are sites where the frequency of occurrence of NHL is relatively common and sites where the frequency of occurrence is relatively uncommon. In contrast, the jaw involvement by NHL is rare. According to Rinnagio et al⁸ among jaw lesions the maxilla is more frequently involved than the mandible, with posterior locations favored over anterior site. Eisenbud et al reported 14 patients with NHL presenting in the jaw. Nine of the patients had lesions in the maxilla and five in the mandible.⁹ The etiology of non-Hodgkin's lymphoma remains unclear; several viruses have been implicated in the pathogenesis of non-Hodgkin's lymphoma.^{10,11} Environmental factors also seem to play a role in the development of non-Hodgkin's lymphoma. Certain chemicals have been linked to development of NHL which includes a variety of pesticides,

organic chemicals and wood preservatives. Thus, certain workers like pesticide applicators, workers in the petroleum, plastic and synthetic industries have slight increased risk of NHL. Immunodeficiency states that seem to predispose to NHL are HIV infection, iatrogenic immunosuppression for organ transplantation and connective tissue disorders.¹¹ Genetic abnormalities like nonrandom chromosomal and molecular rearrangements play an important role in the pathogenesis of many lymphomas. The most common chromosomal abnormality associated with NHL is the t(14;18) (Q32; Q21) translocation that is found in 85% of follicular lymphomas and 25 to 30% of intermediate grade of NHL.¹² Lymphadenopathy is the most common manifestation of NHL. Systemic symptoms like fever, night sweat, weight loss are noticed. About 20% of NHL shows evidence of spleen involvement at presentation and involvement of liver indicates advance disease.^{11,12} Numerous cases of NHL of oral cavity have been reported. In many instances, the oral involvement is the sole expression of the disease or the initial manifestation of generalized disease. NHL arising in the jaws frequently present with nonspecific signs and symptoms such as painless swelling or pain sometimes with numbness, paresthesia, loose teeth and cervical adenopathy.¹⁰⁻¹² Most of the patients with NHL involving the palate complain of dysphagia or sensation of a foreign body in the throat. Our patient also presented with a similar complains of dysphagia and foreign body sensation in the throat. Therefore the symptoms were similar to those of a squamous cell carcinoma and biopsy was performed for confirming the diagnosis of NHL. Usually hematologic and biochemical profiles of the patients are normal. MRI of the head and neck, chest, abdomen and pelvis is the mainstay for staging of NHL. However, concurrent positron emission tomography (PET) with 18F fludeoxyglucose (FDG) and computed tomography (PET/CT) is also a useful method for staging and assessment of the therapeutic response. The presence of positive staining for leukocyte common antigen (LCA) in histological specimen distinguishes malignant lymphoma from nonlymphoid neoplasm. However, diffuse large B-cell lymphomas are commonly positive for CD20 immunohistochemical stains and less commonly positive for germinal center cell markers CD10 and BCL6.¹³ The diagnosis of our patient was confirmed with the help of CD20 markers which was suggestive of diffuse large B-cell lymphoma. The aggressiveness of NHL can be correlated to its histological subclassification. The WHO modification of the revised European-American lymphoma (REAL) classification recognizes three major categories of lymphoid malignancies based on morphology and cell lineage.¹⁴ The categories include B-cell neoplasm, T-cell natural killer cell neoplasm and Hodgkin lymphoma. The NHL can be divided into two prognostic groups: The indolent lymphomas and

the aggressive lymphomas. Indolent NHL types have a relatively good prognosis, with median survival as long as 10 years, but they are not curable in advanced clinical stages. The aggressive lymphomas have a poor prognosis, with a median survival of 2 to 3 years. The treatment option for NHL depends on histological classification and clinical staging of the tumor. In general, the standard treatment for patients with diffuse large B-cell lymphoma is chemotherapy followed by involved field radiotherapy. As the early and initial dose of chemotherapy would prevent the spread of the disease and reduce the radiation field and radiation in most of the cases. RCHOP chemotherapy regimen is considered as a standard treatment for patients with advanced stage of diffuse large B-cell lymphoma.¹⁵ The similar regimen was prescribed for our patient. However, the patient could not survive due to the extensive spread of the tumor.

CONCLUSION

With an increase in the incidence of non-Hodgkin's lymphomas, it has become essential for an oral physician to be aware of this aggressive lesion to aid in the early diagnosis thereby contributing to an increased life expectancy of these patients. The diagnosis of these tumors is complicated by the nonspecific nature of the presenting symptoms. Henceforth, a proper clinical evaluation, histology as well as immunohistochemical evaluation of biopsy specimen may aid in early diagnosis and thus helps in proper management.

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