Non-Hodgkin's Lymphoma of the mandible in HIV patient - A Rare Case Report

Abstract
Non-Hodgkin's lymphoma (NHL) is a lymphatic system tumor originating from either B or T lymphocytes and shows a high malignant potential. In HIV-seropositive patients, NHL of head and neck is mainly found in Waldeyer’s ring, oral mucosa, salivary glands, paranasal sinuses, and laryngeal tissue. Primary NHL rarely affects the bone. When the lesion affects the bones of the jaws, it is rare in the mandible when compared to the maxilla. In the reported cases, only 0.6% are found in the mandible. NHL of the mandible can be difficult to diagnose, and so the prime aim of the present case report is to establish appropriate diagnosis of one of such kinds. Clinically, they may imitate a dental infection with symptoms of pain and discomfort. A delay in diagnosis may lead to a poor prognosis. Herewith, we present a case of NHL on the lower-right mandible in a 40-year-old male. A correlation of clinical findings, radiological examination, and histopathological examination enabled us in early diagnosis and differentiating it from other similar conditions, thus aiding in initiation of prompt treatment.

Keywords: Non-Hodgkin’s lymphoma, B-cell Lymphoma, mandibular swelling, Lymphocytes, HIV

Introduction
Non-Hodgkin’s lymphoma (NHL) is an uncommon neoplasm affecting the lymphopoietic section of the lymphoreticular complex. According to the Surveillance, Epidemiology, and End Results Stat Fact Sheets of the US National Cancer Institute, NHL constituted 4.3% of all new tumor cases and 3.4% of all deaths due to malignancy. The overall risk of contracting it over a lifetime was 2.1%. [1]

The clinical appearance of NHL depends on various factors such as the anatomical location, tumor growth rate, and the organ or tissue involved or displaced. However, although the clinical presentation may vary, the elements that are common include weight reduction, night sweating, anorexia; lymphadenopathy of cervical, inguinal, and axillary hubs. Related associated features may also include pressure on the contiguous tissue by enlarged lymph nodes. The adenopathy of the peripheral region may be slow in progression and can be painless. It is also noted that enlargement or regression of the lymph nodes can happen instantaneously. It might likewise present as asymptomatic in a few situations where the finding is incidental. [2]

The occurrence of NHL in bone is less than 5%, of which mandible accounts for only 0.6%. The etiology of this condition is obscure. Most common chromosomal abnormality associated with NHL is (14; 18) (q32; q21).

Autoimmune disorders are more common in women, but most NHL patients are men. [3] The standard regular finding is pain and swelling in the jaw bone, but quite often, the clinical diagnosis is made as dental infection. [4]

This report presents the clinical presentation of NHL in a middle-aged HIV-positive man with typical dental findings.

Case Report
A 40-year-old male patient, a tailor by profession, attended to the department of oral medicine and radiology, with a chief complaint of a swelling in the lower-right facial area for the past 1 month [Figure 1a]. At first, it began as a small swelling and gradually increased to the present size.

Medical history was positive for persistent weight reduction from 6 months and he also had occasional fever and cough. Family
history was noncontributory. Social history was positive for tobacco smoking. A general physical examination demonstrated that the patient was conscious, cooperative, well oriented, and moderately nourished with signs of anemia. The weight was 52 kg and temperature was 99°F. The extraoral examination revealed mild facial asymmetry with conspicuous bilateral submandibular lymph nodes in which a single, firm, and nontender node on the right side >1 cm fixed to the underlying structures was evident. The local examination also demonstrated a solitary swelling of size 4 cm × 5 cm on the right lower 1/3rd of the face with extension of the lesion 2 cm away from corner of the mouth to 2 cm in front of the tragus of the ear anteroposteriorly and ala-tragus line to mandibular angle superoinferiorly. The swelling was asymptomatic.

Intraoral examination uncovered an exophytic growth of size 5 cm × 6 cm extending out from teeth 44 to 48, which was covered by pseudomembranous slough and erythematous areas over the mucosa with everted margins [Figure 1a]. On palpation, it was tender and firm in consistency. Missing teeth in relation to 46 and 47 were also noted. The teeth were self-extracted by the patient. The remaining dental examination was not significant except with the grade 1 mobility in relation to 44 and mandibular anterior teeth. Based on the history and clinical findings, a provisional diagnosis of primary malignant neoplasm of the mandible was arrived. Differential diagnosis like tubercular granuloma, central mucoepidermoid carcinoma of the mandible, NHL, Hodgkin’s lymphoma, and osteosarcoma of the mandible were included.

A series of radiological and routine hematological investigations were performed. Radiological investigation included orthopantomography, right mandibular lateral occlusal view, magnetic resonance imaging (MRI) of the mandible, and chest posteroanterior X-ray. The mandibular occlusal radiograph uncovered ill-defined radiolucency in the right posterior alveolar ridge. The orthopantomography revealed an ill-defined lesion, with internal structure showing mild radiolucency along with displacement of adjacent teeth from position and missing molar teeth in the right mandibular posterior region. Chest posteroanterior X-ray revealed no significant abnormality. MRI (axial) revealed an irregular intermediate signal intensity mass lesion in the right mandible measuring 43 mm × 34 mm × 54 mm with destruction of the bone and a large extraosseous soft-tissue component with internal septa in the buccal space suggestive of slow-growing mass lesion with a cortical break [Figure 1b].

A routine hematological investigation revealed a decrease in hemoglobin% with an elevated erythrocyte sedimentation rate (ESR) above 45 mm/h when analyzed using Westergren’s ESR. Our laboratory investigation reported that the patient was HIV positive as per Tri-Dot method and it was confirmed by Western blot. An incisional biopsy was performed, and histologic evaluation depicted dense cellular connective tissue comprising of diffuse large lymphocytic tumor cells, which have rounded vesicles and nucleus with 2–3 nucleoli adjacent to the nuclear membrane. There is also the presence of hyperchromatic nucleoli, abundant mitotic figures, and severe vascularity along with extravasated red blood cells, all features suggestive of diffuse large-cell NHL [Figure 1c]. Correlating the history, intra- and extraoral examination, radiological and hematological investigation, and histopathological evaluation, a primary NHL of mandible was confirmed.

Postdiagnosis, the patient was referred to Cancer Institute for further treatment. Patient was started initially with ART along with the chemotherapy for the lesion. Further management of the patient was done by tapering the dose of the chemotherapy and with radiotherapy, as the patient developed complications associated with the AIDS and the chemotherapy given. On follow-up, it was noted that the patient expired due to complications of AIDS.

**Discussion**

NHL provides an early important clue for undiagnosed HIV infections. NHL contributes to around 2% of the neoplasms in oral cavity in patients with AIDS.[5] Groot et al. observed that NHL in HIV-infected patients is higher.[6] Colmenero...
et al. opined that NHL can be the first manifestation of HIV infection. They suggested that biopsy of any intraoral swelling or pathology in patients with AIDS is imperative to rule out NHL.[7] It must be noted that NHL is considered to be the AIDS-defining illness because of the close association between the two.[8,9] Most of these tumors have been found to be seen in AIDS patients. The occurrence of NHL in HIV population is almost two times more often than that in the general population.[9] The percentage of NHL in AIDS increased from 3.6% in 1994 to 4.9% in 1997 in Western Europe.[10] Viral oncogenesis may have a vital role in the development of this tumor, and this is the reason why NHL is found more frequently in immunocompromised patients.[11] It is thought that immune stimulation by HIV reactivation of previous Epstein–Barr virus infection due to defective T-cell surveillance lead to long-term stimulation and proliferation of B-lymphocytes, resulting in the development of AIDS-related NHL.[12,13]

The etiopathogenesis of NHL needs further understanding. Viral infections and immunological elements have also been proposed as major contributing factors. NHL of the mandible is an uncommon entity and majority of them attribute to the B-cell variants. This is characterized by pain and swelling in the jaw bone mirroring to any dental diseases like odontogenic infections, Chronic osteomyelitis, etc prompting to postpone the diagnosis many times, but biopsy of such confusing lesion may prove critical in delineating the disease and is vital for early diagnosis and management.[5,14]

In our case, apart from mild malnutrition, the patient did not show any other specific signs. Extraoral and intraoralexamination revealed mild asymmetry due to swelling and enlargement of lymph nodes.[15] Primary lymphomas consist of a heterogeneous group of neoplasms comprising of reticulosarcoma, lymphosarcoma, Burkitt’s lymphoma, and few other neoplasm of the lymphopoietic portion of the reticuloendothelial framework. It is more common in females. However, in our case, it was a middle-aged male. The occurrence of NHL is common in developed countries than developing nations. Among the developing nations, few of the middle-eastern nations show moderate-to-high intensity. In a study, it was uncovered that the average age-adjusted rate of incidence and percentage of annual change in adjusted rates of age for NHL by sex in five cities of India showed a statistically significant increase in number over a period of two decades.[16,17]

Ann Arbor staging [Table 1][15] is utilized for classifying the degree of illness and the international prognostic index is used to characterize the prognostic sub groups of the disease.[3] The risk parameter of NHL is computed by the International Prognostic Index for NHL.[18,19] Our present case was classified as immunoaffinity extraction (IAE).

NHL of the jaws demonstrates no pathognomonic, radiographic or clinical signs for easy identification. An incisional biopsy taken from the deep portion of the tumor is considered as a gold standard in the diagnosis and categorizing the subtype of this disease. A surface biopsy can delude as results may indicate chronic inflammation or necrosis. A histopathological assessment reveals layers of chronic inflammatory cells, overwhelmingly lymphocytes impersonating an inflammatory reaction. However, pleomorphic and atypical lymphoid cells are the characteristic histologic features of NHL, showing sheets of lymphoid cells infiltrating the bone with atypical mitotic figures, regions of sclerosis, hemorrhage, and necrosis. Immunochemistry helps in accurate diagnosis of the disease, and markers such as leukocyte common antigen (LCA) (CD45) and CD20 confirm the diagnosis.[20]

The management of NHL affecting head and neck relies on the Ann Arbor staging. An indolent assortment might be treated with radiation therapy alone, whereas a disseminated variety requires a combination of radiotherapy and chemotheraphy. Isolated lesions are managed by surgical enucleation. However surgery is combined with radiotherapy and chemotheraphy for better results. The prognosis of the disease depends on stage of the disease which has reported 5 year survival rate for 50% of cases in maxilla and mandible.[4,21]

The survival rate and prognosis depend on early diagnosis, and as dental professionals are the first to encounter such lesions in their patients, their role is vital.

**Conclusion**

NHL of the mandible can be a life threatening disease, as most of the times it carries a risk of delayed diagnosis due to its non-specific symptoms. The present case of isolated mandibular NHL-stage IAE is a rare case which proved to be fatal, also because of the implacable disease AIDS. Most of the patients can’t combat with this disease, as it is the AIDS along with NHL which gives grave prognosis. The oral presentation of NHL in this particular case unmasked the hidden HIV infection, as a diagnostic entity, thereby directing us to selective management of both entities. NHL of mandible warrants a multidisciplinary approach, with insights on its peculiar presentation, as a delay in diagnosis may be devastating.

**Table 1: Ann Arbor staging for lymphoma**

| Stage | Description |
|-------|-------------|
| Stage I | Disease in single lymph node or lymph node region |
| Stage II | Disease in two or more lymph node regions on the same side of diaphragm. Note: Stage II contiguous means two or more lymph nodes in proximity (side by side) |
| Stage III | Disease in the lymph node region on both sides of the diaphragm is affected |
| Stage IV | Disease is widespread, including multiple involvements at one or more extranodal (beyond the lymph node) sites, such as the bone marrow (which is involved commonly), liver, and pleura (thin lining of the lungs) |
Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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