Case Report

Extranodal Non-Hodgkin’s Lymphoma – An unfamiliar presentation in the oral cavity: A Case Report

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ABSTRACT

Non-Hodgkin’s lymphomas represent a group of lymphoid neoplasms that are multifarious and varied in their manner of presentation, response to therapy and prognosis. Oral manifestations present in only 3-5% of the cases of non-Hodgkin’s lymphoma and are rarely the initial manifestation of the disease. Although uncommon, it is essential to be wary of this neoplasm since intraoral manifestations are the sole presenting symptoms in some patients. A case of extra nodal non Hodgkins lymphoma in a 60 year old female involving the nasolabial area is hereby reported. The immunocytoc hemical marker studies were consistent with a B-lymphocyte lineage.

INTRODUCTION

Non–Hodgkin’s lymphomas are a group of neoplasms that originate from the cells of lymphoreticular system. Non Hodgkin’s lymphomas are the third most common group of neoplasms in the oral cavity and maxillofacial region. Majority of them are predominantly of B cell lineage. A proper clinical evaluation, histopathologic and immunohistochemical assessment may aid in the diagnosis and help in management of the disease at an early stage. An infrequent presentation of the same in a 60 year old female patient is hereby reported.

CASE PRESENTATION

A 60 year old female patient complained of a swelling in the upper front tooth region of one month duration. The swelling was insidious in onset, not preceded by trauma or toothache and was constantly and gradually increasing in size. There was no history of any discharge or paraesthesia in the region of complaint. There were no other associated symptoms. The medical and dental history was unremarkable.

Examination revealed a diffuse swelling measuring about 6X4 cms extending from the right nasolabial fold to the left infraorbital margin with obliteration of the philtrum and the nasolabial folds bilaterally. The swelling was non tender and firm in consistency. Intranasal examination divulged no abnormality. The regional lymph nodes were not enlarged or palpable.
Intraoral examination showed obliteration of the maxillary labial vestibule caused by the swelling extending from the canine tooth region bilaterally (Fig. 1).

![Fig. 1 – Swelling of the maxillary labial vestibule](image)

Mucosa over the swelling was intact and of normal color. No evidence of palatal expansion was noted. The swelling was non tender and firm upon palpation. Regional teeth exhibited deep attrition and abrasion, were Grade I mobile and non tender to percussion. Electric pulp testing of the same yielded a delayed response.

Relevant radiographs, failed to reveal the presence of any central or destructive lesion. CT scan of the maxilla showed a well defined soft tissue enhancing mass involving maxillary labial vestibule with no bone destruction with moderate contrast enhancement. The patient was anemic and seronegative for HIV. FNAC from the mass, both extraorally and intraorally showed sheets of small lymphocytes, lymphoid cells with clefted, convoluted and cleaved nuclei with coarse chromatin which was suggestive of an extra nodal non Hodgkin’s lymphoma. A biopsy from the intraoral mass disclosed a neoplasm composed of atypical lymphoid cells arranged in diffuse sheets. The neoplastic cells had indistinct cell margins with vesicular, pleomorphic nuclei and a prominent nucleolus. These findings were consistent with non Hodgkin’s lymphoma. On immunohistochemical staining, the neoplastic cells were positive for LCA, CD-20 (Fig 2) and negative for CD3, CD5, CD10 and Bcl-2 suggestive of a diffuse large B cell lymphoma. The proliferative marker Ki 67 disclosed 40% positivity.
The patient was then referred to a regional institute of oncology where a treatment of six chemotherapeutic regimens followed by involved field radiation therapy has been planned. The patient has received two cycles of the chemotherapy each comprising of Cyclophosphamide 900mg, epirubicin 120mg, oncovin 1.6mg administered IV and prednisone 60mg twice daily for 5 days and is reportedly doing well with a near complete resolution of the swelling involving the maxillary anterior vestibule (Fig. 3).
DISCUSSION

Malignant tumors arising from the lymphoreticular system are called lymphomas. They represent the third most common malignancies of the oral cavity after squamous cell carcinoma and salivary gland neoplasms.\textsuperscript{1,2} Lymphomas have been traditionally categorized as Hodgkin’s disease and Non Hodgkin’s lymphoma (NHL).

The non Hodgkin’s lymphomas include a diverse and complex group of malignancies of lymphoreticular histogenesis.\textsuperscript{3} They occur about thrice more commonly than Hodgkin’s disease and exhibit a greater predilection for dissemination to extra nodal tissues.\textsuperscript{4}

NHL is chiefly a disease of the adults with only 5% of the cases occurring in children. About 50% of the cases occur in individuals who are 65 years of age or older with a male preponderance. Malignant expansion of the B or T cells owing to cytogenic abnormalities is an important etiologic factor in NHL. Although the exact mechanisms remain unknown, chromosomal translocation is considered the genetic hallmark of lymphoid malignancies.\textsuperscript{5} The viruses commonly associated with NHL include EBV, HTLV-1, HHV-8 and Human type C retrovirus.\textsuperscript{4,5} A greater prevalence of NHL in immunocompromised persons has been recognized with the tumors favoring an extranodal site while exhibiting an aggressive behaviour.\textsuperscript{6} However, in our case the patient tested negative for HIV.

While the initial lesion may arise within the lymph nodes, extranodal presentations of NHL are not uncommon with occurrence in the intestine, liver, kidneys, testes, dura, bone, stomach, skin, bone marrow, sinuses and thyroid.\textsuperscript{2,7,8} Oral manifestations present in only 3-5% of the cases of NHL with the oral lesions being rarely the initial manifestation.\textsuperscript{9} This malignancy may develop in the oral soft tissues or centrally within the jaws.\textsuperscript{3} NHL most frequently affects the Waldeyer’s ring, of which the tonsils are most commonly affected. Other sites of occurrence includes the palate, gingiva, salivary glands, buccal vestibule, maxillary sinus.\textsuperscript{1,2,7} Among the jaw lesions, maxilla is more commonly affected than the mandible with a predilection for the posterior sites.\textsuperscript{1,10} In the case reported here, NHL presented as an extra nodal mass in the maxillary labial vestibule region without regional lymph node involvement.

About two-thirds of NHL cases manifest with non-tender lymphnode enlargement persisting for more than two weeks. Patients are classified as “A” (No symptoms) or “B” ( Constitutional symptoms)\textsuperscript{11}. “B” symptoms comprising of systemic signs and symptoms which include fever of unknown origin (>380C), unexplained weight loss (>10% over six months), drenching night sweats, visceral pain and malaise constitute the findings in 40% of the new cases.\textsuperscript{5} Accordingly, our case may be classified as belonging to the “A” type.

Lesions in the oral cavity may manifest as fluctuant swellings predisposed to ulceration. Other manifestations include pain, paraesthesia due to peripheral nerve involvement and tooth mobility.\textsuperscript{4} Individuals wearing dentures may complain of a progressive “tightness” of the affected prosthesis.\textsuperscript{10} In our case, the lesion manifested as a diffuse firm swelling in the maxillary labial vestibule with no evidence of pain or paraesthesia. Radiographic findings include diffuse ill-defined areas of bone destruction, loss of lamina dura, oblique/spiking root resorption.\textsuperscript{4,10} Involvement of the maxillary sinus can present as opacification with eroded cortical walls and a sinus mass in association.\textsuperscript{4} Other presentations may include lowering of
the alveolar bone margin to a condition resembling periodontitis or periodontal abscess. Some lymphomas may additionally exhibit osteoblastic activity giving rise to a mixed radiolucent radiopaque appearance. Our case demonstrated no significant radiographic findings except for a generalized moderate horizontal bone loss owing to the periodontally compromised status of the patient.

Differential diagnosis of NHL in the oral cavity may include odontogenic inflammatory processes, periodontal disease, squamous cell carcinoma or other oral soft tissue malignancies, tumors of the minor salivary glands, tumors of the jaws, benign lymphoproliferative disease and metastatic tumors.

The current and most widely accepted classification system of lymphomas is the Revised European American Lymphoma (REAL) scheme proposed by the International Study Group. This scheme broadly classifies lymphomas into B-cell and T-cell neoplasms and includes a number of entities that arise at extranodal sites. The most recent WHO classification divides NHL as indolent, aggressive and highly aggressive. The most frequently encountered type of NHL includes the diffuse large B-cell lymphoma (DLBCL) that has been classified under the category of aggressive lymphomas. Depending on the gene expression profiles, DLBCL’s has been classified as germinal center B cell like DLBCL’s and activated B cell like DLBCL’s.

Staging of NHL serves a number of important purposes such as determination of the type and intensity of therapy, the overall prognosis of the patient and the potential complications associated with the disease. The Ann-Arbor method is now widely used to stage NHL that takes into account the number of tumor sites involved.

The diagnosis of NHL can be made only by means of a biopsy. Paraffin or frozen section immunohistochemical studies are usually positive for at least one of the various available lymphoid markers. Expression of the cell surface antigens and immunoglobulin proteins depends on the type of lymphocyte and its stage of differentiation or maturation. Additional antibodies may be used to further delineate the subtype of lymphoma and tumor histogenesis. 28% of DLBCL’s depict chromosomal translocations and molecular rearrangements, such as translocation of t (14;18) (q32;q21). In the case presented, the neoplastic cells were positive for CD-20 indicative of a B-cell neoplasm.

Presently the treatment of DLBCL includes a multiagent chemotherapy, typically CHOP (cyclophosphamide, hydroxydoxorubicin, oncovin and prednisone). The role of surgery in DLBCL’s is limited. Patient’s with limited stage disease may receive chemotherapy followed by involved field radiation therapy(IFRT). High dose therapy with stem cell transplant support is the treatment of choice when relapse occurs. Radioimmunotherapy provides yet another novel therapeutic approach for relapse.

The reported 5 year survival rate of patients with NHL is 61.7%. Prognosis depends on the type of histopathologic variant, immunophenotype, staging and the response to therapy. The International Prognostic Index is the most commonly used to establish the prognosis.
CONCLUSIONS
In conclusion, a precise diagnosis of extranodal non-Hodgkin’s lymphoma necessitates appropriate clinical investigations including an immunohistochemical evaluation. Timely treatment promises the best possible prognosis and helps alleviating the physical and psychological morbidity associated with this disease.

CONSENT
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

COMPETING INTERESTS
The author(s) declare that they have no competing interests.

AUTHORS CONTRIBUTIONS
MVG rendered extensive contributions to the design, acquisition, analysis and interpretation of the data. KP and AR have been involved in drafting the manuscript. MVG and KP have given final approval of the version to be published.

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