ABSTRACT
Lymphomas are a malignant neoplasm of the lymphoid tissue. Although Non-Hodgkin’s Lymphoma is fairly common, primary non-Hodgkin’s lymphoma of the oral cavity, with no other nodal involvement in an immunocompetent patient is rare. They then mimic other odontogenic pathologies and pose a diagnostic challenge. An incisional biopsy helps nail the diagnosis in such cases. This paper reports a case of Primary Extranodal Non-Hodgkin’s Lymphoma of Maxilla in a 42 year old male patient and emphasizes the need for early and prompt referrals between physicians and dentists/maxillofacial surgeon which will aid in better prognosis of these rare entities.

Keywords: Extranodal; Maxilla; Non-Hodgkin’s Lymphoma;CHOP

Introduction
Lymphomas are malignant neoplasms affecting the lymphoreticular system. They are classified into Hodgkin’s and Non-Hodgkin’s Lymphomas. Hodgkin’s disease is characterised histologically by the presence of large multinucleated Reed-Sternberg cells. All other neoplasms of the lymphoid system are referred to as Non-Hodgkin’s Lymphoma (NHL) and are predominantly derived from cells of the B’ lymphocyte series. The cervical, axillary and inguinal lymph nodes are typically enlarged and non-tender associated with diffuse symptoms of fatigue and low grade intermittent fever. Extranodal NHL as a distinct entity was first described by Isaacson and Wright in 1983.

Only extranodal presentation of Hodgkin’s disease is rare and in contrast extranodal presentation of NHL is relatively common. However, NHL as a primary symptom in the oral cavity with no other lymph node involved in a healthy immunocompetent patient is rare. Extranodally, NHL can occur in stomach, bowel, skin, lung, orbital tissue, salivary glands, sinuses, thyroid, tonsil, breast, testis, kidneys and oral cavity.

Oral lesions of NHL may develop in soft tissue or centrally within the jaws. They appear as non-tender swellings developing slowly and mimicking a dental abscess of endodontic or periodontal origin. A lesion arising in bone may cause a vague pain mistaken for a toothache. Mucosal ulceration, anaesthesia and loosening of teeth may also be noticed. Sites typically affected in the oral cavity are palate, gingiva, tongue, buccal mucosa, floor of mouth, lips and cheek. Adults over the age of 60 years are most commonly affected, although children may be affected by the more aggressive, intermediate and high grade lesions. All subtypes show slight male predominance. This paper reports a case of Primary Extranodal Non-Hodgkin’s Lymphoma of Maxilla in a 42 year old male patient.

Case Report
A 42 year old healthy male patient was referred to the department of dentistry by a general physician with a chief complaint of swelling in the upper left vestibule over the lateral and canine region since the last three months. He also complained of slight heaviness in that area. Clinically there was a 3cm X 3cm swelling with no ulceration extending from upper lateral incisor to second premolar (Figure 1). Swelling was slightly fluctuant, smooth surface and non-tender. The lateral incisor and canine were tender on percussion. Patient was otherwise healthy with no other similar swellings elsewhere on his body.

Since the orthopantomogram (Figure 2) wasn’t very definitive in diagnosis except for slight radiolucency over the lateral incisor and thinking it to be an abscess related to carious, tender lateral incisor and canine teeth it was decided to treat these two teeth endodontically. As there was no change in the size of the swelling inspite of the root canals, an incisional biopsy was planned for this patient. On raising the mucoperiosteal flap the tissue was whitish grey, slimy and fragile and just slid down into the mouth in toto (Figure 3). Post-operative healing was uneventful.

Histologically, the biopsy revealed diffused infiltrative sheets of large round blue cells. Nuclei of the neoplastic cells were large (at least 3-4 times the size of the resting lymphocytes). Tumour cells were with round, irregular or cleaved nuclear contours, dispersed chromatin, several distinct nucleoli and modest amount of pale cytoplasm. Such cells resemble “centroblasts” the large cells that are seen in reactive lymphoid follicles (Figure 4-6). Immunohistochemistry demonstrated positive CD marker expression for B-cells (CD 20 and CD 79a) and negative results were obtained for T-cells (CD 3). Based on working formulation for classification of NHL a diagnosis of diffused large B-cell NHL was made.

The patient was then referred to a cancer tertiary care centre for further management. Routine blood investigations were normal. PET and CT Scans showed no metabolically active disease anywhere else in the body. Bone marrow biopsy and aspiration showed no involvement. 2D Echo was normal. Only a CT Maxilla revealed a residual 1.5 x 1.2 cm enhancing soft tissue mass and a focal defect. Based on the histologic, immunochemical and full body scans, patient was staged as 1AE (Ann Arbor) Non-Hodgkin’s Lymphoma. Diffuse large ‘B’ cell lymphoma (DLBCL), CD20/CD79a/CD30 positive.

He was treated with chemotherapy. Four cycles of R-CHOP (700 mg Injection Rituximab, 1400 mg Injection Cyclophosphamide, 2 mg Injection Vinristine, 90 mg Injection Doxorubicin, 2 mg Injection Vincristine, 90 mg Injection Doxorubicin, 500 mg Injection Cyclophosphamide, 700 mg Injection Rituximab, 1400 mg Injection Cyclophosphamide, 2 mg Injection Vinristine, 90 mg Injection Doxorubicin) were planned for this patient. On raising the mucoperiosteal flap the tissue was whitish grey, slimy and fragile and just slid down into the mouth in toto (Figure 3). Post-operative healing was uneventful.

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bian and 100 mg Tablet Prednisolone) followed by two cycles of injection Rituximab. During radiotherapy patient received a total dose of 45Gy/25F to the upper left alveolus and left maxillary sinus for consolidation of the lesion. The patient is now in remission and is being regularly followed up and is disease free over the last 24 months (Figure 7).

Discussion

NHL is the third most common malignancy in the oral cavity after squamous cell carcinoma and malignancy of the salivary gland. They are a group of highly diverse malignancy, having a great tendency to affect organs and tissues that do not ordinarily contain lymphoid cells. The exact cause of NHL is still unclear. Viruses could be a potential cause. Certain autoimmune diseases like rheumatoid arthritis, Sjogren’s syndrome could increase the risk of NHL. The risk of developing NHL is higher in patients with a weak immune system like HIV, many times the oral lesion of NHL may present as the first manifestation of AIDS. Patients receiving organ transplants may be at a higher risk of NHL. Among the non immuno-suppressed patients the most common type is diffuse large B cell lymphoma, but mantle cell lymphoma, marginal zone B-cell lymphoma, Burkitt’s lymphoma, lymphoblastic lymphoma, peripheral T-cell lymphoma and anaplastic large cell lymphoma also occur.

Classification of NHL can be quite confusing. There are various versions of lymphoma classification. Rappaport used until 1970, The International Working formulation of Clinical Usage of 1982, Kiel Classification of 1988, the Revised European-American Lymphoma (REAL) classification of 1994, the World Health Organization (WHO) classification of 2001, and the latest update of World Health Organization (WHO) of 2008 which is now used by most haematologist and oncologist. A simpler way of classifying NHL is depending on the cell of origin, either ‘B’ cell or ‘T’ cell. B cell lymphomas are far more common than T cell lymphomas. Classification of NHL’s is also based on clinical aggressiveness. They can be classified as Indolent lymphomas, Aggressive lymphomas, Highly-aggressive lymphomas and Special group of localized indolent lymphomas. Biopsy is critical in this classification. Once the NHL is classified it is staged and graded. They can be divided into either low grade or slow growing called Indolent NHL, Intermediate and High grade or fast growing are called Aggressive NHL.

Staging of patients is very important for their treatment and management. Patients are completely staged when adequate information is available on history, status of peripheral lymph nodes (physical examination), Waldeyer’s Ring (ENT Examination), mediastinal lymph nodes (Chest X-Ray), abdominal lymph nodes, liver, spleen, abdominal CT scan or lymphography, Fluoro Deoxy Glucose (FDG) – PET (Positron Emission Tomography) – CT is a useful tool for staging and diagnosing NHL patients, supplemented with isotope liver and spleen scan as well as peripheral blood and bone marrow cytology and histology. Ann Arbor staging system has four stages, most extra-nodal head and neck NHL fall into stage IE if localized and additional suffix, A - absence of systemic signs or B - unexplained weight loss > 10%, or fever or night sweats. The incidence of oral manifestation of NHL according to international literature is approximately 2% of all extranodal lymphomas. However, Gunjan Shah et al found it to be a rare disease and oral NHL in the Indian subpopulation is more aggressive as compared to Western literature.

The diagnosis of extranodal lymphoma is challenging due to its low index of clinical suspicion when oral soft tissue lesions first appear, they generally appear as non-tender soft to firm swelling with overlying ulceration many a times leading to misdiagnosis. They are confused with pyogenic granuloma, periodontal abscess, osteomyelitis and other malignancies. Incisional biopsy is a definitive diagnostic modality. Biopsy needs to be coupled with immunological studies of the biopsy tissue. Lymphoma malignancy prognosis is revealed by the following factors, age, performance status, number of extranodal sites involved, Ann Arbor stage, and serum level of lactate dehydrogenase (LDH), all of which make up the International Prognostic Index (IPI). This index has allocated NHL patients into two well defined prognostic groups, Good Prognosis (low and low intermediate risk) and Poor Prognosis (intermediate high and high risk). Survival is excellent in localized disease and is less favourable in disseminated disease.

Conclusion

In conclusion, Non-Hodgkin’s Lymphoma of the oral cavity although rare, should be considered in the differential diagnosis of lesions around the oral cavity. A biopsy of the lesion coupled with histopathological and immunological studies of the specimen is the only way to confirm the diagnosis of this challenging entity. The Maxillofacial Surgeon thus plays an important role in detecting this lesion early and improving the prognosis.

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Primary Extranodal Non-Hodgkin’s Lymphoma of Maxilla - A Case Report

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