

Non-Hodgkins lymphoma – A case report and review of literature

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Abstract

Lymphomas are solid tumors of the immune system and include 14% of all head and neck malignancies. Non-Hodgkin lymphomas (NHLs) are a heterogeneous group of lymphoproliferative disorders originating in B-, T-, or natural killer T-cells. They have a wide range of histological appearances and clinical features at presentation, which can make diagnosis difficult. A 58-year-old male patient presented with a 1-month history of swelling in the upper right back tooth region, which developed after extraction. On intraoral examination, there was small nodular lesion proliferation from the extracted socket. Biopsy specimen on histological examination revealed sheets of small round cells with hyperchromatic nucleus resembling lymphoblast. Immunohistochemistry (IHC) confirms the NHL of T-cell origin. This article is an attempt to correlate the clinical presentation and histological importance of small round cell tumors of the jaw and to discuss the differential diagnosis of small round cell tumors. Typically, a multimodal approach is employed, and the principal ancillary technique that have been found to be useful in classification is IHC.

Keywords: Immunohistochemistry, non-Hodgkin lymphoma, T-cell lymphoma

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INTRODUCTION

Lymphomas are a heterogeneous group of malignancies arising from lymphocytes. Over recent years, improved clinical, pathological and molecular data have helped guide an evolution in the classification of lymphomas that is reflected in the 2016 revision of the World Health Organization (WHO) classification. This recognizes >40 mature B-cell neoplasms and >25 mature T-cell and natural killer (NK)-cell neoplasms.^[1] Non-Hodgkin lymphoma (NHL) includes all lymphomas, except Hodgkin's lymphoma (HL). During the past three decades, there have been consistent reports of an increase in the incidence of NHL worldwide. The incidence rates are

about 1.5 times higher in men than in women. The average age at diagnosis is about the sixth decade of life, although certain subtypes of NHL, such as Burkitt lymphoma and lymphoblastic lymphoma, have been diagnosed at a younger age.^[2]

Lymphomas present themselves as enlarged nontender lymph nodes but may involve extranodal regions, commonly involving the gastrointestinal tract and head and neck. Extranodal involvement is much less common in HL than in NHL.^[3]

Recent advances in molecular genetics have significantly deepened our understanding of the biology of these diseases.

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The introduction of gene expression profiling, especially has led to the discovery of novel oncogenic pathways involved in the process of malignant transformation. Equally important, these analyses have identified novel molecular lymphoma subtypes that are histologically indistinguishable.^[4] There is a significant distinction in the clinical course of germinal center B-cell-like, diffuse large B-cell lymphoma (DLBCL), and activated B-cell-like DLBCL, as they have a huge variation in the survival rates after standard treatment.

CASE REPORT

A 58-year-old male patient reported to the college with a chief complaint of swelling and pain in gums in the right upper back tooth region for the past 1 month. Lesion initially started as a small swelling and gradually increased to the present size. Medical history was positive for epistaxis a month back and blood on coughing for 1 month. The patient also gave a history of extraction 2 months in that region after he noticed a loosening of his teeth, which was uneventful. Family history was noncontributory. Extraoral examination revealed mild swelling in the middle-third of the face on the right side [Figure 1].

Intraorally, single large, noduloproliferative growth was seen on the right maxillary ridge, extending from the right second premolar region to maxillary tuberosity area and also up to mid-palate region not crossing the midline [Figure 2]. It was tender on palpation. There was presence of soft-tissue mass protruding from the extraction socket behind 14. The overlying mucosa was reddish pink. The swelling was sessile with ill-defined borders, reddish pink in color and was firm in consistency. Regional lymph nodes were not palpable.



Figure 1: Extraoral photograph showing mild extraoral swelling on the right side of the face

Based on the history and clinical findings, a provisional diagnosis of nasopharyngeal carcinoma of maxillary antrum with a differential diagnosis carcinoma of maxillary antrum was made.

A series of radiological and routine hematological investigations were performed. Radiological investigation included orthopantomography and paranasal sinus view. The orthopantomograph revealed loss of maxillary antral bone with ragged borders on the right side. The bone loss is evident up till the floor of the right orbit. There was presence of soft-tissue shadow over the alveolar ridge with complete destruction of the alveolar bone on the right side. Coronoid and condylar processes were normal [Figure 3a]. Para nasal sinuses view showed destruction of the superior, lateral, and facial wall of the right maxillary antrum, expansion of the malar bone on the right side laterally with involvement of middle and inferior nasal conchae medially. Furthermore, there was destruction of the right infraorbital margin with the haziness of both antra [Figure 3b]. Routine hemogram analysis, urine analysis, and X-ray chest were normal. The patient was negative for HIV and hepatitis B virus.

Incisional biopsy under local anesthesia was done. Microscopic pictures revealed squamous mucosa with underlying connective tissue composed of diffuse, uniform monotonous proliferation of small, round cells with large darkly staining nucleus, and little eosinophilic cytoplasm resembling lymphocytes in loose fibrocellular stroma and comedo necrosis suggestive of lymphoproliferative disease [Figure 4].

Immunohistochemistry (IHC) was performed [Figure 5]. Markers used were CD45 and CD20 which revealed CD45 positivity in tumor cell indicating the tumor cell is



Figure 2: Intraoral swelling seen on the right maxillary ridge

hematopoietic in origin and was CD20 negative indicating that it is not B-lymphocytic in origin.

Based on the above findings, a diagnosis of NHL of T-cell origin was made.

Surgical excision of the lesion was done under general anesthesia, and postoperative radiotherapy and

chemotherapy were planned. A follow-up of 2 years revealed no local relapse.

DISCUSSION

Malignant small round cell tumors is a term used for tumors composed of malignant round cells that are slightly larger or double the size of red blood cells in air-dried smears. This group of neoplasms is characterized by small, round, relatively undifferentiated cells. They generally include Ewing's sarcoma, peripheral neuroectodermal tumor, rhabdomyosarcoma, synovial sarcoma, NHL, retinoblastoma, neuroblastoma, hepatoblastoma, and nephroblastoma. Other differential diagnoses of small round cell tumors include small cell osteogenic sarcoma, undifferentiated hepatoblastoma, granulocytic sarcoma, and intraabdominal desmoplastic small round.^[5] Accurate diagnosis of these cancers is essential because the treatment options, responses to therapy, and prognoses vary widely depending on the diagnosis, and therefore, investigations are needed.

Lymphoma is a general term for a complex group of malignancies of the lymphoreticular system. These malignancies initially arise within the lymphatic tissues and may progress to an extranodal mass (NHL) or to a nontender mass or masses in a lymph node region (HL) that later may spread to other lymph node groups and involve the bone marrow. Lymphoma in the oral soft tissues usually presents as an extranodal, soft to firm asymptomatic lesion, although the mass may also be painful.^[6]

The WHO modification of the Revised European-American Lymphoma Classification recognizes three major categories of lymphoid malignancies, which are B-cell lymphoma, T-cell/NK cell lymphoma, and Hodgkin's lymphoma. NHL is one of the possible cancers in the head-and-neck region, and among extranodal NHLs, this is the second most common site after the gastrointestinal tract. In the head and neck, Waldeyer's ring is the most common site of origin and may be accompanied by cervical node involvement. Nose, paranasal sinus, orbits, and salivary glands are other possible organs affected in decreasing order of frequency, with rare spread to the regional lymph nodes.^[3] NHL has long been recognized as a heterogeneous group of disorders based on clinical presentation, morphological appearance, and response to therapy. In recent years, the use of immunological and molecular biological techniques has led to important advances in our knowledge of lymphocyte differentiation and has provided the basis for a better understanding of the

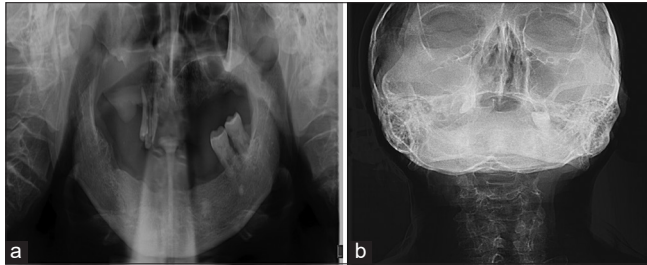


Figure 3: (a) Orthopantomograph, (b) PNS view

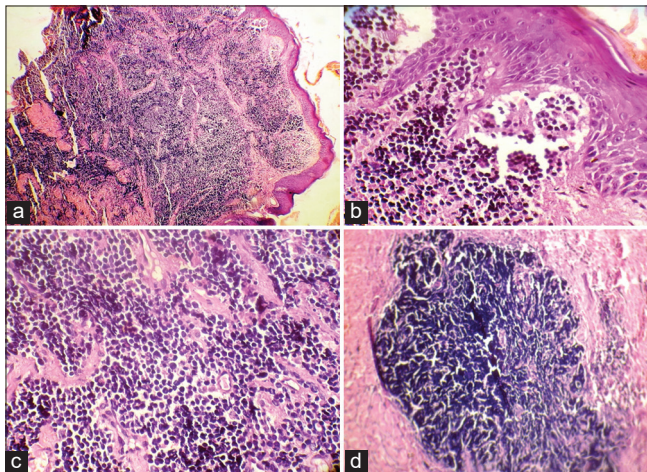


Figure 4: (a-c) Photomicrographs showing squamous mucosa with underlying connective tissue composed of lymphocytes in loose fibrocellular stroma (H&E stain), (a) $\times 4$, (b) $\times 10$, (c) $\times 10$

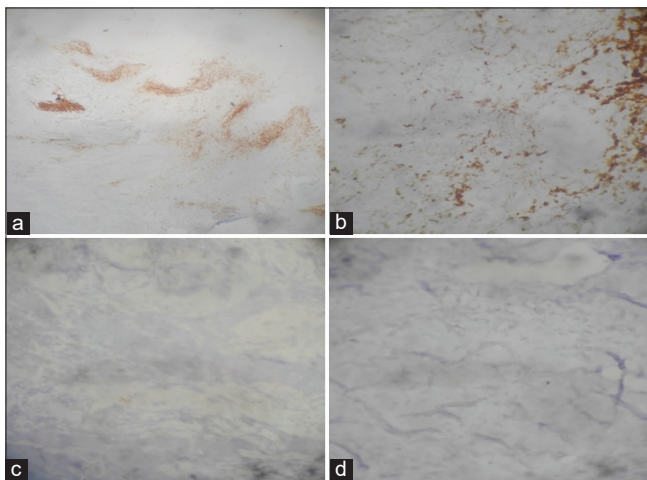


Figure 5: (a and b) CD45, (immunohistochemistry stain, $\times 4$, $\times 40$) (c and d) CD20 (immunohistochemistry stain, $\times 4$, $\times 40$)

cellular origin and pathogenesis of NHL.^[6] Various types of NHL represents neoplastic cells arrested at various stages in the normal differentiation scheme or the gain of a proliferative or anti-apoptotic abnormality, whose precise phenotype depends on the developmental stage, at which the lymphocyte is affected.

T-cell NHLs are uncommon malignancies that represent approximately 12% of all lymphomas.^[7] There are no characteristic clinical features of lymphomas of the oral region, and they depend on the site of the swelling, the lymph node involvement, and/or the presence of metastasis. The most common beginning symptoms are local mass, pain or discomfort, dysphagia or sensation of a foreign body in the throat, in the case of tonsillar NHL.^[5] T-cell NHL commonly presents with extranodal disease and often contains varying amounts of necrosis/apoptosis on biopsy specimens, making differentiation between a reactive process and lymphoma challenging. Immunophenotypic, cytogenetic, and molecular analyses have enhanced diagnostic capabilities and improved classification and prognostication for T-cell NHL. There are 28 different established and provisional mature T-cell/NK cell entities in the 2016 WHO classification of lymphoid neoplasms, broadly subdivided into two groups: peripheral T-cell lymphoma and cutaneous T-cell lymphoma.^[8]

IHC is an integral part of the diagnostic hematopathology. IHC with various antibodies identifies the specific lineage and developmental stage of the lymphoma. Panel of markers is decided based on morphologic differential diagnosis (no single marker is specific), which includes leukocyte common antigen (LCA), B-cell markers (CD20 and CD79a), T-cell markers (CD3 and CD5), and other markers such as CD23, bcl-2, CD10, cyclinD1, CD15, CD30, ALK-1, and CD138 (based on cytoarchitectural pattern).^[9]

Basic immunohistochemistry panel for non-Hodgkin lymphoma

- Expression of CD45 (LCA) rules out an epithelial tumor and suggests the tumor is of hematopoietic origin.

NHL is further subclassified based on the stage of maturation (immature vs. mature) and the cell of origin (B-cell, T-cell, or NK cell).

- CD20 is the most widely used pan-B-cell marker
- CD3 is the most commonly used pan-T-cell antigen
- CD4 is for helper T-cells, CD8 for suppressor cells, and CD57 for NK cells.

In our case, apart from epistaxis and blood after coughing, the patient did not show any other specific signs. Extraoral examination revealed mild facial asymmetry. Primary lymphomas are more common in females. However, in our case, it was an old-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.^[10]

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 chemotherapy. Isolated lesions are managed by surgical enucleation. However surgery is combined with radiotherapy and chemotherapy for better results. The prognosis of the disease depends on the stage of the disease, which has reported 5-year survival rate for 50% of cases in the maxilla and mandible.^[10]

CONCLUSION

Small round cell tumors are difficult to distinguish by light microscopy, and currently, no single test is available, which can precisely distinguish these tumors. Hence to confirm the diagnosis, pathologists should go for several other techniques like IHC. IHC for individual protein markers is used to establish the diagnosis in many instances, and its accuracy rate is also quite satisfactory. Thus, IHC can be helpful in narrowing the differential diagnosis of small round cell tumors, so as the treatment outcome.

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.

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Conflicts of interest

There are no conflicts of interest.

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