

A rare case of high-grade non-Hodgkin's lymphoma with oral and multiple extranodal manifestations

ABSTRACT

Lymphomas are a group of malignant diseases affecting the lymphoreticular system. Lymphoma is the second most common neoplasm of the head and neck after squamous cell carcinoma, but the incidence of lymphomas in the oral cavity and orbit is rare. Non-Hodgkin's lymphoma (NHL) is less predictable than Hodgkin's but has a greater predilection to extranodal tissues. Non-Hodgkin's incidence in extranodal sites accounts for about 20% to 30%, but in the oral cavity, its around 0.1% to 5%. The rarity of incidence in the oral cavity and atypical radiographic features diagnosing a lymphoma is quite a challenge for clinicians. Here we describe a case of 31-year-old male patient with high-grade non-Hodgkin's lymphoma involving oral cavity with metastasis to orbit, skeletal structures, testes, liver, pancreas and nasopharynx, which is quite rare.

Keywords: Extranodal tissues, lymphoma, non-Hodgkin's lymphoma, oral cavity

INTRODUCTION

Lymphomas can be simply defined as malignant neoplasms of lymphocytes and their precursor cells. It has been known traditionally to divide lymphomas into Hodgkin's disease (HD) and non-Hodgkin's lymphomas (NHLs) based on their biological, histological, immunophenotypical differences, and clinical behavior patterns.^[1-4]

Lymphoma is the second most common neoplasm of the head and neck after squamous cell carcinoma,^[2] while in the oral cavity it is preceded by squamous cell carcinoma and salivary gland neoplasm.^[5,6] Lymphoma arising within the oral cavity accounts for less than 5% of all oral malignancies, and approximately 85% of the lesions involve the tonsils and the palate.^[6]

Here we are presenting a case of high-grade non-Hodgkin lymphoma with involvement of palate and metastasis to orbit, testes, skeletal structures, liver, pancreas, and nasopharynx which is quite rare.

CASE REPORT


A 31-year-old gentleman reported to the Department of Maxillofacial Surgery with swelling in the palate bilaterally since 1 month [Figure 1]. He gave a history of root canal treatment done two months back in the upper left back teeth region, following which he noticed the swelling in the palate initially on the same side, which later appeared on the opposite side too. He gave a history of swelling to be small in size, limited to the alveolus, later on extending

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to the midline of the palate, resulting in dysphagia. The patient underwent root canal treatment in relation to 26 two months back. Grade III mobility was noticed in teeth 16, 17, 26, 27 (FDI tooth numbering system), with swelling extending from alveolus to midline of palate bilaterally. The patient had also noticed a swelling in the right hand and scrotum since 1 month with a loss of 10 kg within 3 months.

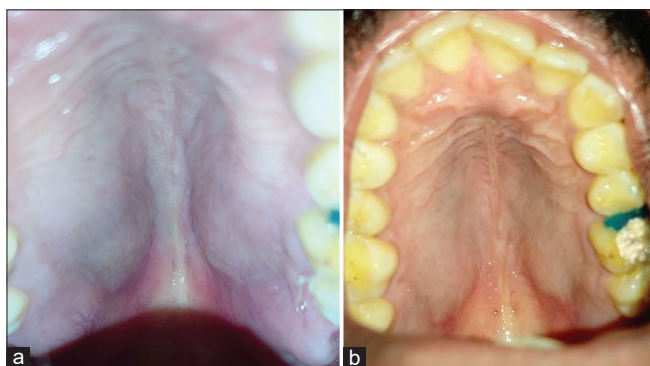


Figure 1: (a) Close view (b) Full mouth view, swelling in palate bilaterally

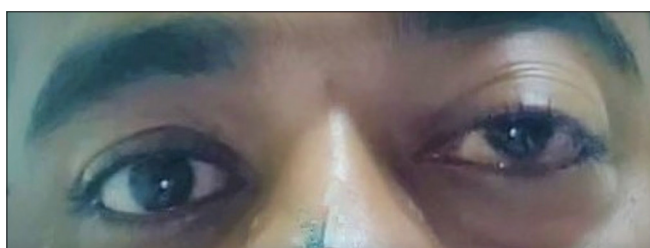


Figure 2: Proptosis of the left eye

These symptoms were followed by the proptosis of left eye [Figure 2] and paresthesia of the left side of the face. The patient was then referred to the Department of Orthopaedics, Urology and Ent for the concerned signs and symptoms.

A CECT Abdomen was done, which showed the presence of liver and pancreatic lesions with the possibility of lymphoma metastasis [Figure 3]. For the swelling of the right hand, X-ray was taken; it appeared as multiple punched out lesion on the 5th metacarpal [Figure 4]. Following this, an MRI of the right hand was also done which confirmed the presence of a lesion in the 5th metacarpal with inflammation around it [Figure 5]. computerized tomography of paranasal sinus indicated complete mucosal thickening in bilateral maxillary antrum with mucosal thickening extending to the right nasal cavity and choana. Also, mucosal thickening involving maxillary ostia and ethmoidal infundibulum causing obstruction of the bilateral osteo-meatal unit with widening and erosion on right side [Figure 6]. Following this, a diagnostic nasal endoscopy was performed, suggesting the presence of lymphoid tissue in the nasopharynx [Figure 7]. Biopsy was taken from the right 5th metacarpal, right testes, left maxillary sinus, and nasopharynx simultaneously by the Department of Orthopaedics, Maxillofacial Surgery and Ent reported to be malignant round cell tumor with the possibility of lymphoma. Routine blood investigations were performed indicating high levels of LDH (lactate dehydrogenase). Based on the results from investigation, we further evaluated the patient with PET CT scan.



Figure 3: CECT Abdomen showing (a) Liver with hypodense, hypoenhancing lesion in right lobe in segment 8 in close contact with Inferior Venacava and cardiac base. (b) Hypodense enhancing lesion in uncinated process of pancreas extending to pancreatico-duodenal groove and multiple small hyperdense lesions in both kidneys

The PET CT showed the following findings [Figure 8]:

Hypermetabolic enlarged lymph nodes in right lower paratracheal, right axillary, abdominal paraaortic, aortocaval, mesenteric, and paracaval regions.

Intensely hypermetabolic soft tissue lesion in extraconal space in the left orbit causing mass effect on the left eyeball.

Hypermetabolic soft tissue thickening in the left ethmoidal sinus.



Figure 4: X-Ray of the right hand with multiple punched out lesions in 5th metacarpal



Figure 5: MRI of hand showing lesion around 5th metacarpal with inflammation of tissues around it. (a) Coronal view. (b) Transverse view



Figure 6: CT PNS showing complete mucosal thickening in bilateral maxillary antrum extending to right nasal cavity and choana. Also, mucosal thickening involving maxillary ostia and ethmoidal infundibulum causing obstruction of bilateral osteo-meatal unit with widening and erosion on the right side

Intensely hypermetabolic ill-defined soft tissue lesions in bilateral infratemporal fossae, around pterygoid plates and posterior aspect of the maxilla on both sides, extending through bilateral pterygopalatine fossae into bilateral nasal cavity and reaching upto nasopharynx (on the right side) as well as involving soft palate and base of the tongue along with thinning and rarefaction of posterior alveoli, medial and posterolateral walls of the maxillary sinus.

Increased metabolic activity around cricoid cartilage and left lamina of the thyroid cartilage.

An intensely hypermetabolic hypodense lesion with central necrosis in segments of the liver.

Mild diffuse increased metabolic activity in bulky spleen.

Multiple hypermetabolic hypodense lesions of varying sizes in both kidneys.

Hypermetabolic lesion involving right testis and increased metabolic activity in left testis

Hypermetabolic soft tissue nodule in the right lumbar region.

Multiple sites of increased metabolic activity in the axial and appendicular skeleton, few show subtle sclerotic changes.

An Immunohistochemistry from trucut biopsy of right testes showed positive for CD 20, Bcl 2, CD 10, Mum I (approx. 60%) with a Ki 67 index of 80-85% while negative for CD 5, Bcl 3, CD 3, Tdt, cMyc, Cyclin D1, CD 23, CD 30 features were consistent with high-grade lymphoma.

The patient underwent eight cycles of chemotherapy with R MCP 842 protocol followed, by which the lesions resolved based on follow up PET CT [Figure 8].

DISCUSSION

Lymphomas are a set of malignancies with pathological behavior ranging from indolent to aggressive and are potentially fatal.^[7]

These malignancies initially arise within the lymphatic tissues and may progress to an extranodal mass (Non-Hodgkin's lymphoma) or to a nontender mass or masses in a lymph node region (Hodgkin's lymphoma) that later may spread to other lymph node groups and involve the bone marrow. Hodgkin's lymphoma corresponds to 14% of all lymphomas,^[8] while Non-Hodgkin's corresponds to 86%.^[9,10] Lymphomas originate in B-cell lines and, less commonly, in T-cell lines.

The most widely used classification of lymphoma is the Ann Arbor staging classification [Table 1], which is based on the anatomic extent of the involvement. This staging was initially introduced for Hodgkin's lymphoma and was later adopted for the classification of NHL.^[11]

The etiology of NHL is unknown.^[2] Several risk factors have been found to increase the incidence of disease. The

risk factors include exposure to pesticides and radiation, long-term immunosuppression, and autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, and Sjögren syndrome.^[12] Also, certain viruses have been suggested as potential causes for this disease,^[2] including the Epstein-Barr virus (EBV), Human T-cell lymphotropic virus 1 (HTLV-1), Human immunodeficiency virus (HIV), Human Herpes virus type 8 (HHV-8, HVSK)^[13] and Hepatitis B, C, and G virus (HBV, HCV, and HGV).^[14] Other microorganisms involved in the genesis of the NHL are *Helicobacter pylori* and Chlamydia.

Extranodal presentations are common in patients with NHL, but the intraoral presentation of lymphoma is an uncommon occurrence.^[6] Also, lymphomas involving the orbits are rare. Common sites of extranodal manifestations are the gastrointestinal tract, especially the ventricle, pharynx, thyroid gland, and skin. In the head and neck region, the most common site is Waldeyer's ring.

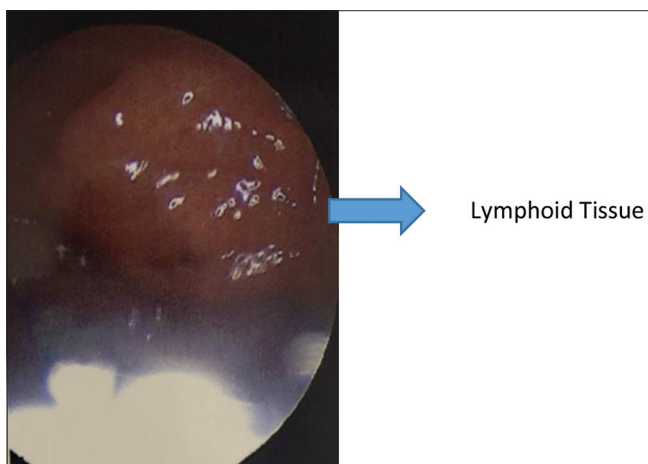


Figure 7: Diagnostic nasal endoscopy depicting presence of lymphoid tissue in nasopharynx

Table 1: Clinical staging of Hodgkin's and non-Hodgkin's lymphomas (Ann Arbor classification)

Stage	Distribution of Disease
I	Involvement of a single lymph node region (I) or involvement of a single extralymphatic organ or site (IE)
II	Involvement of 2 or more lymph node regions on the same side of the diaphragm alone (II) or with involvement of limited contiguous extralymphatic organ or site (IIE)
III	Involvement of lymph node regions on both sides of the diaphragm (III), which may include the spleen (IIIS) and/or limited contiguous extralymphatic organ or site (IIIE, IIIES)
IV	Multiple or disseminated foci of involvement of one or more extralymphatic organs or sites with or without lymphatic involvement

A: asymptomatic. B: presence of B symptoms (including fever, night sweats, and weight loss of $\geq 10\%$ of body weight over 6 months). E: involvement of a single, extranodal site, contiguous or proximal to a known nodal site (stages I to III only; additional extranodal involvement is stage IV). S: splenic involvement. X: bulky nodal disease: nodal mass $> 1/3$ of intrathoracic diameter or 10 cm in dimension

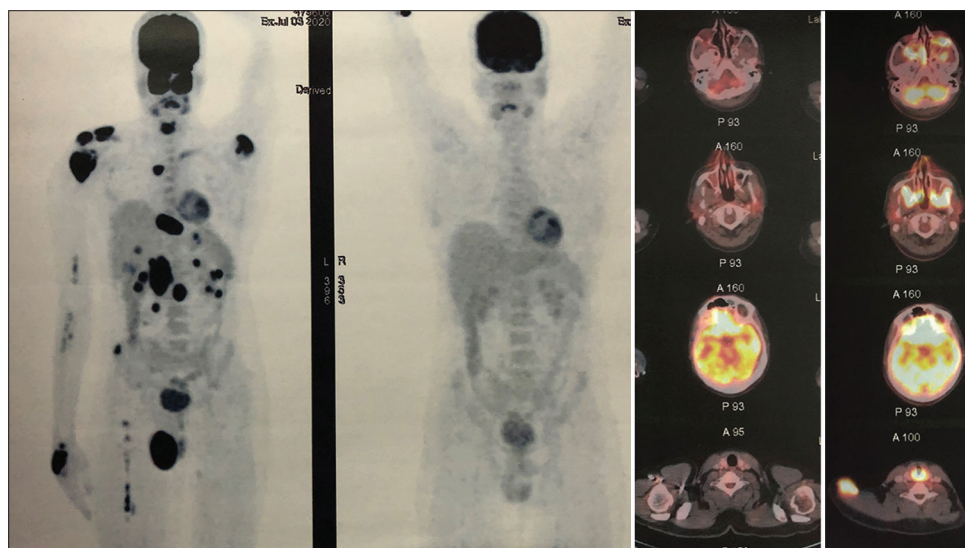


Figure 8: PET CT showing lymphoma metastasis before and after chemotherapy

Oral lymphoma appears as swollen mass followed by ulcerated lesions. Other clinical presentations include hypermobile tooth, paresthesia, pain, palpable lymph nodes, fascial asymmetry and inflammatory-like lesions. Oral signs of NHL appear to resemble benign processes or tumors. Intraoral presentation of NHL as the first sign of AIDS has also been reported.^[15]

Radiographic findings are not specific to lymphomas. Diagnosis is based on histopathological examination with hematoxylin- and eosin-stain together with Giemsa, methyl green-pyronine (MGP), and periodic acid-Schiff (PAS) special stains. Immunohistochemistry of the frozen section should also be carried out for confirmation and classification of lymphomas.

NHL has a worse prognosis than HL because when it is diagnosed, patients are often already at an advanced stage of the disease, and these neoplasms are more aggressive.^[16] Lymphomas of the head and neck are treated with radiotherapy alone or in combination with chemotherapy.^[13]

CONCLUSION

The clinical and radiographic presentation of oral lymphomas are not specific and are similar to many other diseases, such as advanced periodontal disease, osteomyelitis or other malignancies encountered in the oral cavity. In most cases, the involvement of lymphomas in the oral cavity represents part of disseminated disease,^[8] and early detection and diagnosis could promote adequate treatment and a better prognosis.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts

will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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