Case Report

Extranodal large B-cell type aggressive non-Hodgkin’s lymphoma

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INTRODUCTION

Lymphoma is a malignant neoplasm that accounts for 2.6% of all malignant neoplasms.[1] It is the second common malignancy of the head and neck region next to squamous cell carcinoma.[2] It comprises more than 67 subtypes of two closely related cancers that affect the lymphatic system. Generally, lymphomas present as nodal disease, but may involve the extranodal sites, i.e. thymus, spleen, liver, gastrointestinal tract and oral cavity. Primary extranodal lymphomas account for up to 20–30% of all lymphomas.[3]

Non-Hodgkin’s lymphomas belong to a group of neoplasm originating from the cells of the lymphoreticular system that show diversity in their manner of presentation, response to therapy and prognosis. Non-Hodgkin’s lymphoma accounts for 80–90% of all lymphomas. Although primary intraoral lesions in non-Hodgkin’s lymphoma are uncommon, it is important to be aware of them as intraoral manifestations are a presenting symptom in these patients. A 72-year-old Indian male presented with a complaint of asymptomatic swelling in the left side of the face since 1.5 months. A careful clinical evaluation supported by radiologic, histopathologic and immunohistochemical investigations will help in identifying the disease at an early stage, which will result in better prognosis.

Key words: Lymph nodes, non-Hodgkin’s lymphoma, swelling

CASE REPORT

A 72-year-old man reported with complaints of an asymptomatic swelling in the left side of the face since 1.5 months [Figure 1]. The swelling was insidious in onset, gradually increasing in size, and attained the present size. The patient was hypertensive and was on medications for the past 10 years.

Extraoral examination revealed a 4 cm × 3 cm smooth surface swelling involving the left side of the face extending to the lower border of the orbit superiorly and 1.5 cm above the corner of the mouth inferiorly. Medially, the swelling extended a few centimeters away from the ala of the nose and laterally up to 3 cm in front of the ear. On palpation, the swelling was hard and nontender.

Non-Hodgkin’s lymphoma are rare in occurrence with a wide range of histologic appearances and clinical diagnosis. The present report describes a case of non-Hodgkin’s lymphoma of the extranodal site primarily involving the buccal mucosa in a 72-year-old male.
Intraoral examination revealed 2 cm × 1.5 cm swelling on the left side of the buccal mucosa opposite the left maxillary premolar area [Figure 2]. On palpation, the swelling was firm and nontender and was not associated with sinus or pus discharge. No palpable submandibular and cervical lymphadenopathy was evident.

**INVESTIGATION**

A paranasal sinus radiograph revealed the presence of mucosal thickening that was closely associated with the left maxillary sinus. A computed tomography (CT) scan examination revealed the presence of a soft tissue lesion measuring 38 mm × 30 mm × 21 mm on the left side of the face [Figure 3]. The lesion appeared to be in the muscular plane and the underlying bone was preserved. The nasal septum was mildly diverted toward the right side and both the inferior turbinate were hypertrophied. Polypoidal mucosal thickening was seen in the left maxillary sinus suggestive of benign soft tissue neoplasm. For further evaluation, the patient was subjected to ultrasonography of the left side of the face, which revealed the presence of small hypochoic areas in the areas that were closely associated with the swelling region and also on color Doppler ultrasonography examination, which revealed that there was a decrease in vascularity in that region. Differential diagnosis based on the above investigation was suggestive of fungal granuloma, chronic granulomatous lesion, soft tissue malignancy and lymphoma.

An incisional biopsy was carried out for histopathological examination. Grossly, the tissue was creamish white to light brown in color and was soft to firm in consistency. Light microscopic examination of the section stained with hematoxylin and eosin revealed the presence of small and large malignant lymphocytic cells [Figure 4]. The large lymphoid cells were —two

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**Figure 1:** Clinical photograph of a 72-year-old patient showing a swelling on the left side of the cheek

**Figure 2:** Clinical photograph showing an intraoral swelling on the left side of the buccal mucosa opposite the left maxillary premolar region

**Figure 3:** Computed tomography scan revealing a soft tissue lesion on the left side of the face

**Figure 4:** Photomicrograph of hematoxylin and eosin-stained sections showing sheets of small and large lymphocytic cells (10X)
to three times larger than normal lymphocytic cells [Figure 5]. Connective tissue stroma also showed the presence of large, binucleated cells with pale cytoplasm and prominent nucleoli. Few areas also showed the presence of an immature large cell with cleave nucleus [Figure 6] and numerous abnormal mitotic figures [Figure 7]. The histopathological features were suggestive of non-Hodgkin’s lymphoma.

A panel of immunohistochemical markers was also used for confirmation and treatment plan. Immunohistochemistry revealed that the lymphoid tumor cells were strongly positive for pan B cell marker (CD-20) and mild positivity for T cell (CD-3) antigen. Typical large lymphoid cells were also strongly positive for leukocyte common antigen CD-45 and BCL-2 and negative for CD-30, which finally proved the lesion to be a diffuse large B cell non-Hodgkin’s lymphoma. Further bone marrow biopsy showed normocellular marrow spaces with adequate representation of all hematopoietic marrow elements showing no signs of infiltration by non-Hodgkin’s lymphoma. A positron emission tomography (PET) scan was performed to assess the distribution of malignant cells. There was intensive uptake of fluorodeoxyglucose (FDG) in the soft tissue lesion over the left maxilla extending mesially till the left nostril, posteriorly eroding the anterior wall of the maxillary sinus and inferiorly up to the lower eyelid. Intensive uptake of FDG was also seen in the bilateral group of parotid lymph node and mild uptake was seen in the left cervical lymph node, and the patient was grade to the level stage III according to the Ann Arbor classification with the involvement of lymph node and contiguous extralymphatic sites on both sides of the diaphragm.

**DISCUSSION**

Lymphoma is a solid tumor of the immune system that primarily involves the lymph node and rarely involves the extralymphatic sites. Diagnosis of lymphomas is based on the World Health Organization classification and is broadly divided into two main categories.\(^7\)

Non-Hodgkin’s lymphoma covers a wide range of lymphoid neoplasias. The annual incidence rate of the individual diagnosed with non-Hodgkin’s lymphoma has increased since the last few years.\(^8\) Extranodal non-Hodgkin’s lymphoma is a distinct entity and usually accounts for 40% of all non-Hodgkin’s lymphomas. It was first described by Isaccson and Wright in 1983.\(^9\) The diagnosis of oral extranodal non-Hodgkin’s lymphomas is challenging and may
cause relevant problems with their differential diagnosis in view of their rarity in the primary occurrence of non-Hodgkin’s lymphoma in the oral cavity and wide variation in their clinico-radiographic presentations and histologic features. Clinically, when non-Hodgkin’s lymphoma first appear in the oral cavity, they generally appear as nontender, soft to firm swellings that may or may not be associated with ulceration. Usually, in most of the cases, patients present with clinical symptoms like night sweat, fever, weight loss and palpable lymph nodes, but in the present case, no such clinical symptoms and palpable lymph nodes were evident, which may often lead to being misdiagnosed as squamous cell carcinoma, fungal infection or any other soft tissue tumor.\textsuperscript{[10]} Therefore, further investigations must be performed to rule out the possibility of these lesions.

A conventional radiography examination did not reveal any significant difference, but, with ultrasonography examination, lymph node enlargement in the submandiblar and cervical areas gave a significant finding that was not assessed clinically, and proved that the lesion may be associated with lymph nodes. PET examination further improves the accuracy of diagnosis by assessing the uptake of FDG in the region of lymph node and other extralymphatic sites, and proves it to be a soft tissue metastatic tumor.\textsuperscript{[6]}

Histologic examination is paramount in confirming a definite diagnosis. Based on the histopathological finding, the lesion was diagnosed as non-Hodgkin’s lymphoma. Another diagnostic pitfall in connection with non-Hodgkin’s lymphoma is the possibility of its confusion with Hodgkin’s lymphoma. The confusion arises mainly due to the presence of typical multinucleated lymphocytic cells mimicking Reed Sternberg-like cells that characterize the Hodgkin’s lymphoma.\textsuperscript{[6]i} In such an instance, the diagnosis is greatly facilitated by the accurate interpretation of immunohistochemical findings that differentiate non-Hodgkin’s lymphoma from Hodgkin’s lymphoma. The presence of positive staining for leukocyte common antigen CD-45, CD-20 and BCL-20 and immunonegative for CD-30 and CD-3 distinguish the large B cell non-Hodgkin’s lymphoma from Hodgkin’s lymphoma.\textsuperscript{[7]} Correlation and interdependency of advance radiographic, histologic and immunohistochemical examinations help in identifying the disease in the early stage, resulting in better prognosis.

**CONCLUSION**

Non-Hodgkin’s lymphoma often shows an extranodal pattern, especially in the head and neck region. Different patients with primary extranodal locations, particularly in the oral cavity, may be misdiagnosed. In addition to clinico-radiographic findings, additional examinations used in this case are necessary for the early diagnosis and staging of cancer so that more appropriate treatment can be instituted to the specific pathology.

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