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CASE REPORT

Extranodal non-Hodgkin's lymphoma in the malar region – a case report

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Abstract

The incidence of extranodal non-Hodgkin's lymphomas (NHL) in Asian subcontinent is very low. Extranodal NHL in the malar region are uncommon, and the incidence of these lesions in such site is unknown. Here is a case of slowly enlarging mass from the soft tissue over the right malar region, radiographically appeared to have involved maxillary sinus and histopathologically diagnosed as round cell tumour. Immunohistochemistry analysis was suggestive of diffused large B-cell lymphoma. Definitive diagnosis by immunohistochemistry is a must for accurate diagnosis, treatment and better outcome for such lesions.

Introduction

Lymphomas are a heterogeneous group of neoplastic disorders originating from the lymphoreticular system, which usually arise in the lymph nodes[1]. Lymphomas account for 4–5% of all neoplasm, and extranodal involvement in Hodgkin's lymphoma are rare, but its frequency accounts for 25% or more in patients with non-Hodgkin's lymphoma (NHL). The head and neck region has the highest regional incidence[2]. The cause of NHL is unknown. They have varied histological features and clinical behaviour. The major determinants of the clinical course and prognosis are the type of cell origin and pattern of growth within the lymph nodes[3]. NHL generally responds to most modalities of treatment, including radiation therapy, single agent or combination chemotherapy, immunotherapy, or radioimmunoconjugate therapy[3]. Recent studies have shown that radiotherapy is no more used in diffuse large B-cell lymphoma (DLBCL)[4].

Case report

A 51-year-old man presented to the A.B. Shetty Memorial Institute of Dental Studies, Mangalore, India, with asymptomatic swelling in the right middle third of the face for 5 months. Initially, the swelling was of peanut size, which was slowly growing. He had undergone biopsy for the same condition, and the report was suggestive of a non-specific granuloma. Following the biopsy, the swelling grew rapidly to the present size. He gave no history of weight loss, fever, night sweats or sinus disease.

His medical and dental histories were not significant. Physical examination revealed neither abnormal swelling nor lymphadenopathy elsewhere in the body.

On examination, a solitary, ovoid, ill-defined swelling was present over the right malar region measuring 5 × 4 cm, extending from lateral border of the nose to 2 cm ahead of tragus anterior-posteriorly, and from 1 cm above the supra-orbital ridge to the corner of

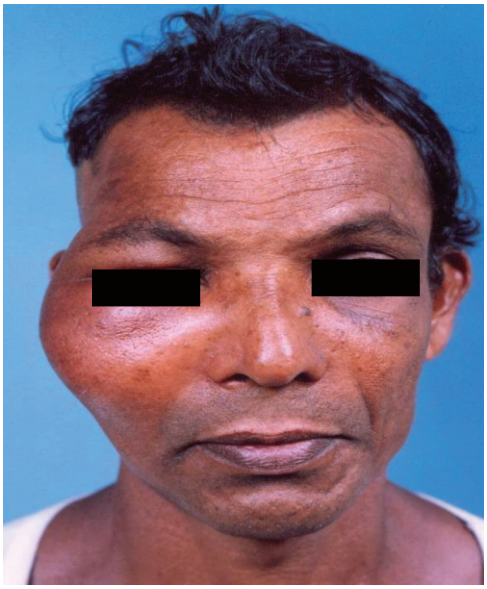

Figure 1 Solitary, ovoid, ill-defined swelling and skin over the swelling was taut.

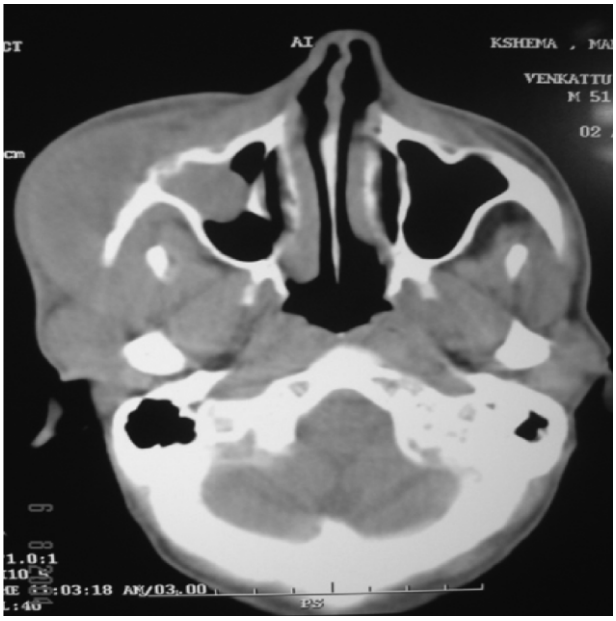

Figure 2 Axial computed tomography showing a well defined hypodense mass with a few areas of cortical erosion, involving the maxillary sinus but not occupying the entire sinus.

the mouth superior-inferiorly (Fig. 1). Skin over the swelling was taut with no secondary changes. No paraesthesia was evident. Eyelid movements were restricted because of swelling. Facial nerve function was normal, and no change in vision was noted.

On palpation, the swelling was mildly tender with well-defined borders. It was firm to hard in consistency; the lesion was fixed to the underlying structures, and it was neither mobile nor reducible; and multiple ipsilateral parotid lymph nodes were palpable, mobile, firm in consistency and non-tender. Intraorally, no sign of the swelling was noted, and salivary flow was normal. Routine laboratory blood investigations were all within normal limits, Enzyme Linked Immunosorbent Assay (ELISA) for human immunodeficiency virus was negative and chest radiograph showed no changes. Intraoral periapical radiograph of 14, 15 and 16, and panoramic radiograph showed no other abnormalities other than the haziness in the right maxillary antrum. A Waters' view revealed an ill-defined radiopaque mass superimposed over the right malar region, the density of which was less than that of bone. Haziness within the right maxillary antrum was noted with lift in sinus air level. Both the medial and lateral walls of the sinus were intact. Axial computed tomography (Fig. 2) at the level of the condylar head shows areas of cortical erosion on anterior wall of maxillary sinus, and a hypodense mass within the maxillary sinus measuring 1.5×1 cm but not occupying the entire sinus. The Hounsfield units 20–30 of the lesion were suggestive of soft tissue mass.

Incisional biopsy was performed extraorally considering its site and accessibility. On histopathological examination, 'Slit like' vascular spaces surrounded by endothelial cells with few mitotic figures and nuclear atypia were seen, which were suggestive of an intermediate vascular lesion. Based on this diagnosis, the lesion was surgically excised using Weber–Ferguson's incision. Specimen showed monotonous sheets of round cells with scanty cytoplasm and dense course nucleus. Nuclear atypia was seen, suggestive of a round cell tumour. To confirm the diagnosis, an immunohistochemical assay was carried out, which demonstrated CD20 positivity and CD3 negativity (Fig. 3). This was suggestive of a tumour of B-lymphocyte origin. A final diagnosis of extranodal NHL (DLBCL) was given and was staged as II–E. (Ann Arbor). Chemotherapy was given with Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone (CHOP) regime, that is, each cycle is repeated every 3 weeks for 6–8 cycles, and patient is on regular follow-up.

Discussion

Lymphomas are solid tumours of lymphoid cells. They mainly involve lymph nodes, spleen and other non-haematopoietic tissues[3]. They are basically classified as either Hodgkin's or non-Hodgkin's lymphoma. NHL comprises a group of closely related yet heterogeneous diseases, each characterised by the malignant

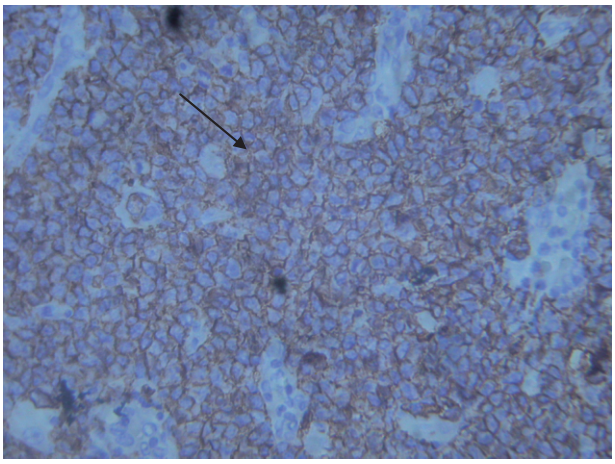

Figure 3 Immunostaining for CD20 showing predominant lymphocyte infiltrates which are CD20-positive cells.

transformation of lymphoid cells but with distinctive morphologic, immunophenotypic, genetic and clinical features[5]. NHL can either be of B-lymphocyte or T-lymphocyte origin[5]. NHL accounts for 5% of new cancers in men, 4% of new cancers in women and 5% of deaths due to cancer each year. Incidence increases with age and peaks in individuals aged 80–90 years. NHL is more common in men than women. The incidence is highest in white people in the USA and lowest in Asia[3].

The cause of NHL is unknown. However, immunodeficiency and some infectious agents like Epstein-Barr Virus (EBV) and Human T-Lymphotropic Virus-1 (HTLV-I) have been suggested in the aetiology[3]. Wotherspoon *et al*. implicated *Helicobacter pylori* in the pathogenesis of gastric lymphomas[6]. Predisposing factors that may be related to the development of NHL are exposure to drugs or infectious agents, previous irradiation, immunosuppression, history of Sjogren's syndrome, and Hashimoto's thyroiditis in association with thyroid lymphoma[2]. In DLBCL, the exact role of these predisposing factors is still debated. Even within DLBCL, there are biological variants that may have different aetiologies[7].

The most common site involved in the orofacial region is the tonsil (34%), followed by salivary glands (15%), thyroid (14%) and sinus/nasal cavity (13%). Other common sites are the tongue, palate and orbit[8]. Primary soft tissue involvement is less commonly described. In a review of over 7000 cases of lymphoma at the Mayo Clinic over 10 years, eight cases of lymphoma that presented as a soft tissue mass were identified. The thigh was the site of presentation in four cases[8]. In our case, the lesion presented as primary soft tissue lesion over the malar region causing cortical erosion and invading into the maxillary sinus; such presentations are very unusual in the head and neck region.

Most common presenting feature is a mass or a swelling (59%), with minimal symptoms: pain (21%), dysphasia (7.9%), weight loss (1.1%), night sweats (0.5%), and nasal obstruction (7.9)[7]. In our case, there was mild tenderness noted. The mean age of presentation is five to seven decades[7]. The age-adjusted incidence rate of NHL in Mumbai, India, is 4.8 per 100 000 men and 2.9 per 100 000 women[9].

Clinically, lymphomas can be categorised using Ann Arbor Staging[2]. Most patients with head and neck NHL have diffuse large-cell type of lymphoma, and approximately 50% present with stage I or II lesions. Most of these are B-cell lymphomas. Sixty per cent to eighty per cent of patients present with local symptoms[2]. In our case, the lesion was stage II E and was diffused B-cell type, which was inconsistent with previous studies. Spread of oral lymphoma is by lymphatics via cervical lymph nodes to extranodal organs, or contiguous spread to adjacent organs, or blood-borne distant metastases[8].

B-cell lineage cases show pan CD20 positivity. The expression of individual antigens is related to different stages of B-cell differentiation, including CD5, CD10, bcl-6, MUM1/IRF4 and CD138, and may help define groups of tumours with different clinical and pathological characteristics[10]. In our case, CD20 positivity and CD3 negativity were noted, which were suggestive of B-cell linage tumour.

The primary differential diagnosis relevant to this case is diffuse mixed small/large cell lymphoma, small lymphocytic lymphoma and extranodal natural killer (NK)/T-cell lymphoma. Extranodal NK/T-cell lymphoma is the most important lesion in the context of orofacial lymphoid lesion because it is the most common lymphoma involving the sinonasal region[11].

Chemotherapy is the most important therapeutic modality, particularly for lymphomas with an aggressive phenotype such as DLBCL[7]. CHOP regime was used in our case. However, radiotherapy is no longer used in the treatment of diffuse large B-cell lymphomas[4].

Hart *et al*., in his review of 580 patients with lymphoma, noted that relatively high (over one third) proportion of patients had excisional surgery, suggesting the importance of diagnostic biopsy before proceeding to definitive surgery, which for lymphoma is usually inappropriate[8]. Biopsy was also performed in our case, re-emphasising the importance of biopsy in cases of localised extranodal lymphomas.

Newer treatment modalities include the use of monoclonal anti-CD20 antibody. Rituximab is a combination of human and mouse antibody with human constant region and mouse variable region. The emergence of R-CHOP regime in the treatment of aggressive NHL has shown promising results, and it should be an area for further clinical research[3,12,13].

Shipp *et al*. in 1993 developed the International Prognostic Index. On the basis of age, tumour stage, serum concentration of lactate dehydrogenase, performance status, and number of sites of extranodal disease, this model identified four risk groups. Adverse risk factors are the following: age older than 60 years, tumour stages III and IV (advanced disease), high serum lactate dehydrogenase concentration, Eastern Cooperative Oncology Group performance status of 2 or greater, and more than one extranodal site of disease. The low-risk group includes patients with either no adverse risk factors or one adverse factor, whereas the high-risk group includes patients with four or five adverse risk factors[3]. Lymphomas have a 5-year survival rate of 50–60% dependent on the age, site of the primary, stage of the tumour and the degree of maturation[1,3].

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