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CASE REPORT

Early-stage diffuse large B-cell lymphoma of the submental region: a case report and review of the literature

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Abstract

Lymphomas represent the third most common group of malignant lesions in the oral cavity and maxillofacial region, following squamous cell carcinoma and salivary gland neoplasm[1,2]. Traditionally, lymphomas are divided into two subtypes, Hodgkin lymphomas (HL) and non-Hodgkin lymphomas (NHL)[3]. The diffuse large B-cell lymphoma (DLBCL) is a rapidly aggressive NHL constituted by big lymphoid cells that can appear as a nodal or extra-nodal disease; about 4% of DLBCL are initially confined to extra-nodal sites[4]. The oral and maxillofacial region is the second most common extra-nodal site, and half of the cases are located in Waldeyer's ring[3].
The tumour may present clinical symptoms and radiographic findings as local swelling, pain or discomfort, ulcer and bone resorption mimicking other pathologic lesions such as periodontal disease, pericoronitis, apical radiolucencies or dental abscesses[5].
We report a case of a patient with DLBCL of the submental region staged at I AE according to the Ann Arbor lymphoma staging system.

Case report

A 65-year-old white woman was admitted to the *Department of Oral and Maxillofacial Sciences of 'Sapienza', University of Rome*, sent by her dentist for the evaluation and treatment of a rapid growing, not painful, fixed lump of the submental region diagnosed as a dental abscess (Fig. 1A,B).

The patient had no significant systemic disease and no smoking habit. Clinical intraoral examination of the soft tissues showed no abnormalities. No lymphadenopathy could be noted. The patient reported no pain when the submental region was palped. A vitality test of both lower canines and incisors was performed. As all teeth were vital, the diagnosis of dental abscess was rejected.

A computerised tomography (CT) with contrast enhancement showed a multilocular tumour measuring 5 × 6 × 6 located in both laterocervical and submental regions (Fig. 2A,B).

Considering the relevant dimensions of the tumour and the absence of squamous cancer related to medical history findings or clinical signs, such as oral and skin primary lesions, the clinicians decided to avoid unnecessary additional tests and to proceed with an incisional biopsy.

Incisional biopsy was performed under local anaesthesia, and multiple specimens were sent for a histological test. The histological examination showed a diffused proliferation of atypical round cells with lymphoid characteristics positive for CD20, Bcl-6 and MUM1 and negative for CD3, CD5 and D1 cyclin. Ki-67 index was 60% (Fig. 3A–D).

The final diagnosis was NHL consistent with extra-nodal DLBCL staged at I AE according to the Ann Arbor lymphoma staging system.

All blood work was normal. Specifically IgG, β-2 micro globulin and lactic dehydrogenase were all within normal range.

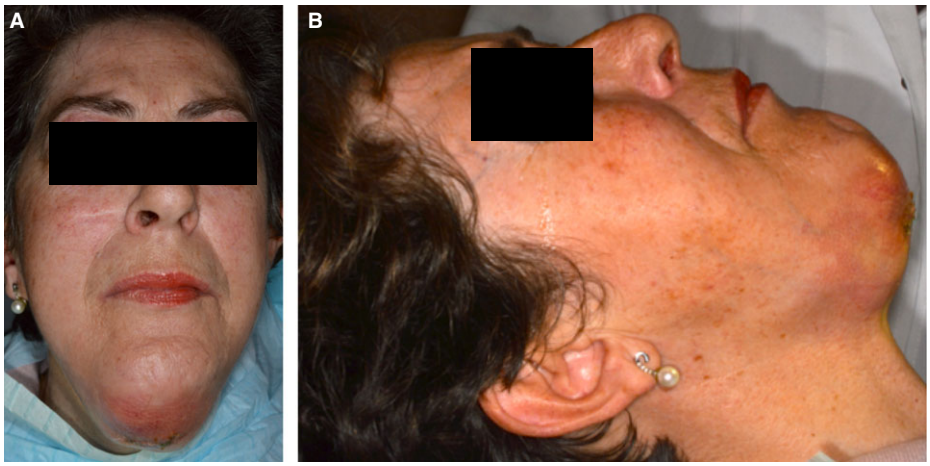

Figure 1 (A, B) Frontal and lateral extraoral view showing the large tumefaction of the submental region after biopsy.

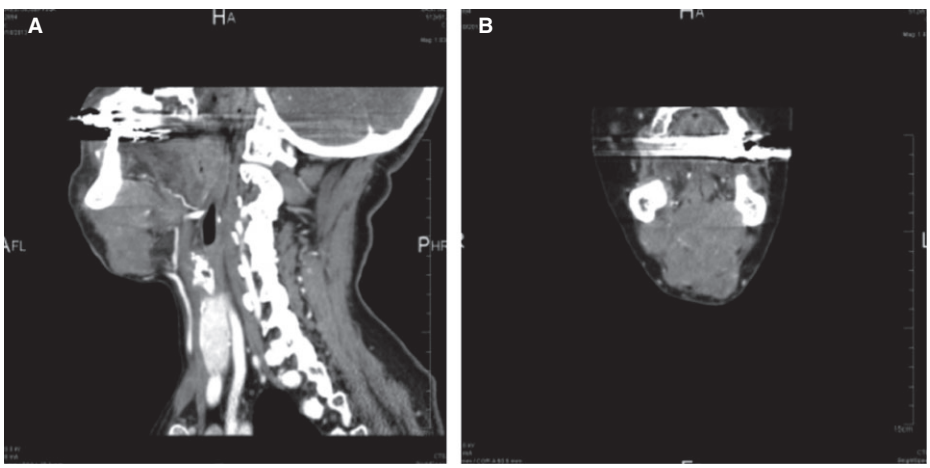

Figure 2 (A, B) Coronal CT scan images with contrast enhancement show a multilocular radiolucent borderline lesion extended both in laterocervical and submental regions.

The patient is under CHOPR treatment monitored at regular intervals by CT scanning.

Discussion

DLBCL is the most common NHL, comprising 30–40% of all cases[6–9]. Little is known about its cause. Differences in incidence among ethnic groups, as reported by Regezi *et al.*, suggest a genetic influence[4]. In 2011, Corti *et al.* reported 11 cases of NHL of oral cavity in AIDS patients, suggesting that acquired or congenital immunodeficiency is a significant risk factor[10]. Iamaroon *et al.* had previously demonstrated that oral NHLs can be caused by an altered immune response to EBV or that specific chromosomal translocation plays a role in the formation of NHLs, causing dysregulation of oncogenes or oncosuppressor genes and allowing unhindered cell proliferation[11].

A lymphoma can arise from regional nodes, and in this case, it is named intranodal lymphoma. Extranodal lymphomas are neoplasms that are often components of a spreading process of a disease, which may involve regional nodes, or they may represent primary extranodal disease[12–14]. Therefore, the definition of intranodal lymphoma and primarily or secondarily extranodal lymphoma is sometimes difficult. Literature reports say that the decision is based on the opinion of the examining physician who may take into account any intercurrent symptoms like lymphadenopathy[15].

The tumour typically affects middle-aged to older adults in the seventh decade. According to the Ann Arbor lymphoma staging system, stage I indicates

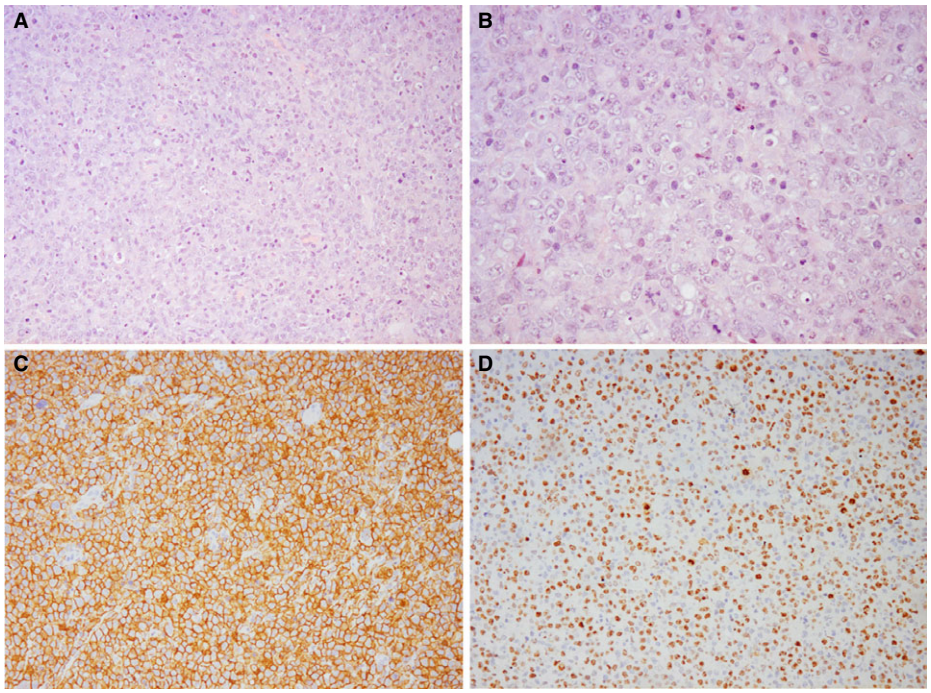

Figure 3 Histological examinations. (A, B) The neoplastic tissue consisted of large lymphoid cells with irregular nuclei and atypical mitosis (H&E stain). (C) Tumour cells expressed the pan B-cell marker CD20. (D) Proliferation fraction as assessed by Ki67 staining.

single lymph node involvement, stage II indicates involvement of lymph nodes on the same side of diaphragm, stage III involves lymph nodes on both sides of diaphragm and stage IV is characterised as diffuse or disseminated involvement. The designation A and B denotes the absence or presence of constitutional symptoms, respectively. The designation E indicates extranodal localisation.

Biopsy, along with tissue-based immunologic studies, is the only reliable way to make a definitive diagnosis. DLBCL consists of sheets of large lymphoid cells with large vesicular nuclei, prominent nucleoli and abundant basophilic cytoplasm[4,9].

In head and neck (HN) region, B-cell lymphomas can appear in any location as demonstrated by De Biase *et al.* who presented the case of a primary and exclusive gingival NHL in the symphysis region[16].

Mian *et al.* showed that the HN region is a relatively frequent site of presentation of extranodal DLBCL that can arise in different anatomical subregions. They reported data from 488 patients affected by stage I/II E HN-DLBCL: 300 were located in the Waldeyer's ring, 38 in the parotid and salivary gland, 48 in the thyroid gland, 53 in the nasal cavity and paranasal sinuses, 24 in the palate and oral cavity and 25 in more than one of the previous involved sites[17].

In 2012, Triantafillidou *et al.* reported 58 extranodal HN-NHL, among them 19 were DLBCL: 6 were I stage, 3 located in paranasal sinus and 3 in Waldeyer's ring; 13 were II stage, 7 located at maxillary mucosa and 6 at mandibular mucosa[3].

Lymphomas can also affect peri-implant tissues as recently showed by the report of Jin *et al.* who presented a case of DLBCL of the peri-implant mucosa mimicking peri-implantitis[18].

Even though HN location is common for DLBCL, there is no evidence in literature regarding this neoplasm located in submental region, suggesting that the physician consider this location as extremely rare.

As found in our patient, immunohistochemical expression of B-cell markers CD20 is commonly seen with variable staining with the germinal centre markers Bcl-2, Bcl-6 and MUM1.

Usually, on radiographic imaging, tumours initially take the shape and form of the host bone and some may be mistaken for a dental abscess. The borders are typically blurred due to the invasive nature of the neoplasm. The internal structure is usually completely radiolucent, with occasional patches of radiopacity as well as reactive bone formation. Widening of the mandibular canal has also been described[5].

DLBCL is considered an aggressive yet treatable tumour with the variable clinical course of a

swelling, painful or painless, with or without ulceration[19,20].

An initial remission rate of 60–80% has been reported, and a 5-year survival rate of about 50% is mentioned considering that the involvement of bone is associated with a very poor prognosis[3].

Prognostic risk factors include age, tumour stage, number of extranodal sites and serum lactic dehydrogenase levels. The most commonly used chemotherapy protocol is CHOP, acronym for cyclophosphamide, doxorubicin, vincristine and prednisone. These can be associated with a monoclonal antibody, rituximab with positive results in terms of survival. This modified protocol is named R-CHOP.

The use of radiation therapy for the treatment of DLBCL is still controversial since some evidences showed that this combination does not provide a survival advantage.

Generally, the prognosis for indolent lymphomas is poor. Even though survival is long, with a mean time interval of 8 years, they are considered incurable.

With aggressive lymphomas, remission is induced in 40% of patients receiving multiple immunochemotherapy. For those who respond well to chemotherapy, the outlook is good and resolution of the disease may occur after few courses of treatment. However, the outlook is poor for nonresponders, and the disease is usually fatal within several weeks[5].

In the majority of cases reported in literature, the neoplasm is associated with endodontically treated teeth. This aspect needs to be taken into account because dentists should be on the alert for clinical situations that fail to respond to conventional therapy and avoid multiple procedures without performing a biopsy causing the delay of treatment of what may be an aggressive, neoplastic condition. Primary extranodal NHL can mimic apical abscesses, and misdiagnosis of this condition can delay both diagnosis and initiation of treatment and influence the prognosis and eventual outcome.

Conflict of interest

The authors confirm that they have no conflict of interest.

Ethical Approval

None required.

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