Diffuse large B-cell lymphoma in the mandible mimicking post-extraction complication Presentation and a 5-year follow-up of a rare case report

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Abstract

Non-Hodgkin lymphomas (NHLs) are a heterogeneous group of malignancies originating from the lymphoid tissues, which can be differentiated by distinct epidemiology, etiology, and clinical characteristics. They can occur in the lymph nodes or as extranodal lesions. The vast majority of extranodal oral NHLs are classified as diffuse large B-cell lymphomas (DLBCL). They are usually found in the maxilla and they rarely occur in the mandible. The aim of this paper was to report a case of NHL with mandibular location by detailing its different clinical, radiological, and histopathological aspects. Herein, we report a case of NHL in the under chin region of the mandible in a 66-year-old male patient. The first diagnosis was post-extraction complication with delayed bone healing. The clinical and standard radiological examinations had no pathognomonic features. However, left labio-chin hypoesthesia and CT examination revealed a malignancy of the lesion without any precision. After performing further diagnostic examinations, including a subsequent biopsy, diagnosis of diffuse large B-cell lymphoma (DLBCL) was made. The patient was therefore treated with chemotherapy and he showed a satisfactory outcome for more than 5 years. Intraoral lymphomas may mimic odontogenic lesions; hence it is important for the dentist to be aware of the various manifestations of NHL to avoid delay and inappropriate treatment strategies.

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1. Introduction:

Lymphomas represent the third most common neoplasm in the head and neck region arising from the lymphoreticular system. They constitute a group of neoplasms of varying degrees of malignancy, derived from the basic cells of lymphoid tissues, lymphocytes, and histiocytes at any stage of their development [1].

Malignant lymphomas are divided into Hodgkin disease and non-Hodgkin lymphoma (NHL) [1].

Non-Hodgkin lymphomas (NHLs) account for around 90% of all malignant lymphomas and Hodgkin lymphomas (HLs) for the remaining 10% [2].

Hodgkin disease typically arises in the lymph nodes and usually occurs in the cervical and mediastinal nodes. However, NHL often presents as extranodal disease [3].

Indeed, nearly 25% of NHL occur in extranodal sites, with the skin, gastrointestinal tract, and central nervous system being the most commonly affected sites. In the oral cavity, the majority of cases occur in Waldeyer's ring, followed by the buccal mucosa, tongue, floor of the mouth, and retromolar area [4].

Diffuse large B-cell lymphoma (DLBCL) is the most frequently reported NHL subtype. It is an aggressive, rapidly growing neoplasm of large lymphoid cells, and it commonly occurs in men older than 50 years [5]. The manifesting symptoms in the mouth cavity include nonspecific swelling, non-healing dental extraction wounds, ulceration, and aposteme. DLBCL may be misdiagnosed as osteomyelitis, periodontosis, pyogenic granuloma, and as malignant tumors, such as squamous cell carcinoma [5].

Only few publications have focused on DLBCL in the mouth cavity, leading to difficulties in diagnosing and understanding the biological characteristics of this disease, choosing a rational treatment, and providing an accurate prognosis [4].

The aim of this report was to describe a rare case of a mandibular NHL mimicking post-extraction complication and to highlight the importance of early diagnosis in improving the prognosis of the disease.

2. Case report:

A 66-year-old male patient was referred to the dental clinic with a chief complaint of swelling in the left side mandibular area under the chin persisting for 60 days, accompanied by left labio-chin hypoesthesia.

The patient reported having a mobile anterior tooth that was extracted in a private clinic.

Extraoral examination revealed a solitary swelling on the left side mandibular area under the chin, measuring about 5 cm of long axis and extending to the oral floor (Fig. 1).

The swelling surface was smooth.

On palpation, the swelling was not tender; it was firm, non-fluctuant, and without thrill or pulsation.

Multiple bilateral submandibular lymph nodes were palpable and not tender. They were firm and fixed to the adjacent tissues. The lymph nodes of others regions were not palpable.

Intraoral examination revealed a delayed healing at the site of tooth 33 (Fig. 2).

Occlusal radiography and occlusal radiography of the chin revealed swelling just in the area under the chin without any osseous lesion (Fig. 3).

Panoramic radiography showed a blurred appearance of the bone at the site of the extracted tooth (Fig. 4).

Craniofacial CT scan examination revealed an infiltration of the left lateral mandibular chin soft tissues and the oral floor, associated with a poorly-limited osteolytic lesion affecting the mandibular crest and the vestibular bone cortex. The chin foramen was in full osteolytic lesion. No enhancement of the lesion was noted after injection of iodinated contrast material (Fig. 5).

Based on these clinical and radiographic findings, a malignant process was suspected. The patient was therefore immediately referred to the Department of Maxillofacial Surgery.

A biopsy of the tumor mass on the buccal floor was taken.

The histopathologic examination of the biopsy showed a fibrous adipose and striated muscular tissue, richly vascularized and crossed by numerous nerve threads, dissociated by a tumor infiltrate of lymphomatous appearance, composed of large cells, non-jointed, of centroblastic type, presenting numerous images of mitosis, enveloping the vascular and nervous structures and dissociating the striated muscular fibres. In addition, it presented a rather abundant reactive lymphocytic population.

The immunohistochemically study carried out on kerosene sections revealed intense and diffuse labelling of the tumor cells with CD20, while CD30 was negative (Fig. 6).

Based on these findings, diagnosis of diffuse large B-cell lymphoma (DLBCL) was made.

The patient was referred to a hematologist-oncologist for evaluation. Several examinations were performed, including thoracic- abdominal-pelvic CT scan and bone scintigraphy.

These examinations showed no abdominal-pelvic metastasis; however, left mandibular hyperfixation was noted at the bone scintigraphy (Fig. 7).

The patient was kept on sequential courses of chemotherapy.

After treatment, the patient completely recovered. Complete tumor remission was observed, which was confirmed by occlusal radiography and CT scan. A favorable clinical evolution with total alveolar healing was noted. Close follow-ups were scheduled, and 5 years after the last cycle of chemotherapy, no signs of tumor recurrence were noted (Fig. 8).

3. Discussion:

Lymphomas are currently classified based on the clinical features, morphology, immunophenotyping, and molecular genetics. Over the years, various schemas have been developed to classify lymphomas [6]. The most widely used schema is the 2008 World Health Organization (WHO) classification, which is based on the principles defined in the Revised European-American Classification of Lymphoid Neoplasms (REAL) [6].

It was updated in 2016 to provide pathologists and hemato-oncologists with the recent advances in understanding the disease [7].

Lymphomas can be divided into two major entities, namely Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Over 20 different subtypes of NHL have been classified according to the specific subtype of lymphoid cells involved [8].

NHLs (Non-Hodgkin Lymphomas) are a heterogenous group of lymphoproliferative malignancies that are much less predictable than Hodgkin lymphomas and have a far greater predilection to disseminate to extranodal locations [1].

The sites for extranodal non-Hodgkin lymphoma are:

1. Waldeyer's ring (Nasopharynx, palatine tonsils, base of the tongue, and oropharyngeal wall).
2. The oral cavity (Palate, gingiva, maxilla, and tongue).
3. The salivary glands.
4. Thyroid.
5. Larynx.
6. The nasal cavity.
7. Paranasal sinuses.
8. The skin [1].

In the oral cavity, lymphomas can appear anywhere in the mouth but they predominate on the hard palate, gingiva, and tongue. The mandible is an infrequent localization of primary osseous NHL [9].

In the present case, the patient presented with swelling of the area under the chin extending to the floor of the mouth, leading to a suspicion of post-extraction complication given the delay in the healing of the site of tooth 33.

NHLs consist of a group of abnormal proliferation of 2 distinct lymphocyte types, B or T and their precursor cells [4].

DLBCL represents the most common type of NHLs, accounting for 40% off all cases. DLBCL is a heterogeneous entity having varied clinical features, morphology, immunohistochemistry, and prognosis. These differences should be carefully analyzed in order to ensure successful management [9].

The median age is 64 years and men are slightly more affected than women [10].

In their study, Van der Waal et al. published the data of 40 cases of primary extranodal NHL of the oral cavity. The Median age according to their study is 59 years (3-88 years) and males are more commonly affected than females [11].

This coincides with the age and sex of the patient included in this study who was male at the age of 66 years.

Diagnosis of lymphoma in the jaws is difficult and it is often delayed for many reasons.

For instance, the clinical and radiographic presentations are not specific for lymphoma. Clinically, lymphoma may cause vague pain and discomfort, which might be easily misdiagnosed as periapical lesion developed from an odontogenic infection [10]. The radiographic changes in the early stages of the tumor may be subtle and they are usually detected only late as an ill-defined radiolucency that might resemble a dental abscess [10].

Conventional radiography of these lesions shows non-defined alveolar margin, loss of cortical limits, widening of the periodontal space, irregular radiolucent lesions, and ill-defined borders [12].

Diagnosis of oral lymphomas may therefore be challenging because there is frequently a low index of clinical suspicion, leading to misdiagnosis and/or delayed treatment [13]. Oral cavity mass can be a rare presentation of a number of conditions, including infections, such as bacterial osteomyelitis, invasive fungal infection and syphilis, inflammatory diseases, particularly Wegener's granulomatosis, and neoplasms, including squamous cell carcinoma and lymphoma [13].

In the present case, standard radiographs (panoramic and occlusal radiographs) were not conclusive. Only CT scan revealed an osteolytic lesion with irregular margins at the site of tooth 33, associated with an infiltration of the soft tissues in the mandibular region under the chin.

Tumors in the head and neck are easily accessible. Biopsy should therefore be immediately performed following suspicious findings [8]. In particular, for NHL with extranodal involvement in the head and neck occurring at a frequency of 20 to 30%, biopsy should always be part of the diagnosis in any head and neck lesions, including those in the oral cavity, major salivary glands, oropharynx, nasopharynx, paranasal sinus, and larynx [8].

In fact, Diffuse Large B-Cell Lymphoma (DLBCL) is characterized by diffuse infiltration of medium to large cells with large nucleoli and abundant cytoplasm, which disrupts and effaces the underlying architecture of the involved tissue. The cells typically express pan-B cell antigens, including CD19, CD20, CD22, CD79a, and CD45. The majority of the cells also express surface immunoglobulin. Approximately 14% of the cases express CD30, which can portend a favorable prognosis [14].

In the present case, the cells strongly expressed CD20. They did not express CD30.

Indeed, CD30 is expressed in various T cell lymphomas and DLBCL. The expression pattern is variable and in DLBCL, CD30 expression is associated with prognosis [15].

The standard imaging assessment includes a thoracic, abdominal, and pelvic computed tomography, with measurement of the lesions that will serve as the initial reference for the treatment response assessment. A PET scanner FDG is also necessary to identify the degree of tumoral extension and to determine the Ann Arbor stage [16].

For our patient, thoracic X-ray, thoracic-abdominal-pelvic CT scan, and bone scintigraphy were performed. These examinations did not show any distant lesions.

Our patient was therefore classified as stage IVA according to the Ann Arbor stage.

Treatment for DLBCL often involves chemotherapy and depending on the clinical stage and the outcome of the treatment, chemotherapy can be combined with radiotherapy. However, its response to chemotherapy

is not always satisfactory and if remission is not maintained, the patient is considered for bone marrow transplantation [5].

The present case was treated with chemotherapy alone and it has so far shown a satisfactory outcome.

The survival of extra nodal NHL of the head and neck depends on the extent of the disease, presence or absence of HIV serology status, histopathology, and Ann Arbor staging. Five-year

survival rate of extranodal NHL of the head and neck was reported by Pazoki et al. and the medial survival rate for stage IE is 10 years [17]. Wolvius et al. reported 34 cases of primary extranodal lymphoma of the oral cavity and the mean survival time was reported to be 38 months with a mean recurrence-free survival time of 31 months. According to Slootweg et al., survival of oral NHL varies according to Ann Arbor stage and it was 70% for those who presented at base line with stage I disease and 20% for stages II-IV disease [17].

The patient´s follow-up is indispensable because of the disease recurrence risk which must

not be neglected.

The national Cancer Institute (NCI) recommends that follow-up visits should include the patient's history, physical examination for lymphadenopathy, abdominal masses, organomegaly, complete blood cell count, and LDH. Additional blood tests and imaging studies may be added for relevant clinical indications but specific tests cannot be currently recommended [18].

In the present case, the patient was followed regularly by his hematologist with clinical, radiological, and biological examinations.

No sign of recurrence was noted over a period of more than 5 years.

4. Conclusion:

Slight clinical symptoms together with clinical and radiological findings may not be clear enough to provide the dentist with specific indications.

The clinician should be aware of the possibility of jaw tumors and should not delay the decision in favor of further radiographic and histological examinations to avoid tumor progression [19].

Clinicopathologic correlation is therefore crucial to reach the correct diagnosis in clinically suspicious cases [10].

Figures:

Fig. 1: Extraoral photograph showing left mandibular swelling under the chin expending inferiorly.

Fig. 2: Intraoral photograph showing delayed healing at the site of tooth 33 associated with swelling on the floor of the mouth.

Fig. 3: (a) Intraoral occlusal radiography, (b) Extraoral occlusal radiography of the chin showing swelling of the area under the chin without any bone lysis.

Fig. 4: Orthopantomogram showing delayed bone healing at the site of tooth 33 with a poorly-limited appearance of the bone.

Fig. 5: (a) Axial CT, (b) Orthogonal cross section of CT dentascan showing a poorly-limited osteolytic lesion affecting the mandibular crest and the vestibular bone cortex, (c) Axial CT without contrast, (d) Axial CT with contrast showing infiltration of the left lateral mandibular chin soft tissues and the oral floor without enhancement of the lesion.

Fig. 6: (a) H and E Stain (Magnification 40X) showing diffuse infiltration by lymphoid proliferation, (b) H and E Stain (Magnification 200X) showing infiltration of the underlying striated muscle, (c) Photomi-

crograph demonstrating tumor positive Immune-Stain of Anti-CD20 Antibody (Magnification 100X), (d) Photomicrograph demonstrating tumor negative Immune-Stain of Anti-CD3 Antibody(Magnification 100X).

Fig. 7: Bone scintigraphy showing left mandibular hyperfixation.

Fig. 8: Extraoral and introral photographs showing complete tumor remission.

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