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Non-Germinal Center Diffuse Large B-Cell Lymphoma Presenting as A Gingival Mass Mimicking Squamous Cell Carcinoma: A Case Report and Literature Review

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Abstract **Case Report**

Background: Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL) in adults. Primary gingival involvement is exceptional and constitutes a major diagnostic pitfall, particularly when associated with mandibular bone lysis and ipsilateral cervical lymphadenopathy, a presentation that closely mimics oral squamous cell carcinoma. ***Case presentation:*** We report the case of a 61-year-old man with no notable medical history who presented with a 3-month history of a right lower vestibular gingival swelling. Facial MRI showed an expansile process of the right lower vestibular gingiva lysing the horizontal ramus of the right hemimandible, with an ipsilateral cervical lymph node larger than 3 cm, initially staged T4a N2a Mx according to the TNM classification used for upper aerodigestive tract carcinomas. Gingival biopsy redirected the diagnosis toward a non-germinal center DLBCL: tumour cells showed intense, diffuse expression of CD20, moderate expression of P53 (40%), and a very high Ki-67 proliferation index (95%), and were negative for CD3, CD5, CD10, BCL2, BCL6, CD30 and TdT. The patient was referred to the haematology department for completion of staging work-up and specialised treatment. ***Discussion:*** This case highlights the clinical and radiological difficulty in distinguishing gingivo-mandibular squamous cell carcinoma from primary gingival lymphoma, and underlines the importance of systematic biopsy for any persistent, atypical gingival swelling. It also stresses the need, once the diagnosis of lymphoma is confirmed, to re-stage the disease according to the Lugano classification rather than the TNM system, which is designed for epithelial tumours. ***Conclusion:*** Early biopsy remains the cornerstone of the diagnostic work-up for atypical adult gingival masses, avoiding diagnostic delay and inappropriate management.

Keywords: diffuse large B-cell lymphoma; gingiva; mandible; non-germinal center B-cell; Han's algorithm; differential diagnosis; squamous cell carcinoma.

INTRODUCTION

Non-Hodgkin lymphomas (NHL) account for approximately 3–4% of all cancers, and diffuse large B-cell lymphoma (DLBCL) is their most common histological subtype, representing 30–40% of adult NHL [1]. While nodal disease remains the most frequent presentation, approximately 40% of DLBCL cases are primarily extranodal and can virtually involve any organ [1].

Primary involvement of the oral cavity, and more specifically of the gingiva, is exceptional, accounting for only about 1% of primary extranodal lymphomas [1, 5]. Clinically and radiologically, this site poses a formidable diagnostic challenge, as it readily mimics a benign dental condition, an abscess, osteomyelitis, or, more concerning, an oral squamous cell carcinoma, particularly when associated with mandibular bone lysis and cervical lymphadenopathy, as reported in several case series [2–6].

We report the case of a patient presenting with a mandibular gingival swelling of 3 months duration, initially staged according to the TNM classification used for upper aerodigestive tract carcinomas, whose biopsy ultimately revealed a non-germinal center DLBCL. Through this observation, we discuss the clinical, radiological, immunohistochemical and therapeutic

features of this rare entity, as well as the diagnostic pitfalls it entails.

CASE PRESENTATION

A 61-year-old man with no notable medical history presented with a right lower vestibular gingival swelling that had been progressively worsening over 3 months.

Clinical examination revealed a firm swelling of the right lower vestibular gingiva, associated with a palpable ipsilateral cervical lymph node.

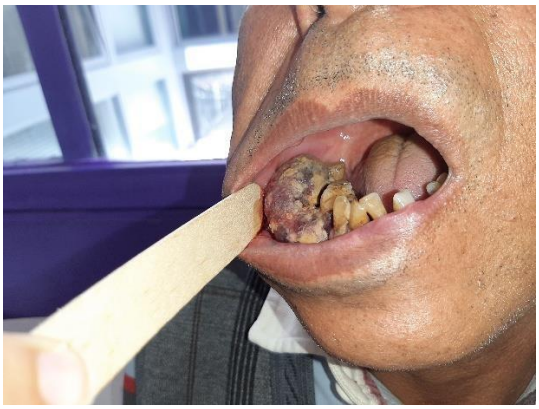

Figure 1: Image of firm swelling of the right lower vestibular gingiva

Imaging

Facial MRI showed an expansile process of the right lower vestibular gingiva lysing the horizontal ramus of the right hemimandible, with an ipsilateral cervical lymph node exceeding 3 cm in its largest diameter. Given this appearance, which was initially suggestive of an oral squamous cell carcinoma, the lesion was classified as T4a N2a Mx according to the 8th edition of the American Joint Committee on Cancer (AJCC) TNM classification for upper aerodigestive tract carcinomas.

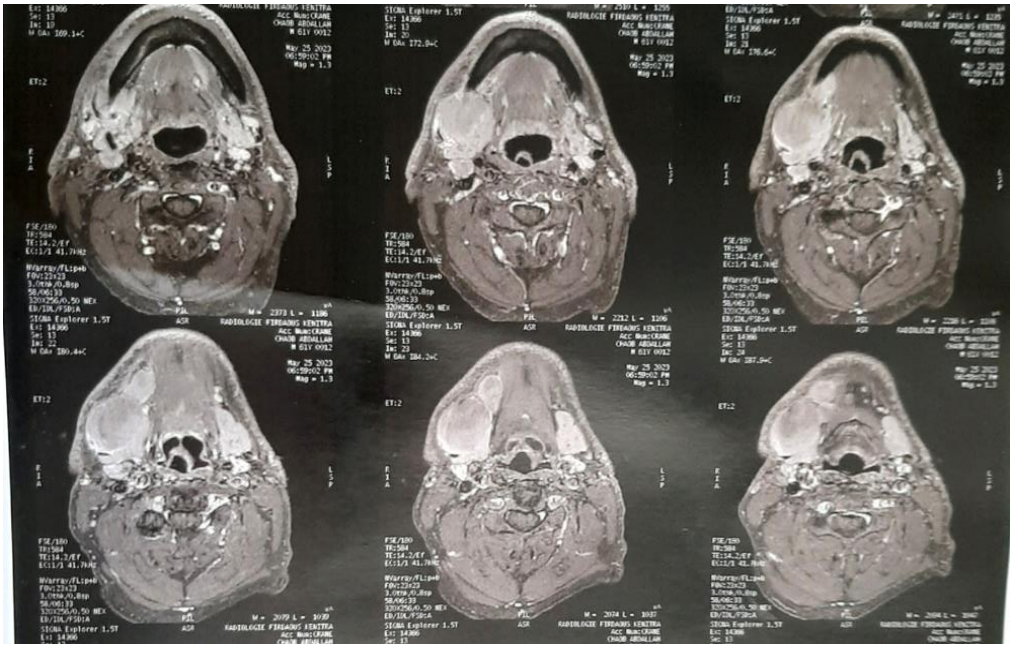

Figure 2: MRI showing an expansile process of the right lower vestibular gingiva lysing the horizontal ramus of the right hemimandible.

Pathology and Immunohistochemistry

A biopsy of the gingival lesion was performed. Standard histopathological examination was morphologically consistent with a large-cell lymphoid proliferation. Complementary immunohistochemical staining further characterised the tumour phenotype (Table 1).

The immunohistochemical profile (CD20 positive; CD10, BCL6 and CD30 negative) was consistent with a non-germinal center (non-GCB / activated B-cell-like) diffuse large B-cell lymphoma, with a very high Ki-67 proliferation index (95%) and moderate P53 overexpression (40% of tumour cells). The

absence of CD3, CD5 and TdT expression excluded, respectively, a T-cell proliferation, infiltration by a CD5+ mantle cell lymphoma, and a lymphoblastic lymphoma.

Table 1: Immunohistochemical findings on the gingival biopsy

Antibody	Staining pattern / intensity	Result
CD20	Intense, diffuse staining	Positive
P53	Nuclear, moderate intensity, 40% of tumour cells	Positive (moderate overexpression)
Ki-67	Nuclear, strong intensity, 95% of tumour cells	Very high proliferation index
CD3	—	Negative
CD5	—	Negative
CD10	—	Negative
BCL2	—	Negative
BCL6	—	Negative
CD30	—	Negative
TdT	—	Negative

The final diagnosis was a gingival localisation of a non-germinal center diffuse large B-cell non-Hodgkin lymphoma.

Management

Given this diagnosis, the patient was referred to the hematology department for completion of the staging work-up (notably 18F-FDG PET-CT, serum LDH, and bone marrow biopsy) and for initiation of specialised systemic treatment, in line with current DLBCL guidelines. Data regarding the complementary staging workup, the therapeutic protocol selected, and the patient's subsequent course were not available at the time of writing, as follow-up is being carried out by the hematology team.

DISCUSSION

A Rare and Deceptive Location

The gingiva is an exceptional site for primary lymphoma: Sugimoto *et al.,* report that it accounts for only about 1% of primary extranodal NHL locations [1], while Deng *et al.,* estimate the frequency of gingival DLBCL with muscle invasion at approximately 0.5% of extranodal lymphomas [5]. Clinically, the presentation is most often misleading: an isolated, sometimes painful, rapidly progressive gingival swelling that can mimic a dental condition, an abscess, reactive hyperplastic gingivitis, or osteomyelitis [1, 4, 6]. Several authors have documented cases initially managed as benign dental disease before persistence of symptoms despite antibiotic and/or periodontal treatment prompted diagnostic biopsy [6].

Our observation illustrates a different, but equally significant, diagnostic pitfall: the combination of mandibular bone lysis and an ipsilateral cervical lymph node exceeding 3 cm immediately suggested an oral squamous cell carcinoma, prompting TNM staging. This same mimicry with epithelial tumours of the oral cavity has been reported by Bhattacharyya *et al.,*[3] and Bugshan *et al.,*[4], who emphasise that neither clinical examination nor imaging can reliably distinguish carcinoma from lymphoma in cases of gingivomandibular involvement with bone lysis; only biopsy with immunohistochemical study allows a definitive diagnosis.

From TNM to the Lugano Classification

This case highlights an important methodological point: the AJCC TNM classification initially used in our patient (T4a N2a Mx) is a staging system designed for solid epithelial tumours and is not appropriate for staging lymphomas. Once the diagnosis of DLBCL was confirmed by biopsy, staging should be revised according to the Lugano classification, which in 2014 modernised the Ann Arbor criteria for the initial evaluation, staging and response assessment of Hodgkin and non-Hodgkin lymphoma, notably incorporating 18F-FDG PET-CT as the reference imaging modality [9, 10]. This change in staging framework has direct implications for the required work-up (PET-CT, LDH, bone marrow biopsy, complete blood workup) and for the treatment strategy, which differs radically from that of a squamous cell carcinoma.

Calculation of the International Prognostic Index (IPI), which integrates age, Ann Arbor/Lugano stage, LDH level, number of extranodal sites involved, and performance status, remains a key prognostic tool in DLBCL, including in the immunochemotherapy era [11].

Contribution of Immunohistochemistry and the Hans Algorithm

Classification into germinal center B-cell-like (GCB) or non-germinal center B-cell-like (non-GCB / activated B-cell-like) subtype classically relies on gene expression profiling, the reference technique but one with limited accessibility in routine practice. The immunohistochemical algorithm published by Hans *et al.,* in 2004 remains the most widely used surrogate tool in clinical practice, based on three markers: CD10, BCL6 and MUM1, with approximately 80% concordance with gene expression profiling [7]. In our patient, negativity for both CD10 and BCL6 is consistent with a non-germinal center profile, in line with the pathology report's conclusion.

This phenotypic distinction carries well-established prognostic value: the non-GCB subtype is classically associated with a less favourable response to treatment and inferior overall survival compared with the GCB subtype under R-CHOP-based immunochemotherapy [7, 8]. A recent Moroccan study conducted at Hassan II University Hospital in Fez, including 106 DLBCL cases classified according to the Hans algorithm, confirmed a clear predominance of the non-GCB subtype (71% of cases) in the Moroccan population, together with a significant association between this subtype, high Ki-67 expression, and poorer outcome [8]. The high Ki-67 positivity observed in our patient (95%) reflects a very high tumour proliferation index, consistent with the aggressive behaviour classically reported for this phenotypic combination [8]. The moderate P53 overexpression (40%) observed in our case is in keeping with molecular alterations frequently described in DLBCL, whose unfavourable prognostic value has been reported by several groups, particularly in non-GCB forms.

Therapeutic Management

The reference treatment for DLBCL has, since the results of the randomised trial by Coiffier *et al.,* published in 2002, relied on the combination of immunotherapy with polychemotherapy according to the R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone), which demonstrated a significant benefit in complete response rate as well as overall and progression-free survival compared with CHOP chemotherapy alone, without a clinically significant increase in toxicity [9]. More than two decades after its validation, this regimen remains the cornerstone of first-line DLBCL treatment, typically administered over 6 to 8 cycles, sometimes combined with additional locoregional radiotherapy in cases of bone involvement or residual mass, as reported in cases of gingival DLBCL with bone or muscle invasion [5].

In our patient, referral to the haematology department for completion of the work-up and specialised treatment follows this standard approach; the precise therapeutic decision (number of cycles, addition of radiotherapy) should be tailored to the definitive Lugano stage, IPI score, and the patient's performance status, elements that were not yet available at the time of writing.

Key Practice Points

This case underscores several practical messages for the ENT clinician and maxillofacial surgeon: any persistent gingival swelling resistant to usual dental or periodontal treatment warrants prompt biopsy, regardless of a radio-clinical appearance suggestive of another aetiology; the presence of mandibular bone lysis and cervical lymphadenopathy alone cannot reliably distinguish squamous cell carcinoma from lymphoma; and, once a histological diagnosis of lymphoma is established, staging and management must follow haematological frameworks (Lugano classification, IPI, immunochemotherapy) rather than those used for solid epithelial tumours.

CONCLUSION

Primary gingival diffuse large B-cell lymphoma is a rare entity whose clinical and radiological presentation can deceptively mimic an oral squamous cell carcinoma, particularly when associated with mandibular bone lysis and cervical lymphadenopathy. Biopsy with immunohistochemical study remains the essential diagnostic step, allowing both confirmation of the lymphomatous nature of the lesion and determination of its subtype according to the Hans algorithm, with major prognostic and therapeutic implications. Once the diagnosis is confirmed, care should be promptly transferred to a haematology team, and staging and treatment should follow lymphoma-specific frameworks rather than those used for solid epithelial tumours.

Declarations

Patient consent: informed consent was obtained for publication of this case and the associated clinical, radiological and pathological data.

Conflicts of interest: the authors declare no conflicts of interest related to this work.

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