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DIFFUSE B-CELL LYMPHOMA OF THE MANDIBLE DISGUISED AS ACUTE OSTEOMYELITIS

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ABSTRACT

Background: Primary bone lymphoma (PBL) is a rare form of extra nodal non-Hodgkin's lymphoma (NHL).
Case description: We describe a 39-year-old-male with no medical history who presented with unilateral facial swelling following a tooth extraction. Initial diagnoses after various presentations over the course of three weeks, based on inflammatory and infectious aetiologies. However, the patient was ultimately diagnosed with diffuse large B-cell lymphoma.
Discussion: Symptoms of PBL are very similar to inflammatory and infectious diseases of the bone, such as osteomyelitis or osteonecrosis. Clinical features of PBL involving the head and neck include persistent jaw pain, tooth mobility secondary to extensive destruction of bone, and in advanced cases, lip numbness and swelling. On examination it may present as an exposed necrotic bone with surrounding soft tissue oedema. Misdiagnosis of these lesions as an infectious or inflammatory aetiology may lead to an unnecessary delay in lymphoma treatment, and subsequently worsen the prognosis if caught at a later stage. Therefore, any concerning lesion, especially in the oral cavity, must be subjected to early histopathological evaluation to differentiate PBL from osteomyelitis and/or osteonecrosis.
Conclusion: This case report highlights the importance of an early histopathological evaluation to prevent delay in the diagnosis of primary bone lymphomas.

KEYWORDS

Osteomyelitis, lymphoma, bone necrosis, diffuse B-cell

LEARNING POINTS

- Resemblance in symptoms: Primary bone lymphoma (PBL) symptoms overlap with bone infections, necessitating careful consideration and differential diagnosis to prevent misjudgment.
- Head and neck manifestations: recognising PBL's signs in the head and neck region, such as jaw pain and bone destruction, aids in timely identification and treatment.
- Timely biopsy significance: swift histopathological assessment for suspicious lesions is critical to avoid delays in diagnosing primary bone lymphomas.

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INTRODUCTION

Non-Hodgkin's lymphoma (NHL) is the seventh most common type of malignancy in males and females in the United States[1]. Primary bone lymphoma (PBL) is a rare and extra nodal type of NHL, occurring in less than 1% of all lymphomas and only 3% of all malignant bony neoplasms[1]. The median age of occurrence is 45 years old, with occurrence more common in males than females[1]. It can manifest in various bones, most commonly in the femur or humerus, followed by bones within the head and neck[1]. The most common type of NHL is diffuse large B-cell lymphoma, followed by mucosa associated lymphoid tissue lymphoma[2]. PBL of the head and neck region presents as persistent jaw pain and tooth mobility, and in advanced cases, lip numbness and swelling[3]. Most of these symptoms overlap with many more common diseases such as toothache, periapical abscess, osteomyelitis of the jaw, Paget's disease or osteosarcoma[2]. Radiographic findings of PBL also can be misleading as they can either be normal or non-specific including lytic (most common) sclerotic or mixed pattern representing necrosis of bone and surrounding oedema[4]. All these mimic findings of other diseases such as acute and chronic osteomyelitis, Paget's disease, multiple myeloma or osteonecrosis, making it challenging to make an early diagnosis. Incorrect diagnosis can lead to delays in starting targeted therapy and subsequently expose patients to unnecessary dental procedures[4]. In this case report, we present a 39-year-old male with worsening facial swelling on the left side initially treated as osteomyelitis.

CASE DESCRIPTION

A 39-year-old-male with no past medical history presented to the Emergency Department (ED) with left sided facial swelling lasting three weeks following a left molar extraction. Symptoms embarked as a toothache four months prior, leading to extraction of #17 tooth with implant placement. Over the course of time, he had persistent, worsening numbness, and tingling of the left cheek, lip and face. He noticed swelling and pain within the month prior to admission which led him to revisit the dental clinic. The patient had an X-ray for his tooth for possible root canal treatment, but a biopsy was not done at that time and no further diagnosis was made. This information was unobtainable. He was prescribed a ten-day course of amoxicillin 500 mg orally twice daily and had #21 tooth extracted once he completed the antibiotics. Following extraction, an additional ten-day course of amoxicillin was prescribed. He returned to the dental clinic approximately one week later with excruciating pain and swelling, for which he was sent to the ED.

On arrival, he was haemodynamically stable without any laboratory abnormalities, including normal C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), comprehensive metabolic panel and complete blood count (normal differential counts and normal eosinophil counts). He appeared well nourished and was not in acute distress. His membranes were moist. There was a firm, indurated swelling without erythema or fluctuance extending from the left angle of the mandible upwards to the midface. It was tender to deep palpation. The swelling impeded palpation of the border of the left mandible proximal to the angle. Interiorly, the uvula was midline and the tongue had full range of motion. However, there was a buccal vestibule swelling noted approximating the left lower, posterior alveolar ridge. The left lower alveolar ridge distal to #20 was oedematous and erythematous, but without purulence or drainage; the #17 residual extraction socket was present without inflammation. There was no avulsion of teeth or intraoral lacerations, and no pain on occlusion. The patient was unable to distinguish pinprick and directionality from mental symphysis to left labial commissure below the lower lip; however, all other cranial nerves were intact and there were no other focal neurological deficits. There were numerous non-tender and mobile cervical lymph nodes, enlarged bilaterally.

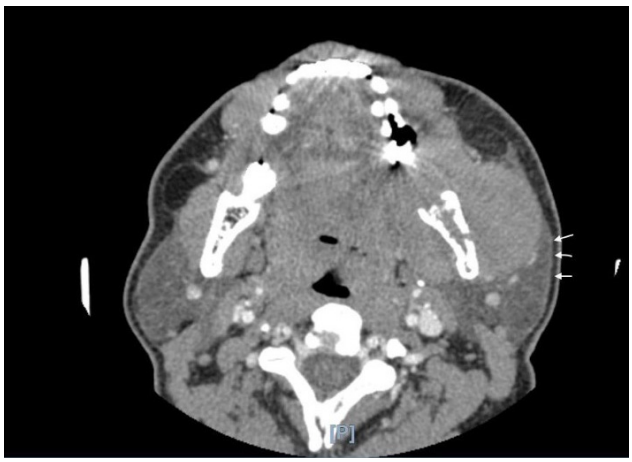

Figure 1. Computerised tomography with intravenous contrast of the maxillofacial area of the jaw showing destruction of the left hemi mandible with associated soft tissue mass involving the master muscle and the pterygoid muscles of the infratemporal fossa (arrows). There is no evidence of an abscess. Reactive adenopathy is noted.

A computerised tomography of the jaw with intravenous contrast demonstrated severe destruction of the left hemimandible *(Fig. 1)*. At this time, the differential diagnosis included severe osteomyelitis versus a neoplastic process. Given the size of the lesion there were minimal inflammatory changes. There was a soft tissue mass effect of the left masseter muscle, and soft tissue swelling of the pterygoid muscles. The Oral-Facial-Maxillary-Services department admitted the patient with concern of osteomyelitis of the jaw, requiring surgical intervention. The Infectious Disease department was consulted for co-medical management.

Through further history it was noted that his mother, sister, and brother all had a history of thyroid cancer (unknown type). The patient migrated from Ecuador 10 years prior, had smoked one cigarette per week for the last 22 years and occasionally drank alcohol. He was not taking any herbal supplements or medications.

During this hospitalisation, he received ampicillin-sulbactam 3,000 mg intravenously every six hours and was started on a

one-time dose of vancomycin 1,000 mg. He underwent a full thickness soft tissue incisional biopsy of the left mandible with intraoperative findings of mandibular soft tissue swelling extending from left body to the pterygomandibular raphe. Superficial wound cultures grew normal oropharyngeal flora. Deep tissue cultures, acid-fast-bacilli and fungal cultures were negative. Pathology returned positive for diffuse large B-cell lymphoma with high proliferation index (>90% on KI-67 stain) *(Fig. 2 and 3)*.

On immunostains, the large cells are positive for CD20, BCL-6 and MUM1, and faintly positive for CD5 *(Table1)*. The large cells are negative for CD10, CyclinD1, CD30, CD34, TdT and PanCK. A stain with c-Myc shows 30%–40% large cells as positive. Most of the large cells are negative to very slightly positive for BCL-2. A stain with Ki-67 shows a high proliferation index (> 90%) in the lymphoma cells. A stain with CD21 fails to reveal any follicular dendritic meshwork. Scattered small reactive T-cells are positive for CD3. These results support a diagnosis of diffuse large B-cell lymphoma (DLBCL), with immunophenotype most compatible with non-GCB (germinal center B-cell subtype) type, with a high proliferation index. Initially, CD5+ DLBCL is usually associated with more aggressive clinical behaviour and poorer outcome; however, the CD5 expression in this lymphoma is very faint and the clinical significance is unclear. In-situ hybridisation for Epstein–Barr virus (EBV)-encoded RNA (EBER), and fluorescence in-situ hybridisation for BCL-2, BCL-6, MYC translocations and 11q aberrations were performed.

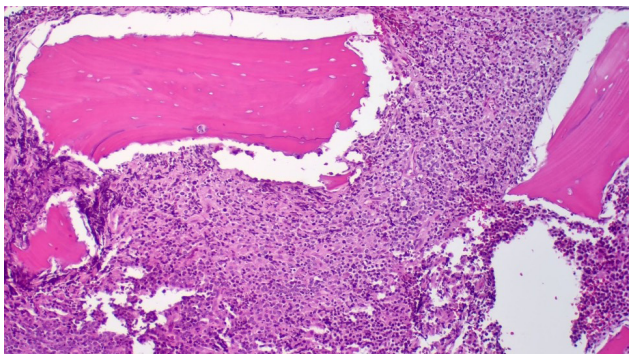

Figure 2. Left mandibular soft tissue and bone biopsy (low power field). Diffuse proliferation of large lymphoma cells with round to slightly irregular nuclei and moderate eosinophilic cytoplasm in the submucosa.

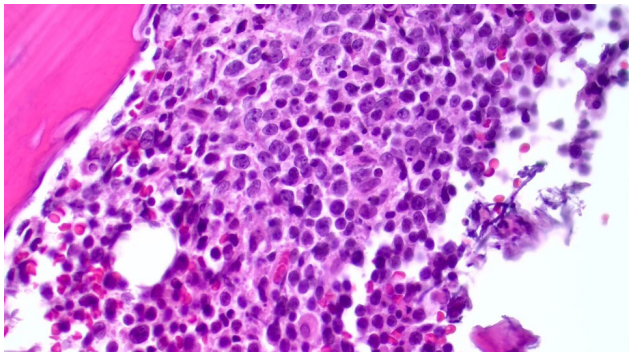

Figure 3. Left mandibular soft tissue and bone biopsy (high power field). Many large lymphoma cells show prominent central nucleoli. Brisk mitotic activities and apoptotic bodies are seen.

Antibody/Test	Clone	Results
PancK (Pancytokeratin)	AE1/3 & PCK26	Negative
CD20	L26	Positive
CD3	Small reactive T cells	Positive
CD10	SP67	Negative
BCL-6	GI191E/A8	Positive
MUM-1 (multiple myeloma oncogene 1)	MRQ-43	Positive (~70-80%)
BCL-2	124	Negative to dimly positive
CD5	SP19	Negative
Cyclin D1	SP4-R	Faintly positive
CD30	BerH2	Negative (<1%)
CD34	QBEnd/10	Negative
TdT (terminal deoxy nucleotide transferase)	Polyclonal	Negative
c-MYC (cellular myc gene)	Y69	30-40%
CD21	2G9	Negative for FDC
Ki-67	30.9	> 90%

Abbreviations - CD: cluster of differentiate; SP: speckled protein; BCL: B-cell lymphoma

Table 1. Immunohistochemistry analysis.

The patient was discharged on a complete seven-day course of amoxicillin-clavulanate 875–125 mg twice daily and met with oncologists in the outpatient setting.

DISCUSSION

Osteomyelitis of the jaw is defined as an infection of bone, involving the cortex, periosteum and adjacent soft tissues[5]. Patients with acute osteomyelitis (OM) often present with fevers, malaise, purulence and/or localised fluctuance surrounding an oedematous and erythematous area, exposure of the bone and high levels of CRP on laboratory studies[6]. Histopathology in acute OM will show necrosis and neutrophilic infiltrates in the medulla, while chronic OM will demonstrate lymphocytic and plasma cells infiltrating the medulla[6]. Chronic OM often presents with low-grade symptoms[6].

Few studies in current literature describe cases of PBL disguised as osteomyelitis[7–11]; there are only a handful of articles which describe PBL manifesting as acute or chronic osteomyelitis[7–11]. Of those, chronic osteomyelitis has been of the ankle or knee joints, and a few of the mandibular bones[7–11]. These articles suggest that a chronic inflammatory process secondary to the underlying PBL malignancy stimulates an infection of the deteriorating bone, such as osteomyelitis[7–11].

Acute OM has imaging findings of periosteal reaction and/or bone marrow oedema, blurring of tissue fat planes, sequestrum formation with overlying involucrum are common in chronic osteomyelitis[4]. Ultimately, both acute and chronic osteomyelitis show various phases of bone destruction seen as lytic lesions on imaging[4]. Invariably, PBL on imaging shows marked non-specific features (no pathognomonic lesion) mimicking other more common conditions such as lytic lesions in infections (osteomyelitis), multiple myeloma, Ewing sarcoma or sclerotic lesions such as in Paget's disease or osteosarcoma[4]. Our patient's radiographic findings included bone destruction, mass effect, oedema, periosteal reaction and lytic lesions, which led to high suspicion of OM. However, it should have raised suspicion for an alternative diagnosis due to failed treatment with antibiotics and additional clinical findings of lip swelling and numbness, and normal ESR and CRP.

Additionally, the poor vascularisation and dense cortex of the mandibular bone makes it a more desirable location than the maxilla for osteomyelitis to occur[6]. This also makes the mandible more prone to infections following procedures, such as tooth extractions[6]. It is possible that our patient did have an infection and/or abscess at one time following his initial procedure; however, given the ambiguous symptoms, and physical and radiographic findings, it is imperative to consider a less likely, but important differential such as PBL.

In acute osteomyelitis, ESR and CRP levels are typically elevated and may rise rapidly over a short period of time. ESR levels can rise to greater than 100 mg per liter while CRP levels can reach several hundred mg per liter[12]. In chronic osteomyelitis, the ESR and CRP levels may not be as high as in acute osteomyelitis[12]. However, they may still be elevated above normal levels and may fluctuate over time[12]. The degree of elevation may also depend on the severity of the infection and the individual's immune response[12]. Moreover, our patient's laboratory studies, including a normal ESR and CRP, did not allude to a diagnosis of acute osteomyelitis; however, chronic osteomyelitis could not be excluded based on that information alone.

Contrary to current literature, our patient did not present with constitutional symptoms such as night sweats or weight loss and did not have haematological abnormalities indicative of a lymphoma either. In prior cases of PBL and concomitant osteomyelitis, patients have demonstrated risk factors such as uncontrolled diabetes mellitus, chronic alcohol abuse, or history of previous old or pathologic fractures, making immunocompromised patients more susceptible in having them both[13].

In this case, the only positive family history is of thyroid cancer (unknown type) in the mother and siblings. On literature review, most thyroid lymphomas are NHLs of B-cell origin. However, with unknown details of the thyroid cancer, association between patient's B-cell lymphoma and thyroid cancer is difficult to make[14].

A histopathological report of our patient's bone biopsy depicted diffuse proliferation of large lymphoma cells with round to slightly irregular nuclei; many large cells had prominent central nucleoli. Brisk mitotic activities and apoptotic bodies were seen. These findings coincide with expected PBL biopsy results of large atypical lymphoid cells with high mitotic division[15]. It can be seen as a localised nodular pattern and/or diffuse pattern invading the bone marrow[15].

The Lugano classification system is the most widely used staging criteria for the diagnosis of PBL[15]. Based on our patient's presentation, he was classified as stage IE, which is disease limited to an extra nodal site as a solitary bone lesion[16].

Current treatment options for PBL include radiation, chemotherapy and surgery. Current studies demonstrate superior results in terms of years of remission and prognosis with a radiation and chemotherapy (cyclophosphamide, doxorubicin, vincristine, prednisone +/- rituximab) combination rather than radiation alone[16]. Occurrence of PBL in the long bones carries the best prognosis The factors associated with the best prognosis include staging of IE, age less than 60 years at time of diagnosis, lack of metastatic disease and a low level of lactate dehydrogenase (LDH)[16].

CONCLUSION

PBL can mimic other conditions such as toothaches, osteomyelitis and abscess. Our patient's diagnosis of PBL was concealed by his recent dental procedures and concern for recurrent infections. It is possible that our patient also had chronic osteomyelitis and PBL, which cannot be differentiated by pathology alone. Although some studies describe concomitant osteomyelitis and PBL, the

occurrences are in the bones of the legs and feet. Seldom do cases describe occurrences in the mandible. With the lack of evidence of acute osteomyelitis, other less likely, but sinister diagnoses such as PBL should be entertained, even if patients lack haematological abnormalities or constitutional symptoms, as seen in our patient.

REFERENCES

1. Zhang X, Zhu J, Song Y, Ping L, Zheng W. Clinical characterization and outcome of primary bone lymphoma: a retrospective study of 61 Chinese patients. *Sci Rep* 2016;**6**:28834.
2. Vardas E, Georgaki M, Papadopoulou E, Delli K, Kouroumalis A, Kalfarentzos E, et al. Diagnostic challenges in a diffuse large B-cell lymphoma of the maxilla presenting as exposed necrotic bone. *J Clin Exp Dent* 2022;**14**:e303–e309.
3. Bugshan A, Kassolis J, Basile J. Primary diffuse large B-cell lymphoma of the mandible: case report and review of the literature. *Case Rep Oncol* 2015;**8**:451–455.
4. Pineda C, Espinosa R, Pena A. Radiographic imaging in osteomyelitis: the role of plain radiography, computed tomography, ultrasonography, magnetic resonance imaging, and scintigraphy. *Semin Plast Surg* 2009;**23**:80–89.
5. Nezafati S, Ghavimi MA, Yavari AS. Localized osteomyelitis of the mandible secondary to dental treatment: report of a case. *J Dent Res Dent Clin Dent Prospects* 2009;**3**:67–69.
6. Lorè B, Gargari M, Ventucci E, Cagioli A, Nicolai G, Calabrese L. A complication following tooth extraction: chronic suppurative osteomyelitis. *Oral Implantol (Rome)* 2013;**6**:43–47.
7. Jayaprakasan P, Warrier A. Primary bone lymphoma of the shaft of the tibia, mimicking subacute osteomyelitis. *Cureus* 2023;**15**:e38070.
8. Peng YH, Wang SJ, Zhao JF, Zha ZA, Han XG, Sun Q, et al. [Clinical features and imaging analysis of primary bone lymphoma of the jaw]. *Zhonghua Kou Qiang Yi Xue Za Zhi* 2020;**55**:383–387.
9. Mika J, Schleicher I, Gerlach U, Adler C-P, Uhl M, Knoeller SM. Primary bone lymphomas thought to be osteomyelitis urgently demand a rapid diagnosis in bone pathology. *Anticancer Res* 2012;**32**:4905–4912.
10. Malik S, Zaki A, Shabbir MU, Hussain T. Plasmablastic lymphoma mimicking osteomyelitis of femur in an immunocompetent individual: a case report. *Cureus* 2022;**14**:e21183.
11. Liu C-W, Tsai T-Y, Li Y-F, Lin L-C, Wang S-J. Infected primary non-Hodgkin lymphoma of spine. *Indian J Orthop* 2012;**46**:479–482.
12. Markanday A. Acute phase reactants in infections: evidence-based review and a guide for clinicians. *Open Forum Infect. Dis* 2015;**2**:ofv098.
13. Hannan CM, Attinger CE. Special considerations in the management of osteomyelitis defects (diabetes, the ischemic or dysvascular bed, and irradiation). *Semin Plast Surg.* 2009;**23**:132–140.
14. Stein SA, Wartofsky L. Primary thyroid lymphoma: a clinical review. *J Clin Endocrinol Metab* 2013;**98**:3131–3138.
15. Krishnan A, Shirkhoda,A, Tehranzadeh J, Armin AR, Irwin R, Les K. Primary bone lymphoma: radiographic-MR imaging correlation. *Radiographics* 2003;**23**:1371–1387.
16. Bindal P, Desai A, Delasos L, Mulay S, Vredenburgh J. Primary bone lymphoma: a case series and review of literature. *Case Rep Hematol* 2020;**2020**:4254803.