

**Primary bone lymphoma of the mandible mimicking osteomyelitis - A difficult differential diagnostic task**

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**Type of Publication:** Case Report

**Conflicts of Interest:** Nil

**Abstract**

**Background:** Lymphomas are malignant diseases arising from lymph nodes or lymphoid system and divided into Hodgins and non-Hodgkin variants. The tumor in most of the cases affects the lymph nodes but in 24% extra nodal sites are involved. The facial bones and especially the mandible rarely is affected.

**Case Report:** A 54-year-old female referred to her dentist with pain and swelling of the right side of the mandible. The mandibular second molar was considered the responsible tooth by her dentist, and it was submitted to endodontic treatment. Next week’s hypesthesia of the ipsilateral site of the lower lip along with pain and mild

swelling lead to the diagnosis of osteomyelitis. Symptoms remained unchanged and a bone biopsy from the mandible showed the presence of a B- cell lymphoma.

**Clinical significance:** In the present case a differential diagnostic dilemma was erected. History of the patient, symptoms, clinical evaluation, and radiologic findings were suggestive of a typical case of osteomyelitis. The patient was free of disease or other symptoms related with lymphoma. The decisive step for diagnosis was the bone biopsy and histologic examination.

**Conclusion:** This case report describes the difficulty and the delay in diagnosis of a primary lymphoma of the

mandible when its clinical symptoms are similar with osteomyelitis.

**Keywords:** Lymphoma, primary, mandible, bone, osteomyelitis, diagnosis

### **Introduction**

Lymphoma is a malignant disease arising from the lymphoid tissue and classified according to clinical criteria for Hodgkin's and Non-Hodgkin's lymphoma. Non-Hodgkin's lymphoma at fifth decade more frequently encountered disease, while Hodgkin's lymphoma affects younger patients. (1) Reed-Sternberg cells are pathognomonic for histological diagnosis of Hodgkin's lymphoma forming a tiny proportion of tumor cells (2). B-cell lymphomas consist the majority of non-Hodgkin lymphomas and more frequently affect the lymph nodes (2).

Non-Hodgkin's lymphoma rarely observed into the oral cavity even though they are classified as the second malignant lesion of the head and neck (3) Skeletal involvement is estimated at 5% with pelvic girdle, fibula, and tibia, humerus and spine to be more frequently affected (4) The oral cavity is rarely affected, and they encountered in the soft tissue of the gingiva, palate, and tonsils or into the jaw bones (5). Mandibular involvement is extremely rare and in cases when mandibular involvement is the primary site of the disease and the clinical symptoms and radiologic features present similarities with well-known dental diseases there is a delay in accurate diagnosis of lymphoma.

The purpose of our paper is to describe a rare case of a primary B-cell lymphoma affecting the mandible mimicking an osteomyelitis, and to alert the clinicians that rarely, hypesthesia of the lower lip could be the first sign of a primary lymphoma.

### **Case report**

A 55-year-old female with free past medical history was referred to her dentist with pain along her right lateral site of the mandible. The dentist performed an endodontic treatment of the right mandibular second molar. However, the pain persisted and a retreatment of the same tooth by an endodontist was performed. Four weeks later the patient complained about mild swelling and pain at the same area and a course of antibiotics were prescribed. Subside of the symptoms observed but 3 weeks later hypesthesia of the ipsilateral lower lip was recorded for the first time. Clinically the diagnosis of osteomyelitis was considered, and extraction of the right second mandibular molar was performed. Three weeks after tooth extraction and healing of the post extraction socket the pain remained severe without relief. A cone beam was performed, and findings of the examination were compatible with osteomyelitis as disorganization of the affected area was observed. (Figure 1, 2) The patient received a new course of antibiotics and pain killers, and a bone biopsy of the affected area was scheduled. However, a new outbreak of the swelling delayed the operation. After relapse of the acute stage a biopsy and exploration of the area revealed a mottled mandible (Figure3), with granular tissue occupying the mandibular bone and investing the internal surface of periosteum. Multiple biopsies were taken from different sites both from the bone and from the soft tissue. Histopathologic findings included destruction of the mandibular bone with invasion by a carcinoma with severe fibrosis.

The malignant cells resembled with large lymphoid cells that in immunohistochemistry were positive for CD20, BCL6, CD10, BCL2 and about 70% of tumor cells showed positivity for ki67 (figure 4A, B, C, D, E, F, G) and the diagnosis of a B-cell non-Hodgkin lymphoma was confirmed. Further investigation of the patient with

PET-CT showed the presence of a large hypermetabolic focus at the right site of the mandible with a high SUV max 33.5 and smaller foci at different bones of the skeleton with lower SUV max 15.1. The patient referred to hematologist for further consideration and treatment.

### **Discussion**

A non-Hodgkin lymphoma is characterized primary when there is not exist involvement of the disease to any other organ or area of the body at least 6 months after the initial diagnosis. (6) It is not uncommon for the lymphomas to present with lymph node enlargement of the neck as the first clinical manifestation, but the mandible rarely is affected. According to clinical studies skeletal bones are infiltrated from the lesion in only 5% of all non-Hodgkin lymphomas. (7) Primary mandibular involvement is estimated about 0.6% of all non-Hodgkin lymphomas and is considered very rare (8). When there is skeletal bone infiltration, other bones such femur, pelvis, tibia, and fibula, humerus, and spine are more frequently infiltrated, while mandible, radius, scapula skull bones are rarely affected. (4) In our case we consider the involvement of the mandible as the primary site as the first clinical signs and the diagnosis performed from this anatomic location and after diagnosis four months after the initial diagnosis, the PET-CT performed after the initial diagnosis of mandibular lymphoma showed the presence of other skeletal involvement that were smaller in dimensions and with lower SUV max than the mandibular site of involvement and without clinical symptoms. Taking into consideration and analyzing all these findings the radiologist considered the mandible as the primary site of the disease. Among the jaws according to some investigators, maxilla is most frequently affected than the mandible, even though it is difficult to distinguish if

the lesion arises from the medullary part of the bone or from the neighboring soft tissues. (9,10,11) However the study of Beal et al (2006) in a sample of 82 patients showed a very rare participation of the mandible with only two cases and without involvement of the maxilla. (4) The body is the most frequently affected area of the mandible. (12,13)

Diagnosis of mandibular lymphoma is challenging, and it is associated with many difficulties as many inflammatory or odontogenic benign or malignant lesions are more often encountered than lymphoma and the differential diagnosis focused initially on clinical situations that more frequently observed. General symptoms such as fever, weight loss and fatigue rarely have been reported in primary bone lymphoma of the mandible (14). This parameter may increase the difficulty in differential diagnosis, as these symptoms are associated with a generalized disease. The initial symptoms of the mandibular lymphomas are pain and/or swelling of the mandible and the swelling initially is attributed to odontogenic etiology. Dental pain and mobility may observe when lymphoma infiltrate the dentate area of the mandible and in some cases, it is associated with numbness of ipsilateral part of the lower lip or with ulceration or with a lesion projecting from an extraction socket. (15) In some cases, the clinical symptom of lymphoma resembles with periapical infection of odontogenic origin mimicking a periapical lesion. (16) In our case the main symptom was a swelling of the right site of the mandible with pain that initially attributed to an oral infection as the patient doesn't have general symptoms. In the course of the disease numbness of the right site of the lower lip was added. This symptom along with the imaging findings from CBCT increased the possibility of an osteomyelitis of the jaw. The latter findings delayed the programmed

bone biopsy; however, the persistence of symptoms leads us to perform the biopsy. During the operation the surgical findings were different from that observed in an osteomyelitis of the jaws including neoplastic tissue infiltrating the mandibular bone and investing the inner site of the periosteum.

Radiographic imaging at the initial stage is subtle and not specific resembling a dental infection. In later stages a destruction of the mandibular bone, loss of cortical bone or enlargement of the mandibular canal may be seen. (1,16,17) A fracture of the condyle has been described in a lymphoma involving the body and the ramus of the mandible along with delay in diagnosis and treatment. (6)

In all the cases bone biopsy is the key examination procedure to establish the diagnosis of lymphoma and to elucidate its type. Large tumor cells with characteristic large nuclei are the histologic feature of NHL but immunohistochemistry with other related examinations is very important for differential diagnosis from other pathologic entities. (13,14)

In our case immunohistochemistry with positivity of CD20, BCL6, CD10, BCL2 of markers and with about 70% of tumor cells showing positivity for ki67 the diagnosis of a B-cell lymphoma was confirmed.

Staging of NHL is critical for treatment selection and for survival rate. Ann Arbor classification is widely used for Hodgkin's and NHL. (10, 18) CT of the total body with contrast medium or scintigraphy are used to investigate the presence of other sites and for staging of the disease. (19) Last year's PET-CT is widely used for staging as it was applied in our case.

### Conclusions

Non-Hodgkin lymphomas of the oral and maxillofacial region are not uncommon, but the mandible is rarely affected. The early diagnosis of a primary lymphoma

involving the mandible is extremely difficult to be conducted. Many common inflammatory neoplastic pathologic entities associated with the presence of teeth may have similar symptoms with lymphoma and they distract the clinician from the correct diagnosis. In our case the delay in early diagnosis was the similarity of symptoms with the ones of osteomyelitis as both entities shared the same clinical and radiologic symptoms. In cases with bone destruction that exceeds the estimated time of clinical improvement, early bone biopsy to reach the accurate diagnosis is suggested.

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#### Legend Figures

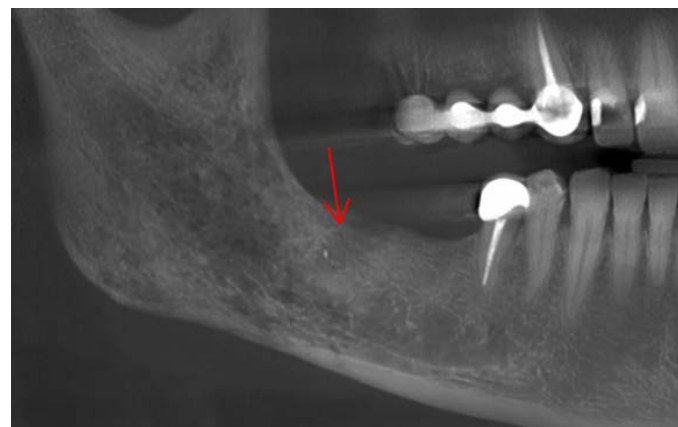


Figure 1: The right side of the mandible showing the healing of the extracted second molar and the mottled area below and behind the extracted tooth.

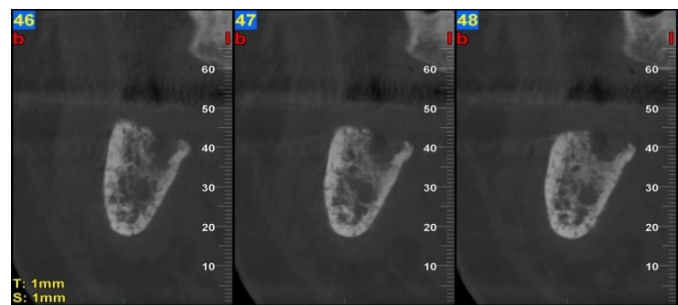


Figure 2: Sections of the mandible showing the mottled mandibular bone.

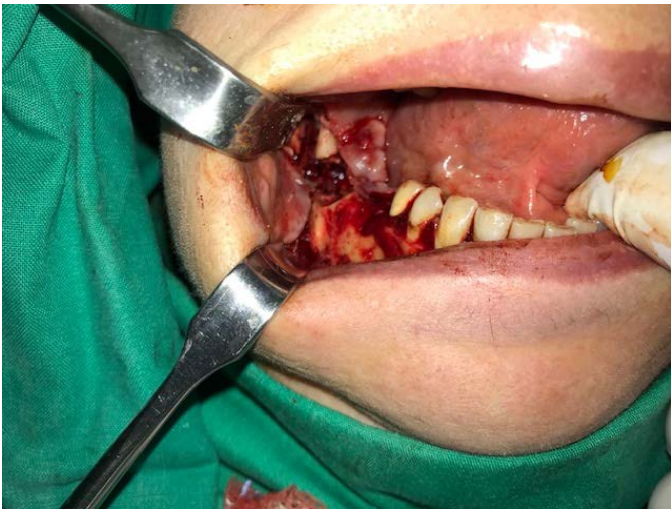


Figure 3: Clinical view of the lesion after releasing the flap.

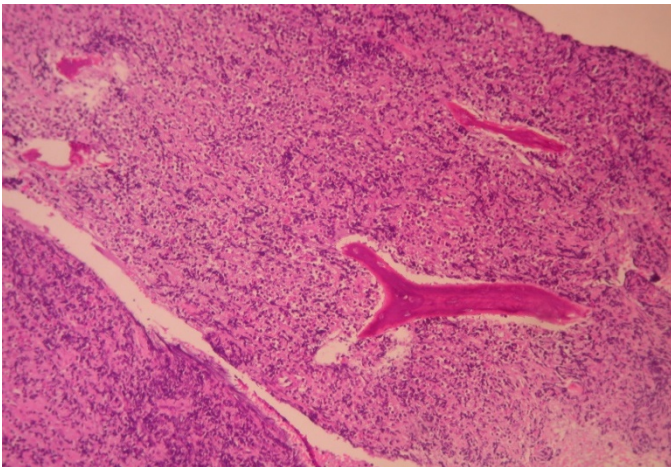


Figure 4 A: Destructive bone invasion by the carcinoma with severe fibrosis H&EX40

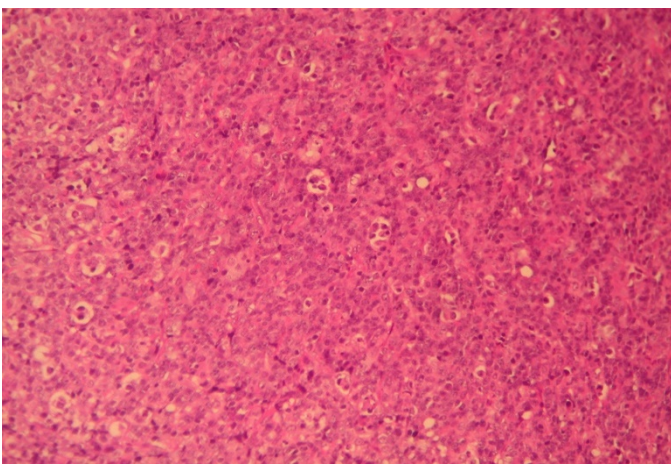


Figure 4 B: Dense diffuse invasion by large lymphoid cells H&EX200

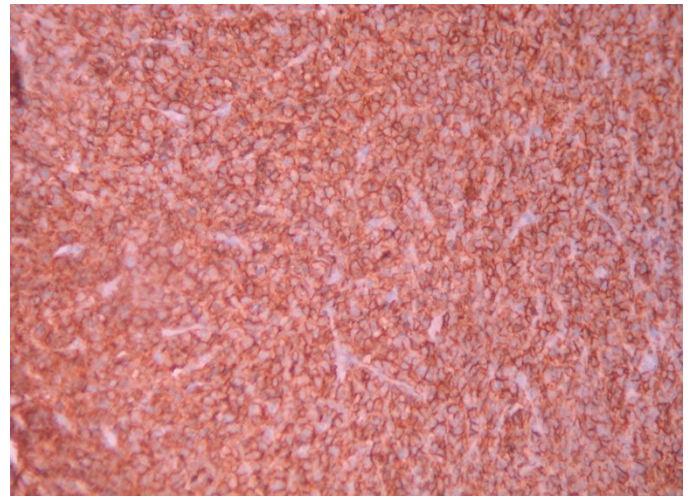


Figure 4 C: The tumor cells are positive for CD20 IHCX200

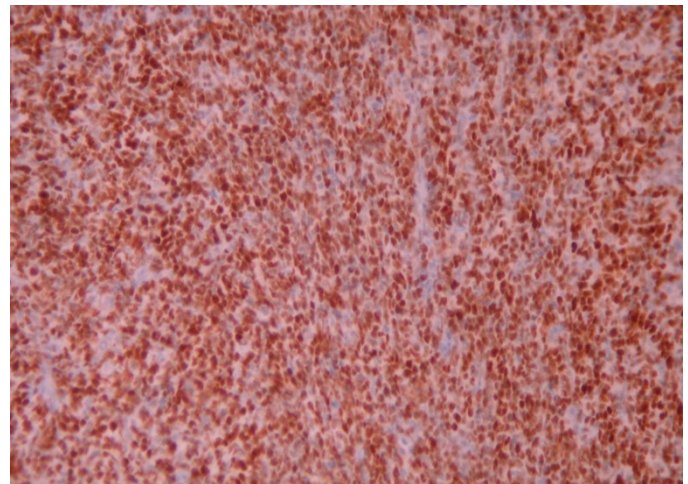


Figure 4 D: The tumor cells are positive for BCL6 IHCX200

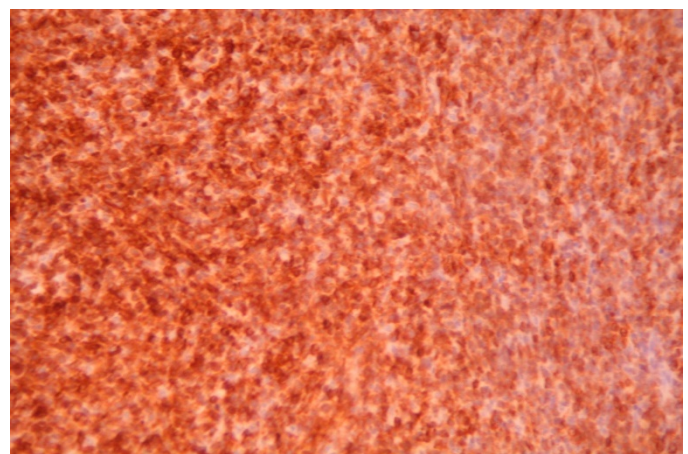


Figure 4 E: The tumor cells are positive for CD10 IHCX200

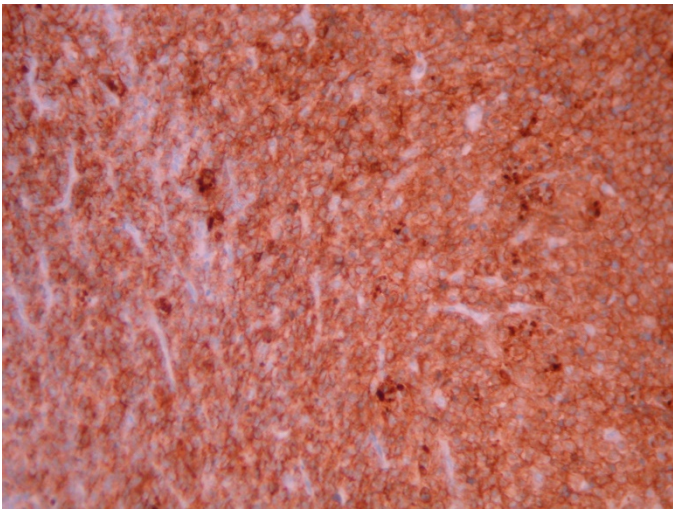


Figure 4 F: The tumor cells are positive for BCL2 IHCX200

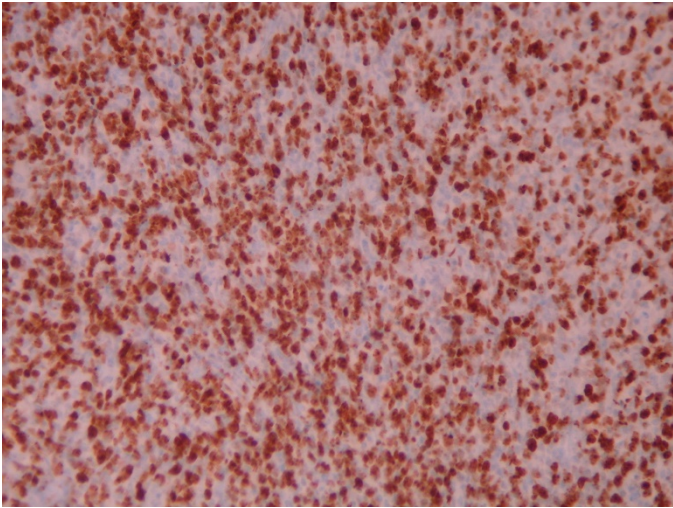


Figure 4 G: About 70% of the tumor cells show positivity for ki67 IHCX200.