CASE REPORT

Unusual presentation of extranodal diffuse large B-cell lymphoma in the head and neck: description of a case with emphasis on radiographic features and review of the literature

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A very unusual radiographic presentation of non-Hodgkin lymphoma (NHL) involving the maxilla is described. The patient was initially managed with antibiotics prescribed to treat what was thought to represent an odontogenic infection. After unsuccessful antibiotic therapy, the patient was referred to an oral surgery clinic where CBCT was performed. CBCT revealed an atypical generalized sclerosis of the affected bone rather than the usual lytic radiographic pattern associated with NHL. Destruction of the sinus floor with infiltration of the sinus was also present. This rare radio-opaque radiographic presentation is described in detail together with the clinical presentation and histopathological findings. The important radiographic features suggesting malignancy that were present in this atypical case of NHL are discussed. A differential diagnosis highlighting the differences between NHL, osteomyelitis and osteosarcoma is also provided.

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Case report

Clinical description of the case

A 35-year-old African-American male with an unremarkable medical history was referred to an oral surgery clinic with a 20 × 20-mm painful, firm and fixed swelling of approximately 2 months' duration involving the right cheek and vestibule from maxillary first molar to the lateral incisor. [Figure 1](#) demonstrates the swelling within the buccal vestibule extending to the lateral incisor. Owing to the presence of gross caries in the maxillary molar teeth, the preceding clinical impression was "odontogenic infection", and the patient was unsuccessfully managed with antibiotics, and incision and

drainage prior to the referral. Management of the patient in the oral surgery clinic included CBCT (described below) as well as an incisional biopsy of the vestibular swelling. Upon initial management and histopathological diagnosis, the patient was referred for treatment to an area hospital.

Microscopic features of the biopsy specimen

Microscopic examination revealed multiple fragments of variably dense fibrous connective tissue containing sheets and vague nodules of discohesive large cells with vesicular cleaved pleomorphic nuclei and abundant, pale amphophilic, often vacuolated cytoplasm. There were frequent mitotic figures including abnormal mitoses. Large cells encroached upon several thick-walled vessels and large nerves. Aggregates of small lymphocytes were often associated with the large cells, and

Figure 1 Clinical features. Clinical images at the time of initial presentation to the oral surgeon. Take note of the location of the swelling within the buccal vestibule extending from first molar to the lateral incisor that does not coincide with the location of the grossly decayed teeth.

crush artefact was prevalent. The lesion infiltrated adipose tissue and striated muscle. Some fragments were surfaced by parakeratinized stratified squamous epithelium of the oral mucosa, and in these fragments, a grenz zone separated the epithelium from the lesion. The large atypical lymphocytes were CD20 positive (*i.e.* B cells) and Epstein Barr virus (EBV) negative, and 35–50% of the large cells were Ki-67 positive (*i.e.* cycling cells). Anti-CD3 antibodies labelled the associated small lymphocytes (not shown). The histopathological diagnosis of diffuse large B-cell lymphoma was established (Figure 2).

Radiographic features

Features associated with lymphoma: The trabecular bone pattern of the right maxilla from the canine to the

tuberosity demonstrated a generalized sclerotic appearance (Figures 3 and 4). Even though the trabecular pattern of the right maxilla was homogeneously radio-opaque, there was no appreciable expansion of the facial or palatal cortex (Figure 4c). Clinically evident swelling was very well demonstrated with significant soft-tissue asymmetry on the CBCT image (Figure 4b). There was opacification of the lower third of the right maxillary sinus, and the adjacent portion of the sinus floor was discontinuous and poorly delineated. On the other hand, the cortical border of the floor of the left maxillary sinus demonstrated normal radiographic appearance (Figure 4a). Otherwise intact maxillary right canine was associated with irregular and diffuse widening of the periodontal ligament (PDL) space on the

Figure 2 Microscopic features. Haematoxylin and eosin (H&E)-stained sections photographed at ×100 (a) and ×400 (b), and immunohistochemistry-stained sections photographed at ×100 (c) and ×200 (d). Included images show sheets and vague nodules of discohesive large cells (a) with vesicular, cleaved, pleomorphic nuclei and abundant, pale amphophilic, often vacuolated cytoplasm (b). Immunohistochemistry for B-cell marker CD20 shows that the large cells are CD20-positive B cells (brown staining of the cell membranes, (c) and proliferation marker Ki-67 reveals numerous cells in cell cycle [brown staining, (d)]. The cell nuclei are blue (c, d).

distal–apical aspect of the root (Figures 3 and 4a). Similar, although less advanced, changes were noted in association with the PDL spaces of the maxillary right first molar and the first and second premolars.

Other features: The maxillary right second and third molars were severely broken down with carious involvement (Figures 3 and 4a). Periapical radiolucencies were associated with the maxillary right second and third molars, consistent with the presence of chronic apical periodontitis. There was vertical bone loss on the distal surface of the maxillary right second premolar, consistent with chronic periodontitis.

Discussion

Lymphoma is a malignant neoplasm of lymphocytes. The two recognized major classes of lymphoma are Hodgkin disease and non-Hodgkin lymphoma (NHL).¹ Hodgkin disease typically arises in the lymph nodes and has a predilection for cervical and mediastinal nodes.¹ By contrast, NHL often presents as extranodal disease.^{1–3} Approximately half of head and neck (H&N) NHL present in the lymph nodes, while the great majority of oral NHL lesions (77%) are reportedly found in the soft tissues and/or bone of the maxilla.^{1,4} Table 1 provides a summary of lymphoma localization in the H&N area. Most NHLs in the H&N area are malignancies of the B lymphocytes, and diffuse large B-cell lymphoma is the most common type (40% of the extranodal NHL in the oral cavity) followed in frequency by mucosa-associated lymphoid tissue (MALT) lymphoma.^{1,3,5} Diffuse large B-cell lymphoma constitutes 85% of NHL involving bone in this area, by far the largest proportion of bone lesions.⁶

Radiographically, lymphoma involving bone typically presents as a poorly defined radiolucency. In a review of 237 cases of primary lymphoma of bone, Mulligan *et al*⁷ found that nearly all the lesions presented as poorly defined radiolucencies (lytic pattern) and only 2% of cases demonstrated a radio-opaque (sclerotic) radiographic pattern. Other studies have also

found radiolucent features to be by far the most common.^{4,5,7,8} This radiolucent radiographic appearance can mimic common odontogenic pathology such as chronic apical periodontitis and chronic periodontitis.

In addition to the radiographic presentation, the clinical presentation of lymphoma in the H&N area has been reported to mimic odontogenic infection and osteomyelitis. The most common clinical feature of NHL of the oral cavity is swelling of soft tissues.^{4,8} Paraesthesia or pain-mimicking odontalgia can occur as well, so it is not surprising that NHL can be clinically misdiagnosed as an odontogenic infection. Yepes *et al*⁹ reported a case of lymphoma that was initially misdiagnosed as a periodontal abscess. Similar to this reported case, the clinical presentation in our case was initially thought to represent an odontogenic infection. The possibility of an odontogenic inflammatory process in our case was supported by pain, swelling and the presence of retained roots in the molar area. Additionally, radiographic features of osteosclerosis are common in osteomyelitis.^{10,11} However, other important radiographic findings associated with osteomyelitis include sequestra and deposition of subperiosteal new bone (periosteal reaction).¹¹ The subperiosteal new bone in osteomyelitis is arranged as one or more layers that align parallel to the cortex.¹¹ Multiple layers appear as an “onion skin” pattern. In our case, neither sequestra nor subperiosteal bone deposition was present. Moreover, osteomyelitis is more common in the mandible than in the maxilla.¹⁰ For example, out of 153 cases of osteomyelitis of the jaws, 128 (83.7%) involved the mandible.¹⁰ Furthermore, there were some key clinical and radiographic features in our case that help distinguish NHL from osteomyelitis. These key features include the extent and location of the intraoral soft-tissue swelling, the extent of sclerosis of the bone, poor delineation of the sinus floor and widening of the PDL around otherwise intact teeth. Intraorally, the swelling was centred over the canine–premolar area and extended anteriorly to the lateral incisor. The swelling therefore did not coincide with the location of the grossly decayed molar teeth or even the vertical bone

Figure 3 CBCT three-dimensional panoramic reconstruction. CBCT three-dimensional panoramic reconstruction demonstrating the generalized sclerotic appearance of the right maxilla extending from tooth 6 (maxillary right canine) to the tuberosity. Take note of the extension of the sclerosis anterior to the grossly decayed teeth (first and second molars) and the vertical defect on the second premolar. Arrow indicates periodontal ligament widening on an otherwise intact tooth 6 (maxillary right canine).

Figure 4 CBCT panoramic reconstruction and axial views. (a) CBCT panoramic reconstruction of the maxilla demonstrating the absence of a well-delineated sinus floor on the right side (thin arrow) vs a well-delineated normal-appearing sinus floor on the left side. Also evident is the periodontal ligament space widening on an otherwise intact tooth 6 (maxillary right canine) and the extension of sclerosis anterior to the grossly decayed teeth (thick arrow). (b) CBCT axial view demonstrating the asymmetry of the soft tissue representative of the clinical picture shown in Figure 1. Arrow indicates the swelling of the soft tissue. (c) CBCT axial view demonstrating the absence of expansion of the right maxilla and the absence of periosteal reaction (arrows).

loss on the distal of the second premolar. Likewise, the sclerotic pattern of the bone extended anterior to the decayed and periodontally involved teeth. The generalized disappearance of an intact sinus cortical border would also be a highly unusual presentation of chronic inflammation of odontogenic origin. On the other hand, NHL of the maxillary sinus demonstrates sinus opacification and destruction of the sinus walls.⁹ Sinus opacification and destruction of the sinus floor were also seen in our case.

Osteosarcoma could be considered on the differential diagnosis of this case owing to an overlap in radiographic and clinical presentations. Osteosarcoma is the most common primary malignant bone tumour

of the jaws, which typically presents with swelling and a history of rapid growth.^{12–15} Although osteosarcoma can arise *de novo* within the jaws, certain conditions such as Paget’s disease of bone, Li-Fraumeni syndrome, polyostotic fibrous dysplasia and a history of radiation therapy are associated with an increased risk of occurrence.^{3,13,14} According to Bennett et al,¹⁴ swelling with expansion of the buccal or lingual plates is evident in the vast majority of cases. The radiographic pattern of osteosarcoma can be osteodestructive, osteogenic or, more commonly, a combination of the two.^{12,15} The osteogenic pattern of osteosarcoma is predominantly radio-opaque, although radiolucent areas are usually present as well.^{12,15} The lack of cortical expansion and

Table 1 Summary of lymphoma localization in the head and neck (H&N) area

<i>Extranodal</i>					
<i>Lymphoma category</i>	<i>Lymph nodes (nodal)</i>	<i>Waldeyer ring</i>	<i>Salivary glands</i>	<i>Jaw bone</i>	<i>Nasal cavity and paranasal sinuses</i>
Hodgkin lymphoma	Most common nodes: cervical	Rare	Rare	Rare	Rare
NHL	>50% of all H&N NHL	Approximately 50% of extranodal H&N NHL	Most common gland: parotid ^a	30–48% of oral NHL	Most common type: nasal NK/T-cell lymphoma

NHL, non-Hodgkin lymphoma; NK, natural killer.
^aSome parotid lesions are nodal, as they arise within intraparotid lymph nodes.

the absence of radiolucent areas are two important features that distinguish our NHL case from osteosarcoma. Widening of the PDL space was identified in nearly half of osteosarcoma cases reported by Fernandes *et al*,¹³ a feature that our case and osteosarcoma have in common. Widening of the PDL space is an important radiographic finding associated with malignant disease and may occur with carcinomas, sarcomas and NHL.^{3,9} Lastly, an important radiographic feature associated with osteosarcoma is a “sunray” or “sunburst” pattern, which was found in over half (55%) of osteosarcoma cases of the jaws but was absent in our case of NHL.¹³ Together, the constellation of the clinical and radiographic features alone in our case does not completely separate NHL from osteosarcoma. These features do, however, point to malignant disease rather than a reactive process that is important to recognize.

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