CASE REPORT

Primary xanthoma of the mandible

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Bone xanthomas are rare and are usually associated with endocrine or metabolic diseases, mainly lipid disorders. In the absence of systemic diseases, the lesion is called a primary xanthoma. Primary mandibular xanthomas are extremely rare. The aim of this report is to describe the clinical and radiographic findings of a primary mandibular xanthoma, discussing the epidemiological features, pathogenesis and differential diagnosis. A 25-year-old man was referred for evaluation of a left mandibular lesion detected in a routine radiographic exam. Radiographically, there was a diffuse, unilocular and radiolucent lesion, with irregular margins located adjacent to the surface from the distal root of the left mandibular third molar. The lesion was excised under local anaesthesia. Microscopically, there were several cells with a foamy and granular cytoplasm and central small, round nuclei, similar to xanthomatous macrophages. No lipid disorders were diagnosed. According to these features, the diagnosis of primary mandibular xanthoma was established. In conclusion, xanthomas of the jaws are rare and all seem to be primary and occur exclusively in the mandible. *Dentomaxillofacial Radiology* (2011) **40**, 393–396. doi: 10.1259/dmfr/51850495

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Case report

A 25-year-old man was referred to a private oral surgery clinic for an evaluation of a left mandibular lesion detected in a routine radiographic exam performed during orthodontic treatment. Medical history was not contributory and the patient denied pain or previous local trauma, including surgical procedures. At the extraoral examination, the face was symmetric, with a normal contour of the inferior portion of the face. On intraoral examination, the patient showed well conserved dentition and oral mucosa with a normal colour and texture without lesions or swelling. It was noted that the patient was undergoing orthodontic treatment owing to the presence of orthodontic brackets fixed to the crown of the teeth. Radiographically, there was a diffuse, unilocular and radiolucent lesion with irregular margins, located adjacent to the surface of the distal root of the left mandibular third molar,

measuring approximately 2.0 cm (Figures 1 and 2). In this region, the upper and lower limits of the mandibular canal were not observed. The left mandibular third molar was intact and no percussion pain, facial paraesthesia or paralysis or periodontal pockets in the distal surface were observed.

As the lesion presented diffuse and irregular margins, and no inflammatory signs and symptoms were observed, a primary or metastatic malignant neoplasm was considered as the main hypothesis of diagnosis. To establish the diagnosis, the patient was submitted to an incisional biopsy of the lesion under local anaesthesia. During the surgical procedure, it was observed that there was no continuity between the lesion and the oral cavity. Additionally, after accessing the local area surrounding the lesion, a bone cavity filled with a yellowish, soft and amorphous tissue was noted; this material was fully curetted and removed without involvement of the inferior alveolar nerve.

Microscopically, there were several cells with a foamy and granular cytoplasm and central small, round nuclei, similar to xanthomatous macrophages (Figure 3).

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Figure 1 Panoramic radiograph reveals a diffuse, unilocular and radiolucent lesion, with irregular margins, located adjacent to the surface from the distal root of the left mandibular third molar (arrow)

These cells were surrounded by scarce fibrous connective tissue and adipocytes. Necrosis, nuclear pleomorphism and mitosis were not observed. Immunohistochemically, the xanthomatous cells presented strong positivity for CD 68 (clone PG-M1, Dako, Glostrup, Denmark, dilution 1:400), confirming the diagnosis of bone xanthoma of the mandible (Figure 4). Owing to the definitive diagnosis of xanthoma, the levels of glycaemia, lipidemia and cholesterolemia of the patient were requested but

did not present any alteration. The patient was under clinical and radiographic follow-up for 2 years and no signs or symptoms of recurrence were observed.

Discussion

Xanthomas are non-neoplastic diseases often found in the subcutaneous tissues, mainly in tendon regions, which commonly represent the manifestation of diseases that affect the lipid, cholesterol or glucose metabolism.^{1,2}

Figure 2 Close view of the lesion in the panoramic radiograph

Figure 3 Numerous cells with a foamy and granular cytoplasm and central small and round nuclei (arrows), similar to xanthomatous macrophages (haematoxylin and eosin stain, original magnification, $\times 200$)

Figure 4 Xanthomatous cells presenting strong positivity for CD-68 (arrows) (streptavidin-biotin-peroxidase method, $\times 200$)

In cases associated with systemic diseases, the lesions are usually multiple. The xanthomas are included in the xanthomatous lesions group, which are composed of macrophages with a large eosinophilic and granular cytoplasm called xanthomatous or foamy cells.¹⁻³

Bone xanthomas are rare, are usually accompanied by cutaneous manifestations and are associated with endocrine or metabolic diseases, such as hyperlipoproteinaemia, hyperlipidaemia and diabetes mellitus.² In the absence of systemic diseases, the lesion is called a primary xanthoma and is very rare.⁴ Bone xanthomas most commonly occur in male patients, mainly between the third and fifth decades,⁵ as in the current case. The most commonly affected sites are the bones of the hand, although cases located in the long and pelvic bones, rib, cranium and vertebrae have been also reported.^{2,4} In the jaws, xanthomas are extremely rare,⁴ all seem to be primary and occur exclusively in the mandible,^{1,6,7} as in the present case. The diagnosis of mandibular xanthomas becomes difficult mainly because of the absence of typical cutaneous manifestations and alterations in lipid values. It is difficult to establish the exact number of xanthomas of the jaws reported in English-language literature because several lesions are described only as xanthomatous lesions or inadequate terms and synonyms are used.⁸

The pathogenesis of the xanthomas consists of lipid leakage from the blood vessels in the site of the lesion, with subsequent phagocytosis of this material by the macrophages. The non-degraded cholesterol accumulates within the cytoplasm, leading to the presence of foamy macrophages. Minor trauma is also involved in the development of xanthomas.⁹ Particularly in primary bone lesions, the xanthomas can apparently occur in a pre-existing lesion, such as a simple bone cyst, aneurysmal bone cyst and fibrous dysplasia.⁶ In the present case, the lesion was within a bone cavity, which could suggest the occurrence of a previous simple bone cyst, although it did not present on radiographic images as such. The lesion presented a close association with

the distal root from the left mandibular third molar, but there was no continuity between the lesion and the oral cavity. This finding strongly excludes trauma or other irritant factors on the local area. Additionally, no metabolic or lipid disorders were observed.

The radiographic appearance may vary. Mandibular xanthoma can appear as a well-defined radiolucent lesion with sclerotic margins or as a diffuse and ill-defined lesion,¹ as was observed in the present case. In similar cases characterized by a diffuse image with irregular and ill-defined margins without inflammatory signs and symptoms, the possibility of primary or metastatic malignant bone tumours should be considered. However, although the upper and lower cortex of the mandibular canal were undefined, paresthesia was not observed. Moreover, owing to the close proximity with the distal surface of the mandibular third molar, some clinical information was essential to exclude an inflammatory lesion, such as the presence of pulp vitality and absence of a periodontal pocket on the distal root surface.

Because of the deposition of calcified material, the bone xanthoma can present as a diffuse radiopacity,⁷ similar to a fibrous dysplasia. A minimum formation of reactive bone can also be observed.¹ However, in the current case, these features were absent. In cranial lesions, the xanthomas usually present themselves as a lytic lesion surrounded by sclerotic margins in some cases.^{3,4} All these features can be observed in a great number of mandibular lesions, such as giant cell central lesions and odontogenic tumours and cysts. Thus, a minute histopathological analysis should be done in order to reach a definitive diagnosis.

Microscopical differential diagnosis includes other bone lesions that produce multiple or single xanthomatous alterations. Among the xanthomatous conditions that usually suggest multifocal skeletal involvement, Rosai-Dorfman disease and Erdheim-Chester disease,^{10,11} in addition to systemic metabolic and lipid diseases such as II and III hyperlipoproteinaemia and diabetes mellitus, should be considered.⁹ Thus, in xanthomatous bone lesions, it is essential to investigate systemic lipid alterations.¹² In this case, no lipid disorders were diagnosed. Other bone diseases that may also present xanthomatous features include Langerhans cell histiocytosis, benign fibrous histiocytoma and fibrous dysplasia,^{3,13,14} which are usually solitary lesions. In this case, histopathological and immunohistochemical analyses, in addition to serum exams, were performed to confirm the diagnosis of primary bone xanthoma.

Surgical excision is the most adequate treatment. The appearance of a lesion during surgical procedure is also important to establish the diagnosis. Usually, the cavity is filled with a soft and yellow mass.¹² In our case, this feature was also observed and the lesion was fully removed by surgical curettage. Nevertheless, in cases of xanthomas associated with lipid or metabolic disorders, the lesions tend to recur after the surgical treatment. Therefore, a therapy for the systemic condition should be also administered.⁹

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