

Case Report

Primary xanthoma of the mandible: a case report

Shin-ichi YAMADA^{1,2}, Saki HAYASHIDA², Shuichi FUJITA³, Tohru IKEDA³, Hiroshi KURITA¹, Masahiro UMEDA²

¹Department of Dentistry and Oral Surgery, Shinshu University School of Medicine

²Department of Clinical Oral Oncology, Unit of Translational Medicine, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences

³Department of Oral Pathology and Bone Metabolism, Unit of Basic Medical Sciences, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences

Xanthoma is frequently observed in patients with endocrine and metabolic diseases. Intraosseous xanthoma is an extremely rare lesion. In cases in which associations with systemic metabolic diseases and lipid diseases are ruled out, intraosseous xanthoma is termed primary xanthoma. We herein report an extremely rare case of primary xanthoma of the mandible in a 27-year-old woman. Lower third molar extraction and extirpation of the tumor was performed under general anesthesia following a clinical diagnosis of a benign tumor in the left mandible. Her previous medical history was not contributory, except for ovarian cystoma. A final diagnosis of primary xanthoma was established. Her last follow-up 4 years after surgery showed no sign of recurrence in clinical and radiological examinations.

ACTA MEDICA NAGASAKIENSIA 60: 161–164, 2016

Key words: xanthoma, mandible, intraosseous foam cell

Introduction

Xanthoma is typically a single or multiple, yellowish, soft papules or small mass lesions arising in soft tissues, such as the skin or over the subcutaneous tissue of tendon sheaths and extensor surfaces, after minor trauma or friction^{1,2}. Xanthoma is frequently observed in patients with endocrine and metabolic diseases¹⁻⁴. Intraosseous xanthoma is an extremely rare lesion⁵. In cases in which associations with systemic metabolic diseases and lipid diseases are ruled out, intraosseous xanthoma is termed primary xanthoma^{3,4,6}. We herein report an extremely rare case of primary xanthoma of the mandible. The histological diagnosis of a surgical specimen was xanthoma.

Case report

A 27-year-old woman was referred to our department for an evaluation of a left mandibular lesion detected in a radiographical examination performed during dental treatment at a private dental clinic. Her previous medical history was not contributory, except for ovarian cystoma. The patient did not have pain, but had a history of local trauma to the left ear bone in her childhood. Preoperative laboratory data, including lipid levels, were normal. No lipid disorders were diagnosed. Facial symmetry was observed without a bulge in the lower portion of the left face. An oral examination revealed no symptoms at the left lower third molar region (Fig. 1). Panoramic radiography showed a unilocular and radiolucent lesion with relatively regular margins located adjacent to the

Corresponding author: Shin-ichi Yamada, DDS, PhD

Department of Dentistry and Oral Surgery Shinshu University School of Medicine 3-1-1, Asahi, Matsumoto, 390-8621, Japan

Tel: +81 (0)263-37-2677, Fax: +81 (0)263-37-2676, E-mail: yshinshin@shinshu-u.ac.jp

Received February 18, 2016; Accepted April 20, 2016

distal root of the lower third molar, measuring approximately 10 x 20 mm (Fig. 2). A computed tomography scan revealed a unilocular and radiolucent lesion with an irregular margin, measuring 22 x 10 x 9 mm, in the left mandibular ramus region (Fig. 3). A fat-suppressed T1-weighted magnetic resonance imaging also showed a unilocular lesion with low signal intensity, measuring 22 x 10 x 9 mm, in the left mandibular ramus region, but, a fat-suppressed T2-weighted magnetic resonance imaging showed high signal density lesion (Fig. 4). A clinical diagnosis of a benign tumor arising in the left mandible was reached. Lower third molar extraction and extirpation of the tumor was performed under general anesthesia.



Fig. 1 Intraoral photograph. There were no symptoms or findings in the left lower third molar region.



Fig. 2 Panoramic X-ray. The lesion had a radiolucent pattern surrounded by thin radiolucency, and a perilesional halo of sclerotic bone (arrows). The left lower third molar was impacted and adjacent to the lesion.

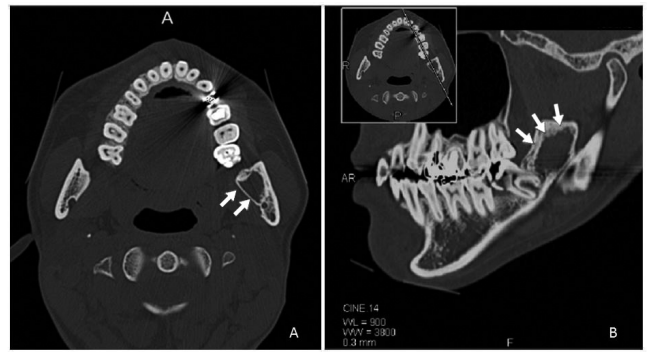


Fig. 3 CT images of the mandible (A: axial plane, B: sagittal plane). CT revealed a unilocular and radiolucent lesion with an irregular margin, measuring 22 x 10 x 9 mm, in the left mandibular ramus region (arrows).

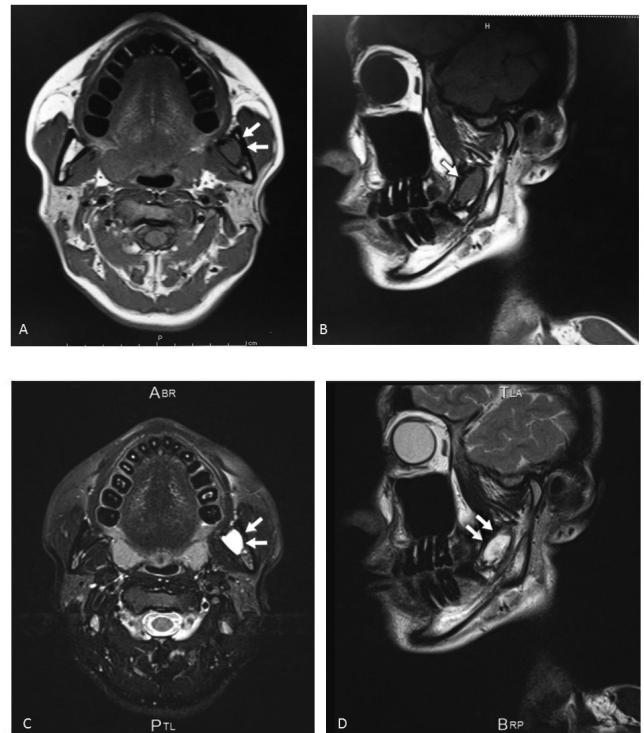


Fig. 4 MR images of the mandible (A: axial plane, B: sagittal plane). A, B: A fat-suppressed T1-weighted magnetic resonance imaging also revealed a unilocular lesion with a low signal intensity, measuring 22 x 10 x 9 mm, in the left mandibular ramus region (arrows). C, D: A fat-suppressed T2-weighted magnetic resonance imaging revealed a same lesion with a high signal intensity (arrows).

During surgery, there was no involvement of the left lower third molar. Therefore, after the extraction of the left lower third molar, a removal of distal bone adjacent to third molar was performed with a bur to access the lesion. A bone

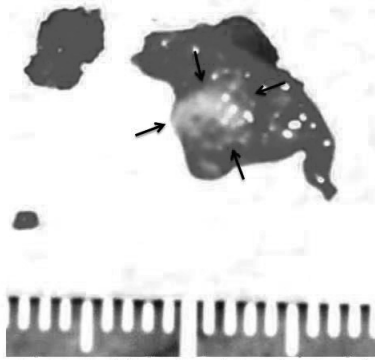


Fig. 5 Photograph of the surgical specimen. The fibrous lesion included a soft, yellowish mass (arrows).

cavity was filled with amorphous tissue. The lesion was removed easily from the adjacent tissue, and included a soft, yellowish mass (Fig. 5).

A histopathological examination revealed that the lesion was composed of the accumulation of foam cells with an abundant amorphous cytoplasm and small round-shaped concentrated nuclei in fibrous connective tissue. An arrangement of foam cells was also noted along the collagen bundles with mild infiltration of lymphocytes. In order to differentiate this lesion from a mucous extravasation lesion (mucous cyst), mucous cell-rich mucoepidermoid carcinoma, and granular cell tumor, mucicarmine staining and immunohistochemical staining were performed for AE1/AE3, CD68, and S100 proteins. Epithelial mucus was not detected in the foam cells. The results of immunohistochemistry, except for CD68, were negative. CD68 localized in the cytoplasm of foam cells as well as the surrounding polyhedral cells. Thus, the origin of these cells in our case was macrophages or histiocytes, and not the epithelium or nervous tissue. Although a demarcated lesion including abundant histiocytic foam cells in the jaw bone was suggestive of radicular granuloma, we rejected the possibility of radicular granuloma because the left lower third molar nearest the lesion was vital and adhesion was not observed between the molar and lesion. The histological diagnosis of the surgical specimen was xanthoma. In addition to clinical findings, a final diagnosis of primary xanthoma of the mandible was reached.

The postoperative course was uneventful. In the last follow-up 4 years after surgery, no sign of recurrence was observed in clinical and radiological examinations.

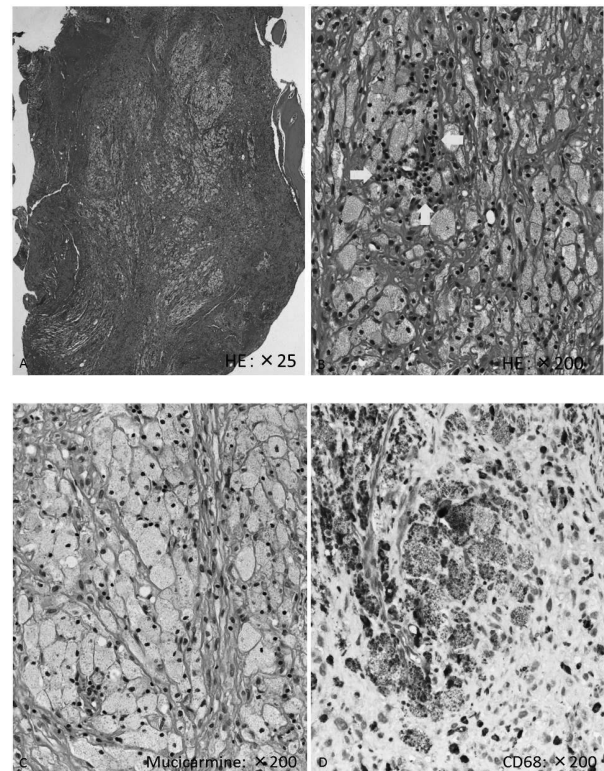


Fig. 6 Photomicrograph of the surgical specimen. A: The accumulation of foam cells was detected in fibrous connective tissue. B: Foam cells possessed an abundant amorphous cytoplasm and small pyknotic nuclei. They were arranged along collagen bundles. Mild lymphocytic infiltration was observed (arrows). C: Epithelial mucus was not identified in foam cells. D: Immunohistochemistry for CD68 revealed a positive reaction in the cytoplasm of scattered polyhedral cells as well as foam cells.

Discussion

Xanthoma is a non-Langerhans histiocytic process that is characterized by lipid-containing macrophages or foam cells⁴). Therefore, xanthoma arising in bone is extremely rare. To the best of our knowledge, seven cases of intraosseous xanthoma arising in the jaw, including the present case, have been reported to date^{3,4,6-9}). Primary xanthoma is more common in males with a 2:1 ratio of males to females^{1,3}), and affects patients between the third and fifth decades of life⁶⁻⁸). Primary xanthoma arising in the pediatric population is infrequent³).

The diagnosis of primary mandibular xanthoma becomes difficult mainly because of the absence of typical cutaneous manifestations and alterations in lipid levels⁶). The differential diagnosis for patients presenting with lytic lesions is broad and depends on the patient's age and the presence of

other disease⁹). In this case, based on the signal intensity of fat-suppressed T1 and T2-weighted magnetic resonance imaging, there were the possibilities of cystic lesions. However, magnetic resonance imaging was reported to show mixed hypointensity-hyperintensity on both T1 and T2 weighted magnetic resonance imaging⁸). The magnetic resonance imaging of primary xanthoma of mandible may be controversial. On the other hand, since a computed tomography scan revealed a radiolucent lesion with an irregular margin, the clinical diagnosis of benign tumors, including such as keratocystic odontogenic tumor and ameloblastoma, was made.

The histopathological characteristics of primary xanthoma are the presence of macrophages, foam cells, cholesterol clefts, and hemosiderin. Although these findings are induced by inflammatory changes in bone, an association with the preceding inflammatory lesion was not found in this case. The pathogenesis of primary xanthoma remains controversial. Lipid leakage from vessels after local trauma or hemorrhage has been suggested as the one of the mechanisms underlying its pathogenesis. Lipid leakage from blood vessels at the site of the lesion, with its subsequent phagocytosis by macrophages, is also suggested to play a role in the pathogenesis of xanthoma²). Non-degenerated cholesterol accumulates within the cytoplasm, leading to the presence of foamy macrophages. Cholesterol clefts also induce an inflammatory giant cell reaction resulting in fibrosis²).

Minor trauma is associated with the development of xanthoma¹⁰). The pathogenesis of xanthoma suggests that it is a secondary phenomenon to some pre-existing processes such as the senescent or degenerative stage of a fibrous defect, giant cell tumor, fibrous dysplasia, simple bone cyst, aneurysmal bone cyst, or brown tumor resulting from hyperparathyroidism¹¹). Although the pathogenesis of this case is also uncertain, the local trauma history of the left ear bone in the patient's childhood may have influenced the pathogenesis.

Bone xanthoma arising in the skull has been associated with hyperlipidemia and hypercholesterolemia^{10,12,13}). Multiple lesions are associated with systemic disease⁶), and xanthomatous bone lesions are reported to occur in all five subtypes of essential hyperlipidemia, as well as in diseases associated with secondary hyperlipidemia¹⁴). It is important to perform a biochemical analysis on serum cholesterol, triglycerides, and proteins in addition to lipid electrophoresis⁴). Due to the exclusion of systemic lipid diseases in our case, a final diagnosis of primary xanthoma was reached.

Xanthoma occurs secondary to hyperlipidemia, and dietary restrictions are recommended for these patients. If dietary control is impossible, medications are suggested. Lesions disappear after hyperlipidemia has been successfully

treated. The long-term prognosis is good, and malignant transformation has not been reported¹⁵). Primary intraosseous xanthoma is treated with curettage, and the prognosis is satisfactory with only partial excision^{2,3,15}). Recurrence has not been reported in cases of xanthoma removed entirely by curettage¹⁶). In this case, the prognosis of the patient was good with extirpation of the lesion. However, a hematological examination, including the lipid profile, amylase, blood chemistry, and hemoglobin A1c, is recommended in order to exclude secondary xanthoma⁸).

References

- 1) Huang GS, Huang CW, Lee CH, et al. Xanthoma of the sacrum. *Skeletal Radiol.* 33:674-678,2004.
- 2) Muthusamy KA, Azmi K, Narayanan P, et al. Bilateral temporal bone xanthoma. Case report. *J Neurosurg.* 108:361-364, 2008.
- 3) Marqués Mateo M, Puche Torres M, Miragall Alba L, et al. Primary mandibular bone xanthoma. A case report. *Int J Oral Maxillofac Surg.* 33:806-807, 2004.
- 4) Harsanyi BB, Larsson A. Xanthomatous lesions of the mandible: osseous expression of non-X histiocytosis and benign fibrous histiocytoma. *Oral Surg Oral Med Oral Pathol.* 65:551-566, 1988.
- 5) Bertoni F, Unni KK, McLeod RA, et al. Xanthoma of bone. *Am J Clin Pathol.* 90:377-384, 1988.
- 6) de Moraes Ramos-Perez FM, de Pádua JM, Silva-Sousa YT, et al. Primary xanthoma of the mandible. *Dentomaxillofac Radiol.* 40:393-396, 2011.
- 7) Slootweg PJ, Swart JG, van Kaam N. Xanthomatous lesion of the mandible. Report of a case. *Int J Oral Maxillofac Surg.* 22:236-237, 1993.
- 8) Morel D, Kelsch RD, Nolan PJ. Primary Xanthoma of the Mandible: Report of a Rare Case. *Head Neck Pathol.* 2015 Aug 8. DOI 10.1007/s12105-015-0643-z.
- 9) de Araujo MR, Scariot R, Uetanabaro L, et al. Primary mandibular xanthoma: case report. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015 Oct;120(4):e177-182. doi: 10.1016/j.oooo.2015.01.015. Epub 2015 Feb 7.
- 10) Bonhomme GR, Loevner LA, Yen DM, et al. Extensive intracranial xanthoma associated with type II hyperlipidemia. *AJNR Am J Neuroradiol.* 21:353-355, 2000.
- 11) Dahlin DC. In *Bone tumors. 2nd ed.* (Springfield: Charles C Thomas) p97.,1967.
- 12) Turk C, Bilginer B, Benli K, et al. Bilateral temporal bone xanthomas in type II hypercholesterolemia. *Turkish Neurosurg.*20:533-535, 2010.
- 13) Broadway SJ, Arnautovic Ki, Zhang Y. Xanthoma of the occipital bone and with preserved inner and outer bone cortex: case report. *J Neurol Surg Rep.* 74:29-32, 2013.
- 14) Chakravarvarthi VK, Aruna E, Rao DNC, et al. Bilateral tibial xanthoma in a normolipidemic patient-report of rare case with review of literature. *Int J Clin Med.* 3:234-237, 2012.
- 15) Huang CF, Cheng SN, Hung CH, et al. Xanthoma of bone in the normolipidic child: report of one case. *Acta Paediatr Taiwan.*41:158-160, 2000.
- 16) Daley T, Dunn G, Darling M. Central xanthoma of the jaws: a clinicopathologic entity? *Oral Surg Oral Med Oral Pathol Oral Radiol.* 119:92-100, 2015.