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Case Report

A Rare Case of a Giant Cell Tumour Caused by Vitamin D Deficiency

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Abstract

Reparative giant cell granulomas are benign masses of multi-etiological nature, which account for 1%–7% of all benign lesions of the jaws. The objective of this case report is to present the relationship between isolated vitamin D deficiency and the development of reparative giant cell granuloma.

Herein, we present the case of a 70-year-old female patient with a painless mass of increased mobility in the mandibular region, and pain in the involved teeth. After histological confirmation and laboratory screening, a reparative giant cell granuloma caused by serious deficiency of vitamin D3 - (25-OH)D was diagnosed. The treatment protocol included surgical removal of the lesion and vitamin D replacement therapy.

In rare cases, this type of lesion can be a primary manifestation of vitamin D deficiency; therefore, it is extremely important to be aware of this pathology.

Keywords

mandible, reparative giant cell granuloma, vitamin D deficiency

INTRODUCTION

The giant cell tumour is not a true neoplasm, but rather a reactive condition caused by factors such as injury, inflammation, or hormonal factors.[1-4] In the jaws, it more often affects the mandible, mainly the molar and premolar areas, and, more rarely, other parts of the mandible such as the condylar process.[5] Cases of unilateral involvement predominate. However, cases of bilateral involvement have also been described.[6] According to their location, giant cell tumours can be classified as central and peripheral. Based on literature data, higher RANKL expression in the central variants is found, which explains their clinical behaviour.[7]

Despite being a benign lesion, giant cell granuloma can occur in two clinical subforms - non-aggressive and aggressive.[8] Signs of aggressiveness include rapid growth, pain, tooth mobility, root resorption, cortical bone lysis, and recurrence.[9] The clinical significance of these benign tumours is determined by the fact that they can mimic a malignant lesion. In non-aggressive forms, a painless swelling in the jaw with a smooth surface is found. Patients with symptomatic lesions are 12 times more likely to develop an aggressive form.[9]

A clinically and histologically similar lesion may occur in the event of elevated parathyroid hormone (PTH) levels with impaired calcium-phosphorus metabolism, which necessitates differentiation from the classic brown tumour

in hyperparathyroidism.[10,11] In some cases, this lesion may occur in secondary hyperparathyroidism due to low serum calcium levels associated with vitamin D deficiency or chronic kidney failure.[12] However, vitamin D deficiency does not result in a decrease in serum calcitriol levels and calcium absorption, respectively, until serum 25-(OH) D level drops to 10 nmol/L.[13] Here we report a rare case of a giant cell tumour of the mandible caused by vitamin D deficiency (<50 nmol/L) without impaired function of the parathyroid glands.

CASE REPORT

A 70-year-old female patient visited our clinic with complaints of swelling and spontaneous pain in the right mandible. Her past history was unremarkable; she had had well-controlled arterial hypertension for 2 years, and before the initiation of systemic treatment, her arterial blood pressure was up to 180/90. Clinical examination revealed a tumour in the mandible, located in the right premolar region. The formation had firm texture and smooth surface, and was painless on palpation. Increased mobility of teeth 43 and 44 was found ***(Fig. 1)****.*

Panoramic radiograph showed a mono-lacunar formation involving the canine and the premolar in this area, without root resorption of the adjacent teeth. Cone-beam computed tomography (CBCT), more specifically images in coronal, sagittal, and axial plane and 3D reconstruction showed a hypodense oval lesion around the roots of teeth 43 and 44, which had homogeneous structure, dimensions of 11.35×9.43 mm and density of 200 HU ***(Fig. 2)****. The boundaries of the process were distinct, perifocal osteosclerosis not observed and interrupted the vestibular compact of the jaw.*

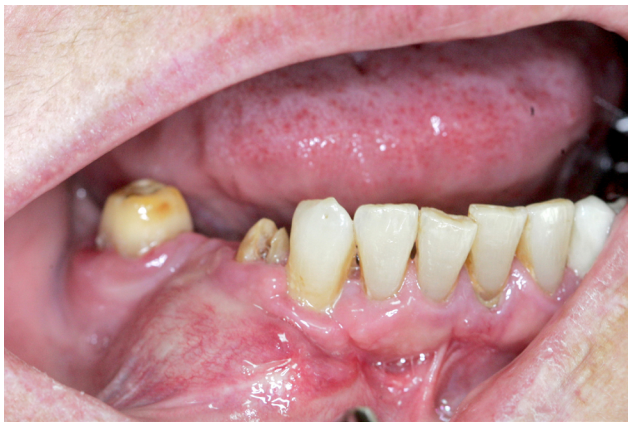

Figure 1. Preoperative clinical appearance.

The histological analysis found stroma rich in spindle-shaped fibroblasts, among which multinucleate giant osteoclast-like cells were disseminated, with less than 20 nuclei in the cytoplasm ***(Fig. 3)****. The giant cells were located near areas of hemorrhage, and some of them - in the vascular spaces* ***(Fig. 4)*** *and around osteoid trabeculae in which central ossification was observed. There were no necrotic foci and atypical mitoses.*

Under local anesthesia with 4% articaine, the patient underwent surgery - resection with margins in healthy bone tissue and extraction of the teeth adjacent to the lesion.

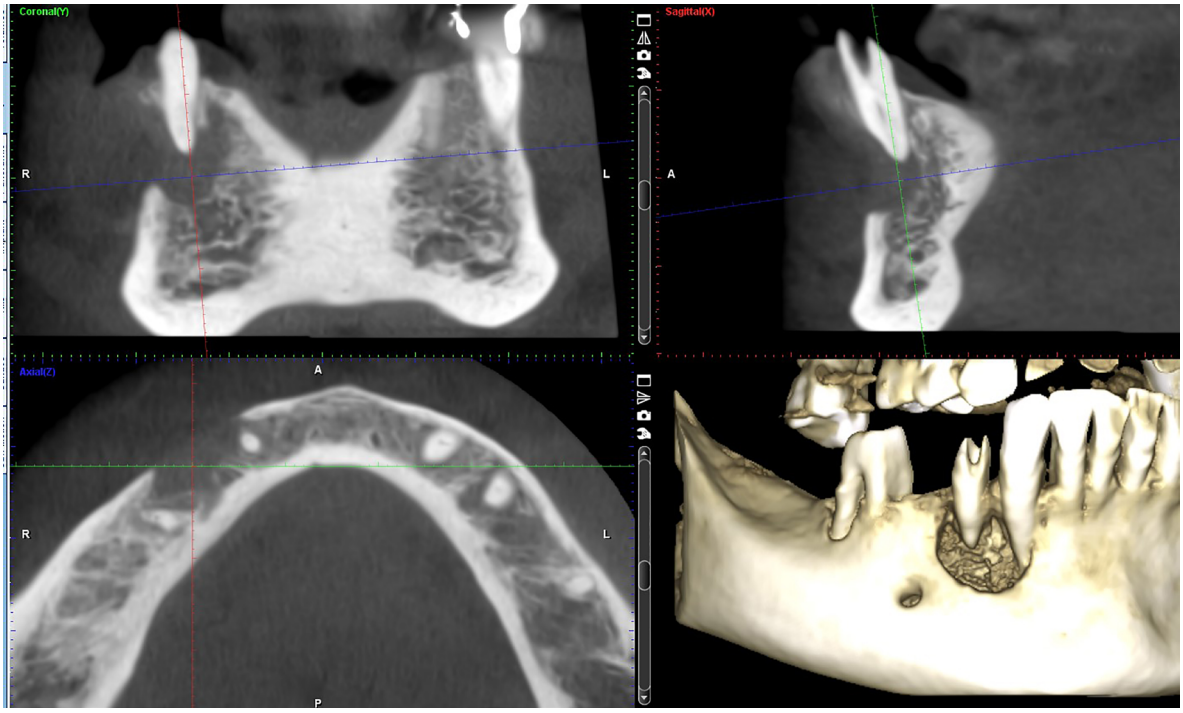

Figure 2. CBCT image of the lesion.

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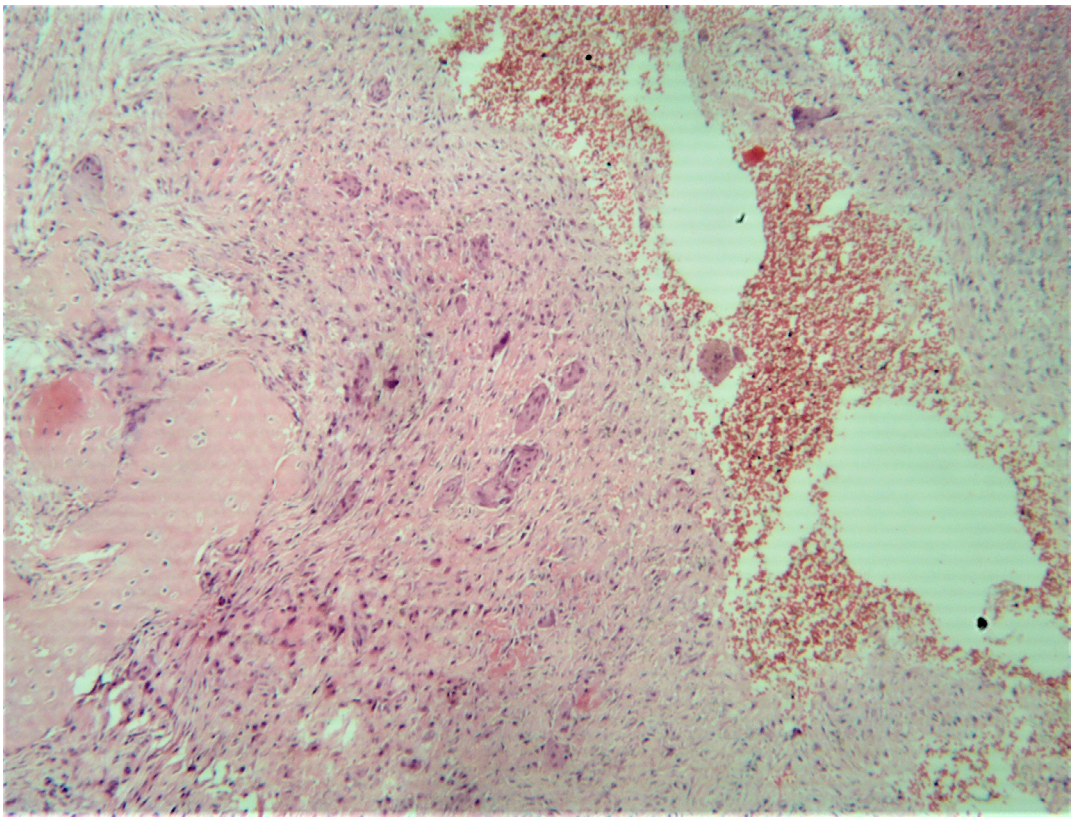

Figure 3. Fibrous stroma with multiple giant osteoclast-like cells in and around a fresh hemorrhage and osteoid trabeculae with a zone of ossification, H&E stain, ×40.

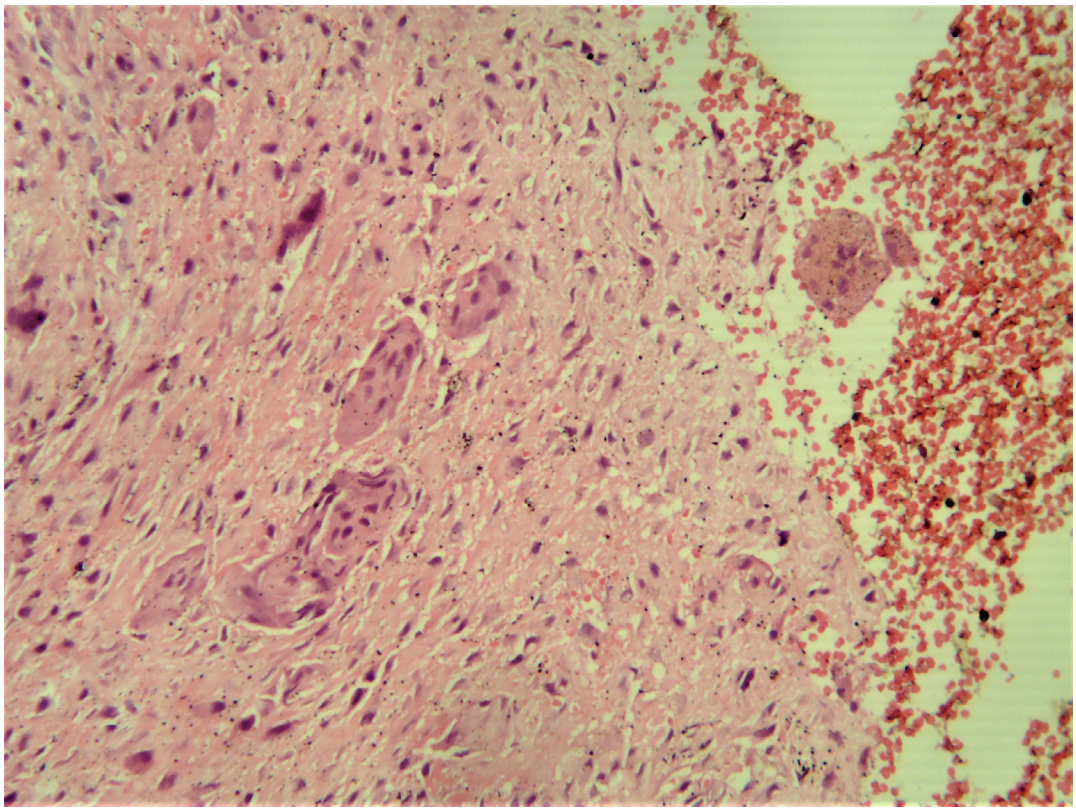

Figure 4. Fibrous stroma with multiple giant osteoclast-like cells near and in a fresh haemorrhage, H&E stain, ×10.

No changes were found during the further examinations performed to assess the gland. Elevated levels of PTH and alkaline phosphatase were found by laboratory screening tests. After further measurement of the level of 25-(OH)D, deficiency was confirmed and replacement therapy was prescribed. During the postoperative period, the surgical field was calm. No changes in the jawbone were found six months postoperatively ***(Fig. 5)****.*

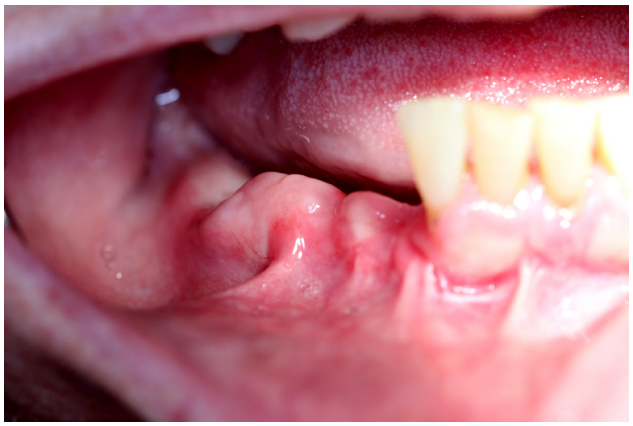

Figure 5. Clinical appearance 6 months postoperatively.

DISCUSSION

The giant cell reparative granuloma of the jaws is a rare lesion, more common in females (in a 2:1 ratio), which can be explained with the relationship between hormone secretion and its manifestation in females.[1,4,6,14] Usually, the lesions affecting the jawbones are more often found unilaterally on the mandible, with possible crossing of the midline and involving the premolar or molar regions, as is in the case presented by us.[1,6,9,11,15] Radiological findings are non-specific for reparative granuloma, and the condition can manifest as a mono- or multi-lacunar formation with distinct or indistinct boundaries, which depends on the clinical behaviour of the formation.[1,2] In this clinical case, the radiographic findings are not informative of the biological behaviour of the lesion because of the unclear boundaries of the formation, which are typically found in malignant conditions. Based on clinical and radiological evidence, giant cell tumours can be classified into aggressive and non-aggressive types; the case described by us is of the non-aggressive type due to the presence of a slowly growing asymptomatic lesion, despite the suspicious radiological findings.[4,12]

Histologically, the lesion consists of fibrous tissue composed of areas of hemorrhage, aggregations of multinucleate giant cells and, in some places, osteoid trabeculae - findings corresponding to the findings in the presented clinical case. Giant cells are commonly located on vascular stroma with hemosiderin deposits. Giant cells are also found in other giant cell lesions such as aneurysmal bone cysts, giant cell tumours, cherubism, and brown tumours. In giant cell tumours, giant cells are evenly distributed, in contrast to giant cell granulomas in which clusters of these cells are observed.[2] Aneurysmal bone cyst was ruled out histologically because blood-filled aneurysmal spaces are observed in this condition. The histological pattern in cherubism is quite similar to that in giant cell granuloma, except in cases where fairly characteristic condensation of perivascular collagen is evident.[6] However, the hereditary nature, the clinical presentation, the bilateral involvement, as well as the higher incidence of cherubism in children are not consistent with the presented case; therefore, this pathology was ruled out. The classic brown tumour is identical to the reparative giant cell granuloma both histologically and radiologically, which necessitates testing the serum calcium, phosphorus, and alkaline phosphatase levels and assessment of both parathyroid glands and renal function.[3] The presence of a brown tumour was ruled out, as our assessment of the function of the parathyroid glands and kidneys found no abnormalities.

Giant cell granuloma as a primary manifestation of vitamin D deficiency is a relatively rare condition described in the literature. In most such cases, impairment of parathyroid glands is found, therefore, it is necessary to assess their function. Primary hyperparathyroidism in 80% of cases is associated with an adenoma, more commonly located in the lower pair of glands or ectopically – in the thyroid gland, the mediastinum or the thymus, and, in rare cases, it is due to glandular hyperplasia (15% to 20%) or carcinoma (<0.5%).[8] In the case presented here, evidence of the above was not found, and an ultrasonographic examination showed structure with normal echogenicity, smooth contours and no focal changes.

The differential diagnosis should also include a brown tumour due to secondary hyperparathyroidism, which may be due to chronic renal failure, vitamin D deficiency, lower intestinal calcium absorption, and liver disease.[11,12] In such cases, the levels of PTH, calcium, phosphorus and alkaline phosphatase should be tested. In primary hyperparathyroidism, laboratory results show hypercalcemia and hypophosphatemia, while in secondary hyperparathyroidism, hypocalcemia and hyperphosphatemia are present, respectively, and in both cases, PTH levels are elevated.[10] In primary hyperparathyroidism, chronically high levels of PTH lead to an increase in calcium levels, and hypercalcemia becomes more severe due to increased production of 1,25(OH)2D. In secondary hyperparathyroidism, hyperphosphatemia causes hypocalcemia and decreased synthesis of 1,25(OH)2D. In isolated deficiency, a drop of 25-(OH)D below 50 nmol/L results in an increase in PTH levels. Until 25-(OH)D reaches values of 10 nmol/L, the deficiency does not result in a decrease in serum 1,25(OH)2D and calcium absorption, respectively, therefore, the serum calcium levels are not affected, which confirms our results.[13,16] An inverse correlation is observed, and as 25-(OH)D levels decrease, alkaline phosphatase levels in-

crease. Elevated levels of PTH (70.08 pg/mL) and alkaline phosphatase (141.65 U/L) were found in this clinical case, with no change in the levels of calcium (2.29 mmol/L) and phosphates (0.79 mmol/L). The results of paraclinical tests clearly showed no impairment of the glands, therefore, a cause related to vitamin D level was sought. Deficiency was proven, with levels of 25-(OH)D of 46.1 mmol/L.

When treating giant cell granuloma, a number of factors must be taken into account such as the anatomical characteristics, the clinical behavior of the lesion[10], and the general health condition of the patient. Treatment is usually surgical, and includes curettage or enucleation of the lesion. Recurrence can occur in the event of a conservative approach or aggressive clinical forms. In cases of vitamin D deficiency, recurrence is usually not observed after surgical treatment and subsequent replacement therapy, and our results confirm this statement.

CONCLUSIONS

Giant cell granuloma can be caused by multiple factors related to patient's general health. In rare cases, this lesion may be a primary manifestation of vitamin D deficiency, therefore, it is essential to be aware of this pathology, to carry out the necessary diagnostic tests and to administer adequate and timely treatment. Vitamin D should be taken into account as an etiological factor for the occurrence of this condition with the view of making correct differential diagnosis with other possible diseases or similar conditions.

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Редкий случай гигантоклеточной опухоли, вызванной дефицитом витамина D

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Резюме

Репаративные гигантоклеточные гранулемы — доброкачественные образования полиэтиологической природы, на долю которых приходится 1–7% всех доброкачественных поражений челюстей. Целью данного клинического случая является представление взаимосвязи между изолированным дефицитом витамина D и развитием репаративной гигантоклеточной гранулемы.

Здесь мы представляем случай 70-летней пациентки с безболезненной массой повышенной подвижности в нижнечелюстной области и болью в поражённых зубах. После гистологического подтверждения и лабораторного скрининга диагностирована репаративная гигантоклеточная гранулема, обусловленная выраженным дефицитом витамина D3-(25-OH)D. Протокол лечения включал хирургическое удаление очага поражения и заместительную терапию витамином D.

В редких случаях этот тип поражения может быть первичным проявлением дефицита витамина D; поэтому крайне важно знать об этой патологии.

Ключевые слова

нижняя челюсть, репаративная гигантоклеточная гранулема, дефицит витамина D