Protet Stomatol, 2025; 75(4): 398-404
DOI: 10.5114/ps/215024

Unusual presentation of mandibular ameloblastoma resembling hyperparathyroidism – a case report

Nietypowy obraz szkliwiaka żuchwy przypominający nadczynność przytarczyc – opis przypadku

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KEY WORDS:
ameloblastoma, mandible, brown tumour, hyperparathyroidism

HASŁA INDEKSOWE:
szkliwiak, żuchwa, guz brunatny, nadczynność przytarczyc

Summary

A case of ameloblastoma is reported, which resembles both clinical and radiological presentation of brown tumours of hyperparathyroidism in the mandible. A 70-year-old man was treated for a mass in the lower jaw. Some laboratorial exams confused the authors regarding ameloblastoma and brown tumour from hyperparathyroidism.

Ameloblastoma is regarded as the most usual odontogenic tumour. It is a benign tumour of the enamel organ without enamel formation. This tumour generally occurs in the middle-age group with the highest frequency observed at 33 years of age. Ameloblastoma occurs in all areas of jaws, but the lower jaw is most frequently affected. Within the mandible, the molar angle ramus area is affected three times more often than the premolar and anterior regions combined. Laboratory and radiological examinations were fundamental in establishing the final diagnosis.

To the authors' knowledge, this case was the second unconventional case of benign ameloblastoma associated with hypercalcemia reported in the literature.

Streszczenie

Przedstawiono przypadek szkliwiaka, który zarówno klinicznie, jak i radiologicznie przypomina obraz brunatnych guzów nadczynności przytarczyc w żuchwie. 70-letni mężczyzna był leczony z powodu zmiany w żuchwie. Niektóre badania laboratoryjne wprowadziły autorów w błąd co do różnicowania szkliwiaka i brunatnego guza w wyniku nadczynności przytarczyc.

Szkliwiak jest uważany za najczęstszy nowotwór odontogenny. Jest to łagodny guz w obrębie szkliwa bez wytworzenia szkliwa. Guz ten występuje zazwyczaj w grupie wiekowej średniej, a najwyższą częstotliwość występowania obserwuje się u osób w wieku 33 lat. Szkliwiak występuje we wszystkich obszarach szczęk, ale najwięcej przypadków obserwujemy w żuchwie. W obrębie żuchwy, gałąź kąta trzonowego jest trzy razy częstszą lokalizacją niż obszar zębów przedtrzonowych i zębów przednich razem wziętych. Badania laboratoryjne i obrazowe były kluczowe dla ustalenia ostatecznego rozpoznania.

Zgodnie z wiedzą autorów, opisany przypadek jest drugim niekonwencjonalnym przypadkiem łagodnego szkliwiaka związanego z hiperkalcemią opisanym w literaturze.

Introduction

Ameloblastoma, constituting the second most prevalent odontogenic neoplasm, comprises approximately 1% of all head and neck tumours, and around 11% of odontogenic tumours, representing a benign yet aggressive entity derived from the odontogenic epithelium.[1,2] This tumour typically manifests as a painless, gradually expanding jaw swelling, characterized by unilocular or multilocular expansive radiolucency, predominantly observed in the mandibular molar/ramus region.[3] Although the maxillary occurrence of the tumour is most frequent in the molar area, occasional instances in the anterior region, maxillary sinus and nasal cavity have been documented. The peak incidence is noted in the third and fourth decades of life, demonstrating a consistent sex distribution but with a potential increase in prevalence from the first to the seventh decade.[2] Surgical intervention with wide resection is recommended for ameloblastoma due to its propensity for high recurrence rates.[3,4]

Brown tumours, bony lesions arising in the context of hyperparathyroidism (HPT), occasionally involve the jaw bones. Clinical diagnosis of these tumours is confirmed by establishing HPT.[5–7] Intraorally, brown tumours present as painful, rigid, visibly apparent and palpable swellings. Treatment for primary HPT with bone lesions, including brown tumours, focuses on surgical removal of the parathyroid adenoma or hyperplastic glands, or medical intervention. Spontaneous resolution of the bone lesion is anticipated following correction of the patient's hormonal status; hence, surgical excision of a jaw-based brown tumour is generally discouraged unless the lesion attains significant size and becomes symptomatic.[8]

This report documents a case of ameloblastoma in the mandible of a 70-year-old man exhibiting both clinical and radiological similarities to brown tumours associated with hyperparathyroidism. It underscores the critical need for accurate diagnosis, as misidentification could lead to incomplete and inappropriate treatment, given the disparate treatment protocols for these two distinct pathologies.

Case report

A 70-year-old male was referred to our maxillofacial clinic complaining of a painful lesion that appeared on the right mandibular ridge five months previously. The patient had lost all the teeth 10 years before and had been using dentures since then. He had no remarkable medical history and denied smoking or addiction habits. No apparent lesion or lymphadenopathy was observed in the extraoral examination. There was no facial palsy or any paresthesia of the mental or infraorbital nerve.

On intraoral examination, a 2.5×2.0 cm sessile lesion was observed in the anterior right side of the mandible. The lesion exhibited fluctuant to firm consistency with a smooth surface and a colour similar to that of normal mucosa. The lesion expanded the medial and lateral cortical plates, but no ulceration of the overlying mucosa was found. Additionally, swelling occurred on the right side of the mandible (Fig. 1a-1b). The patient's consent form was signed and approved by the patient. This study was approved by the Bioethics and Research Committee of the Mashhad University of Medical Sciences (IR.MUMS.sd.1399.298).

After aspirating the lesion and sending it for cytology, the report indicated a proteinaceous fluid without cells. On radiological examination using panoramic imaging (OPG) and computed tomography scan (CT scan), a destructive expansive radiolucent lesion (3.5×3.0 cm) with well-defined borders was observed on the right side of the mandible (Fig. 2a, 2b).

Pre-operative laboratory test results for the patient were abnormal with a high calcium level of 12 mg/dl (normal range: 8.6-10.3 mg/dl),

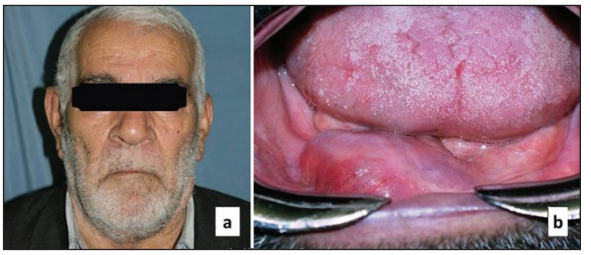

Fig. 1a-1b. A: the swelling of the right side of the mandible was noted. B: on intraoral examination the 2.5 x 2.0 cm sessile lesion was seen on the anterior right side of the mandible.

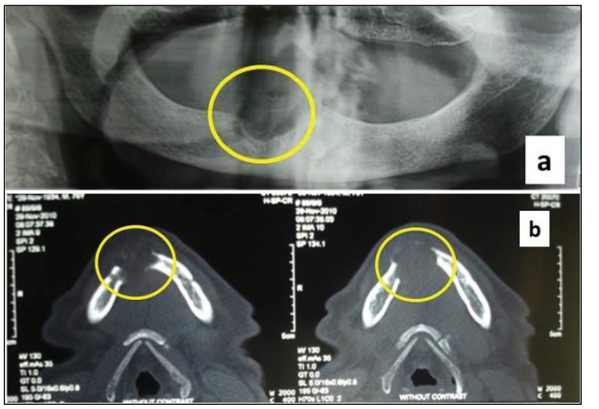

Fig. 2a, 2b. On X-ray examination of OPG (a) and CT Scan (b), the destructive expansive radiolucent lesion (3.5 x 3.0 cm) with well-defined border was seen on the right side of the mandible.

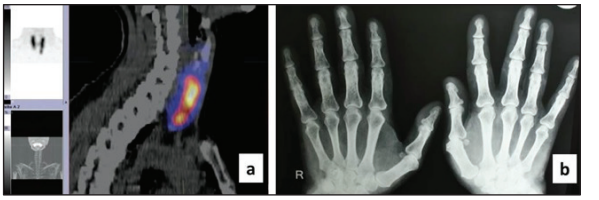

Fig. 3a, 3b. On the nuclear image of the parathroid glands, no adenoma was apparent (a), but the patient had subperiosteal bone resorption in the phalange bone (b).

high phosphorous level of 6.8 mg/dl (normal range: 2.7-4.5 mg/dl), high parathyroid hormone (PTH) level of 102.9 pg/ml (normal range: 15-65 pg/ml), and low 25OH-Vit.D3 of 7.1 ng/ml (normal range: 20-32 ng/ml) (Table 1).

After consulting the internal medicine service to rule out the brown tumour of the jaw, hand radiography, kidney sonography to check for possible renal stones, urology consultation, parathyroid sonography and nuclear medicine scanning were requested. Interestingly, the patient had no kidney stones, myopathy, or muscle pain, and in the nuclear imaging of the parathyroid glands, no adenoma was apparent. However, the patient had subperiosteal bone resorption in his phalangeal bone (Fig. 3a, 3b).

Based on the findings, the patient was diagnosed with hypercalcemia and a brown tumour of the jaw associated with secondary hyperparathyroidism. Medical treatment of Vitamin D 5000 u/week for eight weeks and evaluation of 24-hour urine calcium levels were prescribed. However, since the patient had a painful and symptomatic lesion, an excisional biopsy under general anesthesia was performed. The lesion was attached to the surrounding mucosa and was sent for histopathological evaluation.

Pathologic reports from two different centres for the lesion came back as a follicular type ameloblastoma. Through microscopic observation, a neoplasm composed of palisading columnar cells around an epithelial nest in a fibrous stroma was seen with a pattern similar to that of ameloblasts in the enamel organ. In the centre, loosely arranged cells were noted, mimicking the stellate reticulum of the enamel organ (Fig. 4).

The patient returned to the clinic from his hometown six months later with no sign of recurrence. Laboratory tests were checked again, and surprisingly, PTH level was 51.8 pg/ml, calcium level was 9.1 mg/dl, and phosphorous level was 4 mg/dl, all of them in the normal range, and 25OH-Vit.D3 level was 32.57 ng/ml (Table 1).

The patient's postoperative course was favourable and associated with a rapid improvement in hypercalcemia and normalization of the PTH level. Postoperative examination at the 12-month follow-up showed no recurrence or metastasis.

Table 1. Changes in the patient's laboratory tests, pre- and post-operative values and comparison to normal references

Laboratory tests	Pre-operation	Post-operation	References
Calcium	12 mg/dl	9.1 mg/dl	8.6-10.3 mg/dl
Phosphor	6.8 mg/dl	4 mg/dl	2.7-4.5 mg/dl
PTH	102.9 pg/dl	51.8 pg/dl	15-65 pg/dl
Vitamin D	17.1 ng/dl	77.8 ng/dl	30-74 ng/dl

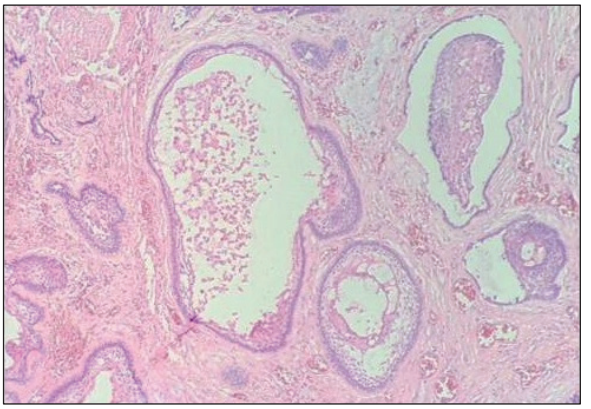

Fig. 4. Histopathological examination showed that neoplasm composed of palisading of columnar cells around epithelia nest in a pattern similar to that of ameloblast of enamel organ in fibrous stroma was seen. Central to these cells were loosely arranged cells that mimic stellate reticulum of the enamel organ.

Discussion

Ameloblastoma represents a benign tumour arising from the odontogenic epithelium and stands as a prevalent and clinically significant odontogenic tumour. It displays an aggressive nature, characterized by a relatively high rate of recurrence. While it can manifest anywhere in the mandible or maxilla, its most frequent occurrence is observed in the mandibular molar–ramus area.[3,6,9]

Ameloblastomas, categorized as a type of odontogenic tumour, exhibit diverse clinical and histological characteristics, leading to their classification into three categories based on presentation, treatment modalities and prognostic outcomes: multicystic or conventional, unicystic, and peripheral.[4] The presentation of these tumours varies, with patients often manifesting symptoms such as a slow-growing mass, malocclusion, loose teeth or, less commonly, paresthesia and pain. Notably, a significant number of cases are incidentally diagnosed through radiographic observations in asymptomatic patients.[3,4] From a radiographic perspective, conventional ameloblastomas typically display distinctive traits, presenting as unilocular or multilocular radiolucencies with well-defined borders.[2] These features contribute to their identification during imaging examinations, facilitating the diagnostic process.

Histologically, the majority of ameloblastomas showcase follicular or plexiform patterns. However, variations such as basaloid, granular cell, or desmoplastic patterns may also be encountered. It is noteworthy that the specific histological patterns observed do not appear to be directly linked to the tumour's behavior or prognosis, as they are considered irrespective of these clinical aspects.[4,10] This histological diversity emphasizes the complex nature of ameloblastomas and underscores the importance of a comprehensive histopathological examination for accurate diagnosis and treatment planning. While the patterns may vary, the classification and understanding of these variations contribute to a more nuanced approach in managing patients with ameloblastomas,

taking into account the diverse nature of these intriguing odontogenic tumours.

Current trend in surgical treatment of ameloblastoma is either conservative or radical. The conservative approach includes enucleation, curettage, or surgical excision with peripheral osteotomy. The tumour has a strong propensity to recur after conservative surgical removal.[4] Many researchers recommend excising a 1.5–2 cm margin beyond the radiological extent to ensure all microcysts are removed.[6]

Radiologically, brown tumours, representing the terminal phase of hyperparathyroidism (HPT), exhibit distinctive features that aid in their identification and characterization. These tumours most commonly affect the ribs, the clavicles, the pelvic girdle and the mandible. Intraorally, brown tumours present as palpable, painful, and visibly evident hard swellings, providing clinical indicators for further investigation.[8]

When observed radiographically, brown tumours manifest as well-demarcated lesions with either a monolocular or multilocular osteolytic appearance. In the mandible, these tumours often lead to the expansion and thinning of the cortical bone. Notably, brown tumours in the jaws may contribute to root resorption and loss of the lamina dura. In some instances, they can present as space-occupying masses within the sinus cavity, adding complexity to their radiographic presentation.[5,8]

Beyond the maxillofacial region, skeletal radiographic findings associated with brown tumours include subperiosteal resorption of bone, typically affecting the medial aspect of the middle phalanges. Additionally, erosion of distal digital tufts and margins of multiple joints may be observed. These features contribute to a comprehensive understanding of the systemic impact of brown tumours on the skeletal structure.[8]

Histologically, brown tumours are characterized by soft tissue masses composed of giant cells within a fibrovascular stroma. Cystlike spaces lined by connective tissue and foci of hemorrhage releasing hemosiderin are also observed in histopathological examinations. These distinctive features collectively contribute to the tumour's appearance as a friable red-brown mass, providing a histological basis for the term "brown tumour".[5,8] The radiological and histological features of brown tumours underscore the importance of a multidisciplinary approach for accurate diagnosis and appropriate management, particularly in the context of hyperparathyroidism.

Primary hyperparathyroidism (HPT) is characterized by PTH hypersecretion, triggered by adenomas in 85% of all cases, while secondary HPT results from chronic renal failure. Patients with a history of dialysis and/or renal failure are often suspected of secondary HPT.[8] Parathyroidectomy is the preferred treatment for brown tumours associated with HPT, aiming to normalize parathyroid function, leading to a decrease in size or disappearance of the tumour.[5] Additionally, medical treatment, including calcium carbonate, vitamin D and aluminum hydroxide antacids for hyperphosphatemia, may prevent or alleviate significant bone disease associated with secondary HPT. The bone lesion tends to resolve spontaneously after correcting the patient's hormonal status, and surgical excision of a brown tumour of the jaw is generally not recommended unless the lesion is large and symptomatic.[8]

The presented case of ameloblastoma was associated with hypercalcemia and hyperparathyroidism, resembling the clinical and radiological presentation of brown tumours. PTH targets the kidney and bone to closely govern systemic homeostasis of calcium and phosphorous ions.[9] The present case exhibited hypercalcemia, a common metabolic complication in malignancies, categorized into humoral hypercalcemia of malignancy and local osteolytic hypercalcemia. While many cases of ameloblastic

carcinoma with hypercalcemia were reported, only one case of benign ameloblastoma associated with hypercalcemia was found in the literature.[7,11–13] Our case represents the second reported case of benign ameloblastoma associated with hypercalcemia. In 2012, *Ota* et al. reported a case of a 32-year-old Japanese woman with ameloblastoma associated with hypercalcemia.[3] Despite apparent similarities, the extent of the two tumours is contrasting.

PTH-related protein (PTHrP) was first discovered as a protein generating hypercalcemia, commonly observed during the terminal phase of malignant tumours such as squamous cell carcinoma of the tongue, lung cancer, breast carcinoma with metastatic bone deposits and in patients with multiple myeloma with hypercalcemia.[9,14] PTHrP, the second member of the PTH family, comprises 139 amino acids and mimics not merely the genomic structure of PTH but also its protein configuration.[9,14] In contrast to the systemic hormonal impact of PTH, PTHrP locally controls tissue functions.[14] Besides malignant tumours, PTHrP is present in normal keratinocytes, lactating mammary tissue, placenta, parathyroid gland, the central nervous system, and various other sites suggesting a widespread physiological role.[5,14] PTHrP was localized in ameloblast-like and stellate reticulum–like cells and squamous metaplasia and is required for tooth eruption. It has been reported to be involved in ameloblast function and maturation and to influence the growth of epithelial tissue, as well as the differentiation of keratinocytes.[7,14] The proposed role of PTHrP expression in ameloblastoma is central to local bone resorption, contributing to the destructive and infiltrative growth of this tumour, especially in acanthomatous types.[9,14]

In conclusion, this case report underscores the diagnostic challenges posed by the rare coexistence of ameloblastoma and hyperparathyroidism, presenting clinically and radiologically akin to brown tumours. While ameloblastoma, as the second most common odontogenic neoplasm, necessitates surgical resection due to its benign yet aggressive nature, brown tumours, representing the terminal phase of hyperparathyroidism, typically require intervention targeting hyperparathyroidism with surgical excision of the jaw lesion reserved for large symptomatic cases. The rarity of ameloblastoma associated with hypercalcemia adds complexity, emphasizing the need for nuanced diagnostic approaches. The role of PTH-related protein in ameloblastoma highlights potential mechanisms for local bone resorption.

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Zaakceptowano do druku: 2.12.2025 r.

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Declaration

The authors would like to appreciate the continued support of the Research Council of Mashhad University of Medical Sciences and Student Research Committee of Mashhad University of Medical Sciences, Mashhad, Iran. The authors also express their gratitude to Dr Armaghan Salehi for preparing this article.

Ethical Approval: All procedures performed in this study involving the human participant were in accordance with the ethical standards of our institutional research committee and with the 1964 Helsinki declaration. The patient's ethical consent form was signed and approved by the patient. This study was approved by the Bioethics and Research Committee of Mashhad University of Medical Sciences (IR.MUMS.sd.1399.298).

Funding: None. This study was self-funded.

Conflict of interests: The authors have no conflict of interest to declare.

Patient consent: Authors have a written and signed consentment term.

Authors contribution: All authors contributed equally to this manuscript. All authors read and approved the final manuscript.