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Dental Science – Case Report

Brown Tumour in the Mandible and Skull Osteosclerosis Associated with Primary Hyperparathyroidism – A Case Report

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Abstract

BACKGROUND: The hyperparathyroidism (HPT) is a condition in which the parathyroid hormone (PTH) levels in the blood are increased. HPT is categorised into primary, secondary and tertiary. A rare entity that occurs in the lower jaw in association with HPT is the so-called brown tumour, which an osteolytic lesion is predominantly occurring in the lower jaw. It is usually a manifestation of the late stage of the disease. Osteosclerotic changes in other bones are almost always associated with renal osteodystrophy in secondary HPT and are extremely rare in primary HPT. This article reports a rare case of a brown tumour in the mandible as the first sign of a severe primary HPT, associated with osteosclerotic changes on the skull.

CASE REPORT: A brown tumour in the mandible was diagnosed in 60 - year old female patient with no previous history of systemic disease. The x - rays showed radiolucent osteolytic lesion in the frontal area of the mandible affecting the lamina dura of the frontal teeth, and skull osteosclerosis in the form of salt and pepper sign. The blood analyses revealed increased values of PTH, calcitonin and β – cross-laps, indicating a primary HPT. The scintigraphy of the parathyroid glands showed a presence of adenoma in the left lower lobe. The tumour lesion was surgically removed together with the lower frontal teeth, and this was followed by total parathyroidectomy. The follow - up of one year did not reveal any signs of recurrence.

CONCLUSION: It is critical to ensure that every osteolytic lesion in the maxillofacial region is examined thoroughly. Moreover, a proper and detailed systemic investigation should be performed. Patients should undergo regular check-ups to prevent late complications of HPT.

Introduction

The main hormone that regulates the calcium metabolism in the body is the parathyroid hormone (PTH). It is secreted by the parathyroid glands, and its release is dependent on the plasma concentration of ionised calcium. The lower the concentration, the higher the secretion of PTH is. The primary function of PTH is to normalise the level of calcium in the blood. It demonstrates its activity by activation of osteoclasts, subperiosteal bone resorption, catalysing the vitamin D synthesis in the kidneys and increasing the reabsorption of calcium in the kidneys.

The hyperparathyroidism (HPT) is a condition where PTH is increasingly released from the parathyroid glands. It is categorised into primary, secondary and tertiary [1].

The primary HPT is, in most of the cases, a result of a gland adenoma, and rarely occurs due to malignancy [2]. It is characterised by hypercalcemia. The secondary HPT is a consequence of the hypocalcemia, where the glands increase the production of the hormone to mobilise the calcium from the bones to correct the condition [3]. The tertiary HPT is a condition developed after a long period of increased PTH secretion from the glands. Additionally, another form of HPT exists, known as a paraneoplastic syndrome or pseudohypo-parathyroidism, in which PTH is released into the bloodstream from ectopic parathyroid - like a gland.

A rare entity that occurs in the lower jaw is the so-called brown tumour, which is an osteolytic, cystic -

like lesion filled with soft tissue composed of fibrovascular stroma and giant cells [4]. They are called brown tumours because of the colour that they get as a result of the haemorrhage in the tissue, and the hemosiderin deposits [5][6] The frequency of occurrence of brown tumours in the primary and secondary HPT is 4.5% and 1.5 – 1.7%, respectively. The overall incidence is 0.1% [7]. It is thought that brown tumours are a late manifestation of HPT and nowadays they are not as often detected as before due to the early diagnosis of the endocrinologic condition. Osteosclerotic changes in other bones are almost always associated with renal osteodystrophy in secondary HPT and are extremely rare in primary HPT [8][9][10]. They are usually limited to the pelvis, spine, skull and ends of the long bones.

This article reports a rare case of a brown tumour in the mandible as the first sign of a severe primary HPT, associated with osteosclerotic changes on the skull with the so-called salt and pepper sign.

Case report

Sixty-year-old female referred to our clinic, complaining about discomfort and swelling in the front area of the mandible. The obtained medical data did not show any history of chronic or malignant conditions. According to the patient, the swelling in the vestibulum was gradually increasing with time. The patient did not complain about pain, stiffness or other subjective symptoms. The clinical investigation revealed solid, rounded formation in the vestibulum extended between the canine teeth in the lower jaw. There were no fluctuations, no tenderness and no colour or surface changes of the mass. No fistulas or pus were detected. All the lower incisors were mobile, indicating loss of the surrounding bone. Further examination tools were used: a complete blood analysis and panoramic x-ray were performed.

The blood analysis showed increased values of parathyroid hormone, osteocalcin and β - cross-laps (Table 1). No other significant alterations of the blood parameters were present. The x-ray showed a cystic-like radiolucent lesion in the mandible, extending from the roots of the second premolars from the one side to the second premolars to the other side (Figure 1). The lesion almost reached the lower edge of the body of the lower jaw. A severe reduction of the bone density was observed in the affected area, as well. Also, the lamina dura of the incisors and right canine was also affected. The similar lesion was detected on the x-ray in the left distal area of the mandible body, but that finding was not associated with any clinical signs or symptoms.

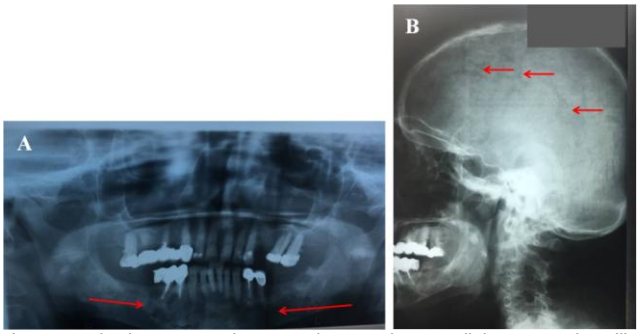

Figure 1: A) The panoramic x-ray shows a huge radiolucent cystic - like change in the frontal area of the mandible (red arrows), extending to the lower edge of the mandible and affecting the lamina dura of the lower frontal teeth; B) The red arrows on the lateral x-ray of the skull show osteosclerotic changes on the calvaria (salt and pepper sign)

The profile x-ray of the skull showed the lesions of the mandible from another perspective, but it also revealed osteosclerotic changes on the calvaria. These changes were addressed as salt and pepper sign.

Table 1: Laboratory tests and findings in the patient that lead to set the diagnosis

Tested parameter	Found value	Normal range
PTH	1312 pg/ml	15-65 pg/ml
Osteocalcin	56.4 ng/ml	15-46 ng/ml*
B - crossLaps	1.57 ng/ml	0.556 ng/ml*
Total Vit. D (25 - Hydroxyvitamin D)	30.88 nmol/l	25-110 nmol/l
Na^+	141 mmol/l	130-150 mmol/l
K^+	4.2 mmol/l	3.3-5.6 mmol/l
Ca^{2+}	1.64 mmol/l	1.16-1.29 mmol/l **

*in postmenopausal women; **in adults 60-90-year old.

Considering the obtained data from the blood and x-ray analyses, a working diagnosis of a brown tumour in the mandible as a result of HPT was set. Two-Phase scintigraphy of the thyroid and parathyroid glands was performed, and it showed accumulation of the Tc99m beyond the lower pole of the left thyroid lobe, extending sub-clavicular and posteriorly (Figure 2).

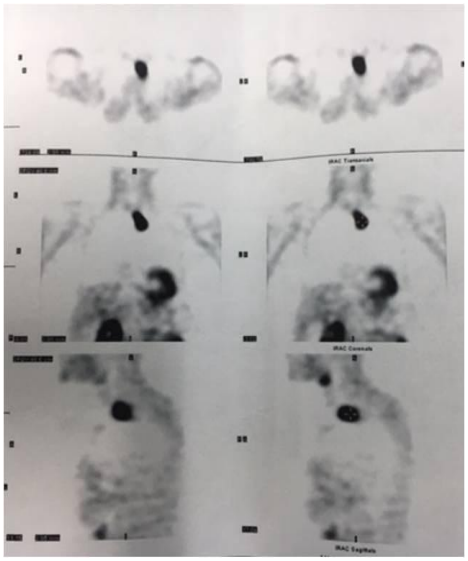

Figure 2: The scintigraphy of the parathyroid glands show accumulation of the isotope in the lower left parathyroid lobe, extending below the clavicle and posteriorly. This finding indicates a presence of gland adenoma

The extension was with a diameter of 4 cm, indicating a presence of adenoma of the parathyroid gland. In the absence of signs of renal failure and ectopic parathyroid glands, the HPT was determined as primary. The treatment plan included surgical removal of a brown tumour from the frontal area in the mandible, followed with excision of the gland adenoma (Figure 3).

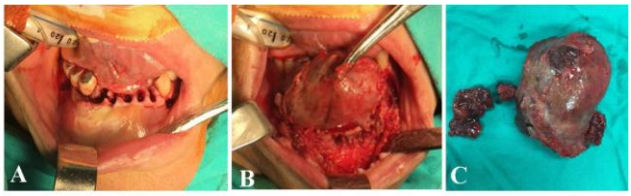

Figure 3: A) Preoperative look of the affected area. The lower frontal teeth were extracted due to severe mobility; B) Intraoperative view of a brown tumour (clamped lesion); C) A tumour was excised completely in one piece

We extracted the lower incisors and right canine due to the severe mobility. An intraoral buccal vestibular incision was made, and the mass was removed in one piece. The histological examination proved the working diagnosis of a brown tumour. The adenoma of the parathyroid gland was also removed, after which the level of PTH was gradually decreasing. No signs of recurrence of a tumour were noted in the following year.

Discussion

The clinical presentation of HPT in the early stages is not often abundant. Later, it may include renal calculi, osteoporosis, peptic ulcers, pancreatitis or neuropsychiatric symptoms [11][12][13][14]. Since HPT changes the bone metabolism, the bones are likely to become affected. Most involved bones are the ribs, clavicles, pelvic girdle and the lower jaws [15].

The brown tumours in the jaws associated with HPT represent reparative granuloma, rather than a true neoplastic process. These changes are due to the reduction of the bone density and its filling with granulation tissue. The lytic lesions on the bones, including the jaws and skull, as showed in our case, are signs of the terminal stadium of HPT. The technological advancements and the possibility of early diagnosis greatly decreased the incidence of these findings [16]. Thus, they are rarely seen in the developed countries [17]. However, this case showed that they still can represent a clinical entity that requires great attention.

A brown tumour associated with primary HPT is more frequently seen in the lower jaw, rather than in the upper jaw. The simultaneous finding in both jaws is extremely rare [18]. The females are three times more likely to be diagnosed with a brown tumour than the males when the disease is progressing to the late stage [3]. A brown tumour in this case, in addition to the bone resorption of the body of the mandible, affected the periodontal apparatus of the frontal teeth which lead to the severe mobility. This loss of the surrounding bone of the teeth was also demonstrated in previous studies and was a radiologic feature within 6 - 55% [15][19].

The diagnosis of a brown tumour cannot be solely set by the histological findings because they are not specific for this condition. The usual findings are mononuclear stroma cells accompanied by multinuclear giant cells [20][21]. These giant cells can be found in other lesions, like aneurismal bone cysts, giant cells granulomas, cherubism and Langerhans histiocytosis [22][23]. Therefore, the definite diagnosis should incorporate the clinical, biochemical, histological and radiological signs. The increased levels of PTH and osteocalcin indicated an increased release of the hormone from the glands. The level of calcium was also elevated due to the bone resorption, as an effect of the action of PTH. B - cross-laps, which are a specific marker for degradation of mature type I collagen during bone resorption, were also elevated. Furthermore, the scintigraphy showed increased uptake of the used isotope in the right parathyroid glands. The skull changes were a sign of general reduction in the bone density. All these findings, accompanied with the lytic lesions seen on the radiographs, depicted the condition of primary HPT.

The principle treatment of the primary HPT associated with bone changes and highly increased blood markers is partial or total parathyroidectomy. It is assumed that after the removing of the reason for HPT, the bone changes will spontaneously regress [13][14][24,25]. This claim is supported particularly for the small tumours and has been demonstrated in previous studies [19]. However, in cases when the tumour dimensions interfere with the function and every - day activities of the patient, the surgical removal is a reasonable solution [26][27]. This was the case with our patient. The growth of the lesion severely damaged the frontal teeth and was a reason for considerable discomfort during eating and even not taking any action. After the surgical removal of the jaw lesion and the gland adenoma, no signs of recurrence were detected in the follow up of one year.

This report shows that HPT may not be diagnosed until the late stages of the disease, despite the technological advancements and available diagnostic tools. The huge brown tumour in the mandible and the osteosclerotic skull changes were the initial signs of primary HPT in our patient. Therefore, it is critical to perform a detailed systemic investigation in the cases of suspect osteolytic lesions in the maxillofacial area. Moreover, rising the awareness and emphasising the importance of regular check-ups are also encouraged. These measures will

prevent the late complications of the disease that can be easily diagnosed in its early stages.

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