



Primary Hyperparathyroidism Presented with Peripheral Brown Tumor in the Oral Cavity: A Case Report

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Abstract

Brown tumor is a non-neoplastic lesion which resulting from abnormal bone metabolism caused by hyperparathyroidism. We report a rare case of peripheral brown tumor related with primary hyperparathyroidism which simulating a peripheral giant cell granuloma of the jaws.

Key words: Primary hyperparathyroidism, brown tumor, maxillar giant cell granuloma

(Rec.Date: May 27, 2014 Accept Date: Jun 16, 2014)

This paper reported as a poster presentation at ECE 2014 Congress (May 3-7 in Wrocław, Poland).

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Introduction

Parathyroid hormone (PTH) is the chief regulator of calcium homeostasis in the human body. Primary hyperparathyroidism (PHPT) occurs in a setting of excessive PTH secretion with an autonomous parathyroid gland, which results in hypercalcemia [1]. Most patients with PHPT have a single adenoma (about 80% of cases), but multigland disease can occur in 10%-15% of cases and double adenomas in 4%-5% [2]. Parathyroid carcinoma is a rare cause (usually less than 1% of patients) of hyperparathyroidism [3,4]. There is a great variation in the manifestations of PHPT. The clinical presentation of PHPT ranges from a severe disease with nephrolithiasis and metabolic bone disease to mild asymptomatic disease [5,6]. The most common clinical presentation of PHPT is asymptomatic hypercalcemia with an elevated or higher normal intact PTH level. Patients with hypercalcemia may present with vague constitutional symptoms, anorexia, lethargy, or polydipsia and polyuria [7-9]. Less specific features of PHPT are fatigue, proximal muscle weakness, mild cognitive disturbances, hypertension, left ventricular hypertrophy, valvular calcification and cardiovascular mortality [2,10]. Classic skeletal lesions, which are bone resorption, bone cysts, brown tumours and generalized osteopenia, occur in less than 5% of cases [11]. PHPT affects compact bone more than trabecular bone with particular sensitivity in the cortices of long bones leading to subperiosteal bone resorption (seen as periosteal elevation on plain radiography) [12]. PHPT is prone to cause loss of the lamina dura [13].

Giant cell lesions of bone share similar clinical, radiological and histological features. The most challenging differential diagnosis is between giant cell tumour and brown tumour due to hyperparathyroidism. Giant cell lesion associated with hyperparathyroidism is commonly named as “brown tumour”. Brown tumour, also called osteitis fibrosa cystica, represents the terminal stage of the bone remodelling processes occurring as a result of peritrabecular fibrosis and osteoclastic activity [14,15]. Brown tumours can occur as solitary or multiple lesions in any bone. The term of “brown tumour” comes from the colour of the lesion; which results from the vascularity, haemorrhage and deposits of haemosiderin [16]. Histologically, brown tumours are characterized with numerous giant cells, diffused or arranged in clusters, in a background of mononuclear oval-to-spindle stromal cells. They appear highly vascular and haemosiderin deposition may be abundant. Histologically, brown tumours may be indistinguishable from giant cell tumours of the bone, and correlation with clinical and

radiographic studies is essential in making the correct diagnosis. Brown tumours are usually soft, painless, minimally tender, and appear elastic on palpation. Symptoms result from the considerable dimensions of the tumour and its localisation, but in most cases maxillary brown tumours are not painful. Radiographically, they appear as well demarcated monolocular or multilocular osteolytic lesions. The mandible is the predominantly affected site in the maxillofacial area. Maxillary involvement is rare [17-22].

Case Report

A 50-year old man was admitted to the Oral Medicine Department in Samsun Oral Medicine Hospital for evaluation of an oral cavity lesion. Physical extraoral examination was not remarkable and facial deformity was not observed. In his medical history there was no renal failure or any disease including bone metabolism. In physical intraoral examination there was a sessile swelling on the anterior region of the maxilla, 27x16x13 mm in diameter. The lesion was surgically removed and histopathological analysis revealed a tumour, including ovoid to spindle-shaped mesenchymal cells with focal aggregates of multinucleated giant cells throughout the lesion (Figure 1).

The patient was referred to our outpatient clinic of Endocrinology and Metabolism at the Samsun Training and Research Hospital. He had no symptoms or signs of hyperparathyroidism. In his medical history, other PHPT related diseases such as hypertension, cardiac dysrhythmia and nephrolithiasis were not present, either. Physical examination of the patient revealed no additional pathologies. Blood analysis demonstrated a PTH level of 355 pg/mL (normal range:15-65). Serum calcium and alkaline phosphatase levels were also higher [10.6 mg/dL (8.7-10.4); 430 U/L (45-129), respectively] than normal limits whereas the phosphorus level was lower. The blood urea nitrogen (BUN), and the creatinine levels were within normal limits. Pathological biochemical tests of the patient on admission are summarized in Table 1. Neck ultrasonography revealed a solitary lesion on the right parathyroid region (Figure 2). Dual phase 99mTc-sestamibi parathyroid scintigraphy imaging (Tc99 m MIBI) detected a mass close to the inferior right thyroid gland, compatible with a parathyroid adenoma (Figure 3). These findings confirmed the patient's PHPT diagnosis. The patient was investigated using multiple direct bone graphs. No foci suggestive

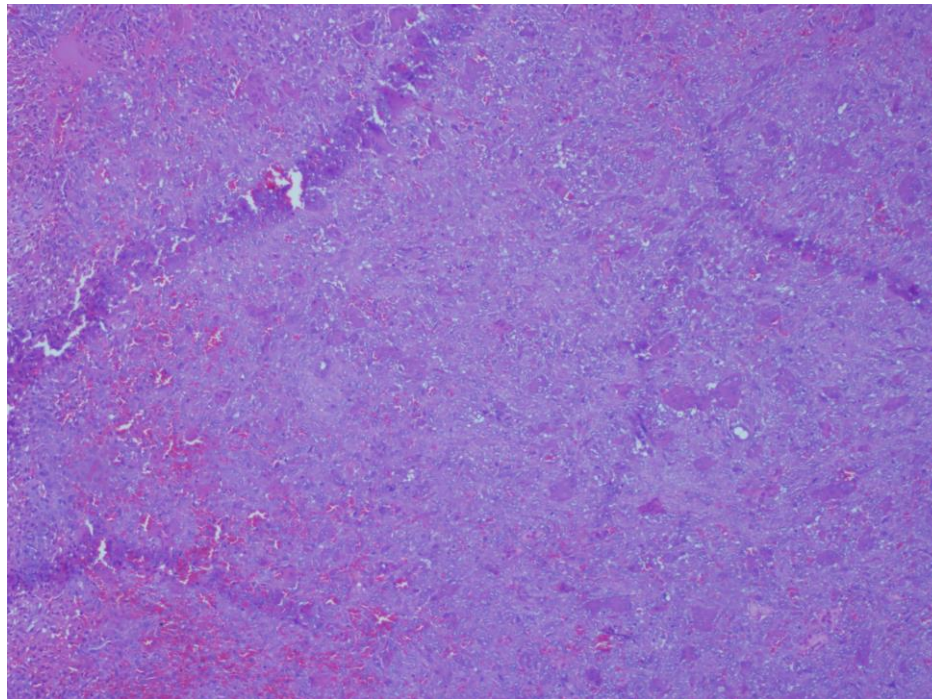
of another brown tumour were identified. No cardiac pathologies were detected from his physical examination or electrocardiographic findings.

Informed consent was obtained from the patient. And, the patient underwent parathyroid surgery. After removing the parathyroid adenoma the serum calcium level decreased to 8 mg/dL and the PTH to 5.6 pg/mL. Calcium treatment was administered intravenously to the patient for three days and treatment was subsequently switched to calcitriol 0.5 µg tablet 2x1 and calcium 1000 mg tablet 3x1. Seven days after parathyroidectomy, serum calcium was 8.5 mg/dL and he was discharged. The patient is still on routine follow-up at our endocrinology outpatient clinic and has normal serum calcium levels.

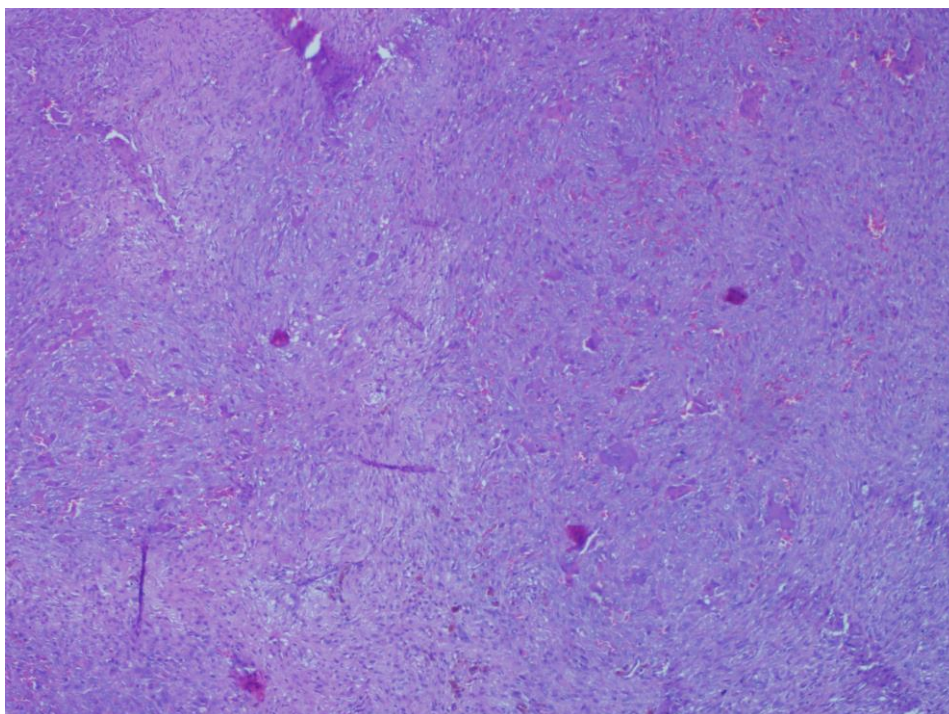
Table 1. Biochemical tests of the patient showing abnormalities

Parameter	Patient	Normal Range
Calcium	10.6 mg/dL	8.7-10.4 mg/dL
Phosphorus	1.9 mg/dL	2.4-5.1 mg/dL
Albumin	4.2 g/dL	3.2-4.8 g/dL
Alkaline phosphatase	430 U/L	45-129 U/L
Parathormone	355 pg/mL	15-65 pg/mL
25-OH-vitamin D	25 ng/mL	25-80 ng/mL

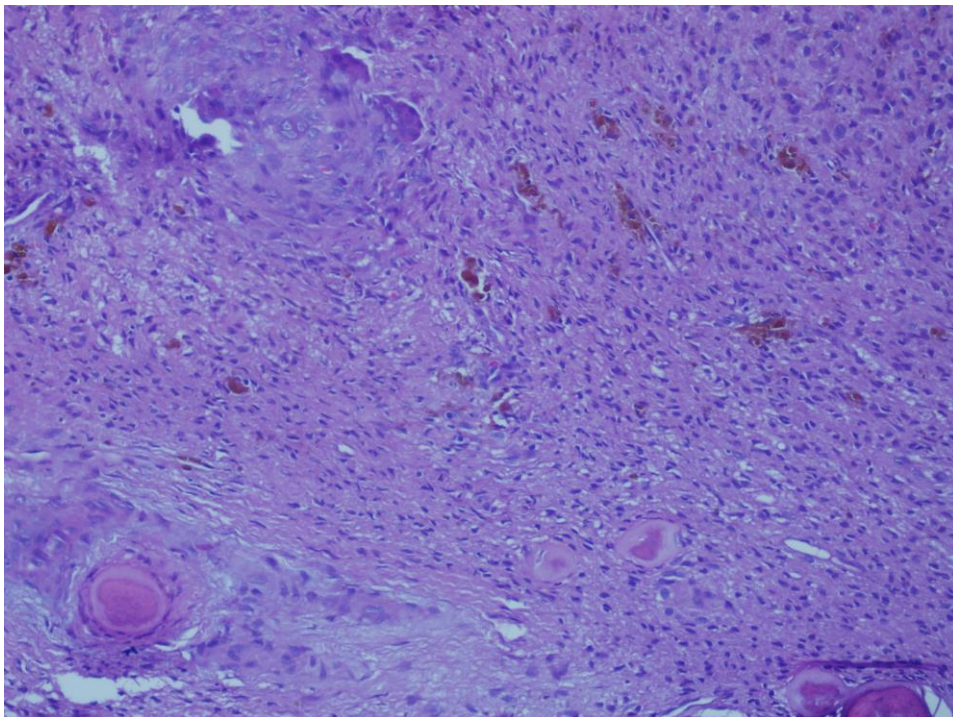
Figure 1. Histopathological appearance of the lesion. Mononuclear ovoid and multinucleated giant cells. (1a. 10x10, 1b. 10x10, 1c. 10x40, 1d. 10x20)



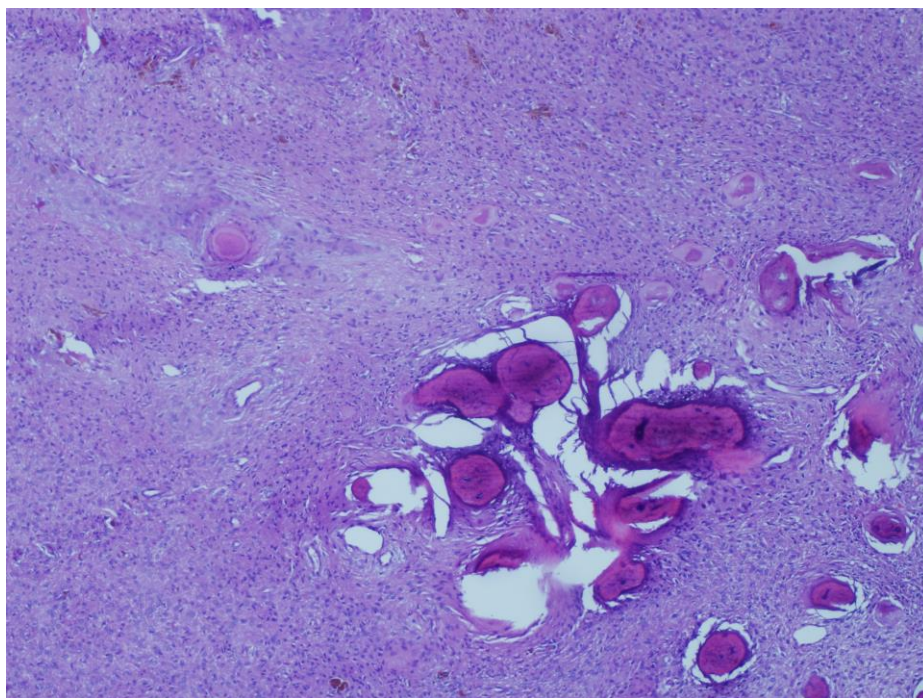
1a.



1b.



1c.



1d.



Figure 2. Neck ultrasound shows well-defined homogenous hypoechoic solid mass lesion in relation to the posterior aspect of the inferior pole of the right lobe of thyroid.

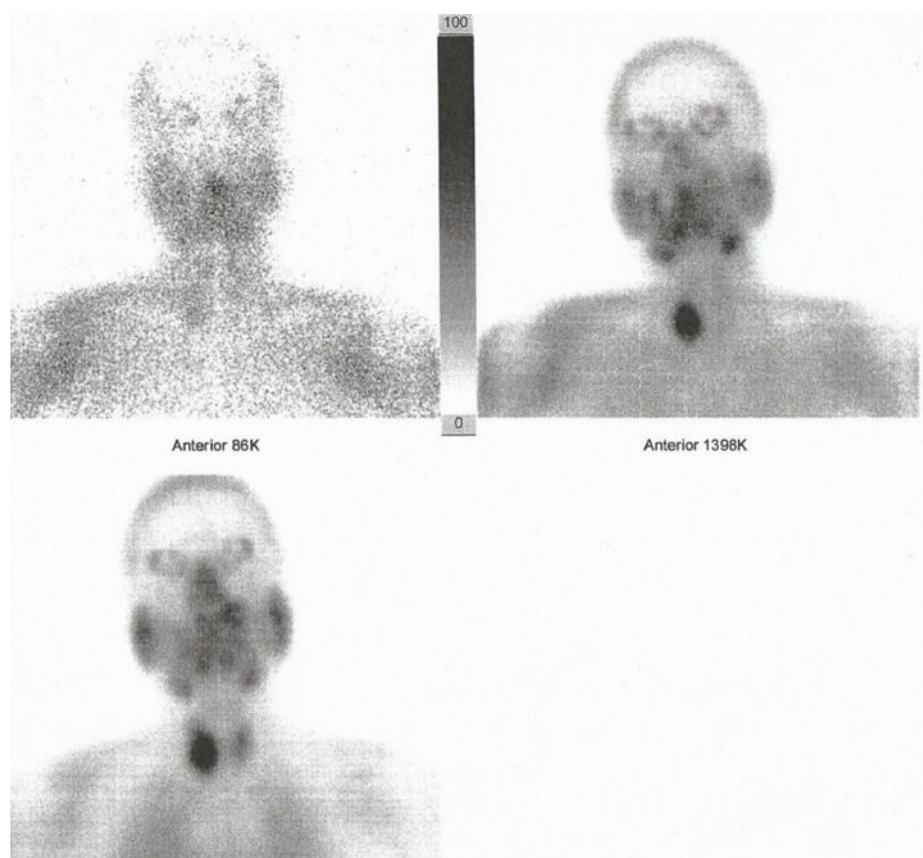


Figure 3. Tc99m-sestamibi parathyroid scintigraphy, revealed an area with increased uptake in the lower right thyroid lobe and another area with marked uptake lower than this level.

Discussion

PHPT is one of the most common endocrinological disorders [1]. Single gland parathyroid adenoma is the most common cause of PHPT. A single adenoma usually indicates sporadic disease, whereas hyperplasia of the four glands suggests familial disease (multiple endocrine neoplasia type 1 or 2A). Although PHPT is generally an asymptomatic disease detected by an incidental finding of hypercalcemia; in several cases, it has been diagnosed by overt bone disease. Bone involvement is the late manifestation of PHPT [19]. The brown tumour is a type of giant cell lesion and appears as multiple expansive osteolytic lesions of the bone. The ribs, clavicles, pelvic girdle, hand and the mandible are the bones which are most involved [20,21]. Peripheral manifestation of brown tumour on the oral cavity is rare, and the clinical appearance simulates peripheral giant cell granuloma. It is very difficult to distinguish histopathologically brown tumour from other giant cell lesions. So, the clinical diagnosis is

made based on the association with PHPT [22]. There are very few cases presented in current literature, similar to ours i.e. brown tumour due to PHPT localized in the maxillary region.

The most useful therapy for patients with brown tumours is surgical excision of bone lesions and therapy (surgical or medical) for primary or secondary HPT. If PHPT is due to a parathyroid adenoma (or adenomas), parathyroidectomy is the definitive cure. Surgery has a very high long-term success rate and minimal morbidity [7,8]. Most authors also agree that the best treatment for brown tumours is to cure the underlying PHPT. When a successful parathyroidectomy for PHPT has been performed, partial or total recovery of osteitis fibrosa cystica patterns has been described [23,24].

Medical therapy, such as calcimimetics, may gain in popularity with hypercalcemia patients who cannot undergo surgery. Although studies show that cinacalcet, versus placebo, effectively lowers both calcium and PTH levels, there is no significant increase in bone mineral density [25-27]. Multiple studies have shown that bisphosphonates improve bone mineral density on dual energy X-ray absorptiometry (DXA) scans in patients with PHPT [28,30]. If preservation of bone mineral density is the primary goal of treating asymptomatic PHPT, the agent of choice should be a bisphosphonate [7].

Conclusion

We present a rare case of maxillary brown tumour associated with PHPT simulating a peripheral giant cell lesion. We also strongly emphasise the need for group consultation between oral and maxillofacial surgeons, dentists, endocrinologists and radiologists.

Disclosure statement: No conflict of interest

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