Primary hyperparathyroidism presenting as a giant cell tumor of the jaws

Wojciech Pawlak [1], Anna Bohdanowicz-Pawlak [2], Marek Bolanowski [2], Jadwiga Szymczak [2], Grażyna Bednarek-Tupikowska [2], Klaudiusz Łuczak [1]

1 Department of Cranio-Maxillofacial Surgery, Wrocław Medical University, Poland
2 Department of Endocrinology, Diabetology and Isotope Therapy, Wrocław Medical University, Poland

Correspondence to: Anna Bohdanowicz-Pawlak, MD., PhD.
Department of Endocrinology, Diabetology and Isotope Therapy,
Wrocław Medical University
Pasteura 4, 50-367 Wrocław, Poland.
TEL: +48 71 7842550; FAX: +48 71 3270957;
E-MAIL: anna.bohdanowicz-pawlak@am.wroc.pl

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Abstract

OBJECTIVE: Giant cell tumors of the maxillofacial skeleton are uncommon, they are usually late manifestation of primary hyperparathyroidism. A series of five clinical cases in four women and one man presenting as the giant cell lesions in the maxilla and/or mandible are discussed.
METHODS: Biopsy of the lesions, biochemical and hormonal analyses, densitometry and parathyroid scintigraphy were carried out.
RESULTS: Biopsy of the lesions showed giant cell tumor of bone. The medical history and laboratory analyses showed primary hyperparathyroidism. Bone density loss was documented and scintigraphy revealed the presence of parathyroid adenomas in four cases. Surgical treatment of hyperparathyroidism, and in the second step – after 6–12 months – the subsequent excision of residual brown tumors in all cases was performed.
CONCLUSIONS: One should have in mind that osteolytic bone lesions may be due to metabolic disease of the bone. Accurate diagnosis enabling the proper treatment should be carried out, avoiding unnecessary harm to the patients.

CASE REPORT

INTRODUCTION

Giant cell tumors of the maxillofacial skeleton are uncommon and can be classified as brown tumors of hyperparathyroidism (HPT), true giant cell tumors or reparative giant cell granulomas. Brown tumors develop in bones, presenting as well-demarcated, circumscribed osteolytic lesions. Involvement of the spine, the pelvic bones, the shoulder, the sternum, the palate and the jaws has been reported (Martinez-Gavidia *et al.* 2000; Rosenberg & Nielsen 2001; Daniels 2004; Triantafillidou *et al.* 2006). Brown tumors are made up of mononuclear stromal cells mixed with multinucleated giant cells with hemorrhagic infiltrates and hemosiderin deposits are found. Because it is difficult to histopathologically distinguish brown tumor from other giant cell lesions a clinical diagnosis of brown tumors is made with the finding of HPT (Whitaker & Waldron 1993; Rosenberg & Nielsen 2001; Ciorba *et al.* 2004; Etemadi *et al.* 2009). Parathyroidectomy to control primary hyperparathyroidism (PHPT) is the treatment of first choice for brown tumor because

normalization of parathyroid function should lead to a reduction in size or disappearance of the tumor (Keyser & Postma 1996; Suarez-Cunqueiro *et al.* 2004; Sanroman *et al.* 2005).

Primary hyperparathyroidism is the most common endocrine disorder after diabetes mellitus and thyroid dysfunction. The disease is characterized by hypersecretion of parathormone (PTH) from parathyroid gland(s), which is caused by adenomas in 81%, hyperplasia in 15% and carcinoma accounting for 0.5–4% of cases (Daniels 2004; Triantafillidou *et al.* 2006). The diagnosis of PHPT has classically been based on the demonstration of increased serum level of PTH, hypercalcemia, hypophosphatemia, hypercalciuria and hyperphosphaturia. About 80% of cases of PHPT are diagnosed when a routine assay shows hypercalcemia in patients who are asymptomatic or during evaluation of osteoporosis. It is generally accepted that brown tumors and dental changes are late manifestations of hyperparathyroid bone disease (Bolanowski & Pluskiewicz 2002; Sanroman *et al.* 2005; Vera *et al.* 2011).

A series of five clinical cases, previously not diagnosed towards PHPT, presenting as the giant cell lesions in the jaws are discussed.

MATERIAL AND METHODS

We present 5 cases of giant cell tumors in the jaws, developed in 4 women and one man. Two cases of the tumors involved the mandible, one case involved the maxillary sinus and two cases involved both the maxilla and mandible. Biopsy of the tumor in all patients showed numerous osteoclast-like giant plurinuclear cells, without necrosis and mitoses or histological signs of malignancy, the picture compatible with giant cell tumor of bone. The medical history of patients and biochemical exploration showed the existence of primary hyperparathyroidism as the cause of the bone lesion – brown tumor. The clinical characteristics of patients, treatment and results of follow-up are shown in Table 1. Blood tests demonstrated elevated serum PTH and calcium concentration and low serum phosphorus level, hypercalciuria was proven also. Bone density in forearm and lumbar spine was evaluated (Table 2). Scintigraphic examination revealed the presence of parathyroid adenomas in four cases. Surgical treatment of PHPT – hyperparathyroadenomectomy and in the second step – after 6–12 months – the subsequent excision of residual brown tumors in all cases was performed.

RESULTS AND DISCUSSION

Osteitis fibrosa cystica is a diffuse resorptive process of the bone resulting from hyperparathyroidism. Nowadays, it occurs less frequently because HPT is diagnosed and managed earlier. Typical skeletal findings consist of subperiosteal bone resorption in the phalangeal tufts, absence of lamina dura of the teeth, focal areas of demineralization in the scull and generalized osteoporosis (Keyser & Postma 1996; Bradoo *et al.* 2009). Brown tumors are focal lesions found within these areas of bone resorption. They represent the terminal stage of HPT. In the past, bone lesions as brown tumors were recognized in 80–90% of patients with HPT but the last years these rates have been declined to 15–10% (Triantafillidou *et al.* 2006) or even < 5% (Vera *et al.* 2011). These tumors have been reported to occur in 4.5% of patients with PHPT and in 1.5–1.7% of those with secondary hyperparathyroidism (SHPT) (Keyser & Postma 1996; Giumaraes *et al.* 2006; Etemadi *et al.* 2009). All of our patients demonstrated brown tumors resulting from PTH overproduction by solitary parathyroid adenomas. PHPT is more common among people above 50 years old and is three times more common in women than in men (Daniels 2004; Vera *et al.* 2011). In our patients there were 4 women

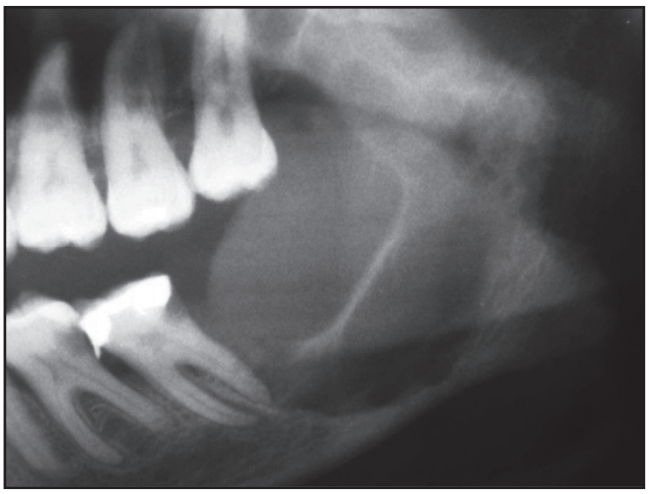

Fig. 1. Part of the panoramic x-ray reveals osteolytic lesion in left mandibular angle with features of expansion and destruction of bone structures.

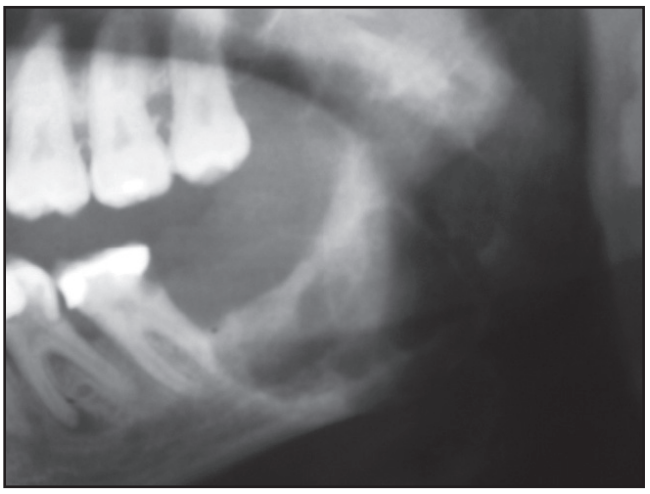

Fig. 2. Part of the panoramic x-ray reveals regress of the tumor mass and signs of the bone rebuilding after excision of parathyroid adenoma.

and one men in ages 32–66 years. Brown tumors most often involve the ribs, clavicles, pelvic girdle and mandible. Mandibular involvement has been reported in 4.5% patients with HPT (Merz *et al.* 2002; Suarez-Cunqueiro *et al.* 2004). Involvement of the maxilla is very rare (Merz *et al.* 2002; Bradoo *et al.* 2009). Among our patients there were 2 with involvement of both maxilla and mandible (patients no 3 and 4) and one (no 5) with involvement of maxillary sinus. Peripheral manifestation of brown tumor in the oral cavity is rare (Giumaraes *et al.* 2006). Intraorally, brown tumors present as painful, hard clearly visible and palpable swelling, they were observed in two out of five our patients. They can be difficult to distinguish histologically or radiographically from other types of giant-cell tumors. True giant-cell tumors are more infiltrative lesions with unknown cause (Moss *et al.* 2001; Curtis & Walker 2005; Park *et al.* 2012). Radiographically brown tumors appear as well-defined lytic lesions of the bone (Fig 1). Oral radiographic manifestations include a generalized loss of lamina dura surrounding the roots of the teeth, loss of cortication around the inferior alveolar canal and maxillary sinus. The radiographic differential diagnostics often includes metastatic disease and multiple myeloma (Rosenberg & Nielsen 2002; Merz *et al.* 2002; Su *et al.* 2010). The practice of checking serum calcium

Tab. 1. Clinical characteristics of patients and their treatment.

No	Age (yrs) sex (F/M)	Location and medical history	Treatment (sequence)	Follow-up
1	32 F	Left mandible. History of PHPT – asymptomatic. Left-side PT adenoma.	Surgical removal of PT adenoma. Removal of mandibular tumor after 6 months.	After 3 years free of the disease, no recurrence of brown tumor.
2	57 F	Right mandible. History of PHPT – nephrolithiasis for 15 yrs. Left-side PT adenoma.	Surgical removal of mandibular tumor. Removal of the left-side PT adenoma after 8 months	2 years later – free of the disease, no recurrence of brown tumor.
3	42 F	Right maxillary sinus. History of PHPT – asymptomatic. Left-lower PT adenoma.	Surgical removal of the left-lower PT adenoma. Removal of maxillary sinus tumor 6 months before	3 years later free of the disease – not follow up now.
4	66 F	Left maxilla and left mandible. History of PHPT – nephrolithiasis for 13 yrs, right nephrectomy because of hydronephrosis, osteoporosis. PT adenoma without MIBI location	Surgical removal of the left-side PT adenoma gland. Removal rest of mandible and maxillary tumors after 12 months	One year after surgery free of the disease.
5	32 M	Right maxilla and right mandible. History of PHPT – nephrolithiasis, nephrocalcinosis. Left-lower PT adenoma.	Surgical removal of the left-lower PT adenoma. Removal of maxillary and mandible tumor after 6 months	One year after surgery free of the disease.

F – female, M – male, PHPT – primary hyperparathyroidism, PT – parathyroid gland

Tab. 2. Laboratory characteristics of patients.

No	Age (yrs) sex	pPTH (pg/ml) N: 11–67	sCa (mmo/l) N: 2.0–2.55	sPh (mmol/l) N: 0.8–1.6	uCa (mmol/24h) N: 2.5–6.0	AP (U/l) N: 100–290	DXA Forearm (ultradist.) T-score	DXA Forearm (1/3 radius) T-score	DXA Lumbar spine(L2–L4) T-score
1	32 F	136	3.0	0.61	8.5	290	–0.66	–1.61	–1.26
2	57 F	158	2.65	0.9	8.2	281	–3.21	–1.62	–1.78
3	42 F	756	3.19	0.65	–	668	–3.16	–3.27	–3.42
4	66 F	674	3.09	0.58	8.0	612	–4.79	–5.47	–
5	32 M	466	3.3	0.5	6.0	277	–1.0	–1.6	–0.6

F – female, M – male, pPTH – plasma pararthyroid hormone, sCa – serum calcium, uCa – urinary calcium, sPh – serum phosphorus, AP – alkaline phosphatase, DXA – dual energy X–ray absorptiometry

on routine blood screens has led to earlier diagnosis of PHPT. It is especially rare for advanced bone disease, such as brown tumor, to present in the absence of other symptoms of hypercalcemia. In our patients the brown tumors were the first diagnosed symptoms of PHPT, they were not suspected as hyperparathyroid having in the past in spite of nephrolithiasis (asymptomatic in one and complicated in two out of five patients) It is therefore necessary to remind practitioners of the possibility of being confronted with advanced PHPT with extensive bone disease – brown tumors.

Increased serum parathyroid hormone levels, hypercalcemia, hypophosphatemia and hypercalciuria demonstrated in all our patients indicated the presence of primary hyperparathyroidism. The bone density assessed by DXA especially in forearm – 1/3 distal radius was decreased in 3 out of our patients (reflecting cortical bone loss, typical for HPT) compared to ultradistal part (trabecular bone) indicated presence of PHPT also (Bolanowski & Pluskiewicz 2002). In women no 2 and no 5, they were postmenopausal, the density in 1/3 distal radius was higher (Table 2). The cause of PHPT in all of cases were sporadic, solitary parathyroid adenomas. All patients underwent a surgical removal of parathyroid gland adenoma. Excised parathyroid tumors showed histological characteristics of adenoma. Treatment of jaws brown tumors is dependent on the evolution of biochemical parameters after excision of parathyroid tumor. In benign parathyroid disease the jaw lesions have been reported to regress spontaneously, partially or completely, after 6 months to 5 years and the patients age is a relevant factor in the duration of the healing (Yamazaki *et al.* 2003; Daniels 2004; Bradoo *et al.* 2009). These observations suggest that surgical intervention is not necessary. Surgical excision of the brown tumors is indicated if the lesion is large and disfiguring or if the affected bone is weakened. We observed partially regression of tumors after parathyroidectomy in our patients (Fig 2 – patient no 1). All patients underwent excision of parathyroid adenoma and after 6–12 months the residual mandibular tumors were excised. Diagnosis of hyperparathyroidism and brown tumor should be considered in any patients with hypercalcemia and destructive bone mass. Bacause the PHPT may be recognized by presence of an osteolytic lesion with giant cells and because the bone osteolytic changes are often suspected as neoplasm we should investigate all giant cell lesions to exclude primary hyperparathyroidism. We should have in mind that osteolytic bone lesions may be due to metabolic disease of the bone. Accurate diagnosis enabling the proper treatment should be carried out, avoiding unnecessary harm to the patients.

Conflict of Interest Disclosure

There is nothing to disclosure

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