CASE REPORT

Parathyroid adenoma diagnosed on the basis of a giant cell tumor of parieto-occipital region and multifocal bone injuries

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Abstract

Brown tumors are rare skeletal manifestations of hyperparathyroidism (HPT) that may mimic cancer metastases. Histopathologically, they are difficult to differentiate from other giant cell lesions. A case is presented of 41-year-old woman with giant cell tumor in parieto-occipital region with injury of external bone lamina, growing into the skull cavity. The mass was suspected of being neoplastic. Numerous osteolytic lesions in the skull skeleton and multifocal bone injuries were observed, also. Elevation in calcium (5.91 mEq/L) and parathormone (1188 ng/mL) concentrations and hypercalciuria (52 mEq/24 h) suggested the diagnosis of HPT initially manifesting as a brown tumor of the skull. Further exploration confirmed the existence of parathyroid adenoma as a cause of the disease. The key treatment for the condition was surgical excision of the adenoma followed by the normalization of parathyroid function and significant reduction in size of skull tumor and other lesions.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is caused by benign or malignant neoplasms of the parathyroid gland, parathyroid hyperplasia or parathyroid cysts. The disease is characterized by hypersecretion of parathormone (PTH) from parathyroid gland(s), which is caused by adenomas in 85% of all cases. It is rarely caused by parathyroid carcinoma. Most cases are identified by hypercalcemia, hypophosphatemia and hypercalciuria in routine multipanel serum testing (Martinez-Gavidia *et al.* 2000; Merz *et al.* 2002; Curtis &Walker 2005; Youanes *et al.* 2005). Less than 5% of PHPT cases are recognized by the presence of brown tumors, histologically indistinguishable from giant cell tumors (GCT) which are the highly vascular lesion. A definitive diagnosis is only possible on comparing the clinical manifestations and radiological and laboratory test results that differentiate the lesions (Merz *et al.* 2002; Suarez-Cunqueiro *et al.* 2004; Etemadi et al 2009; Pawlak *et al.* 2013). The practice of checking serum calcium on routine blood screens has led to earlier diagnosis of PHPT (Bradoo *et al.* 2009; Vera *et al.* 2011). In recent years, it has been recognized that patients

with PHPT may present normal range of plasma calcium concentrations (Emin *et al.* 2004; Vera *et al.* 2011). Brown tumor, also known as generalized osteitis fibrosa cystica comprises only a small percentage of osteolytic bony pathologies. It is caused by hyperparathyroidism which may be primary, secondary or tertiary (Whitaker & Waldron 1993; Curtis & Walker 2005). PHPT due to parathyroid adenoma is one of the leading causes of brown tumor. It is generally accepted that brown tumor is a late manifestation of hyperparathyroid bone disease. It has become increasingly rare to find generalized osteoporosis or osteitis fibrosa cystica with brown tumor as first manifestations. The 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 most commonly the jaws has been reported (Bradoo *et al.* 2009; Yamazaki *et al.* 2003; Ciorba *et al.* 2004; Pawlak *et al.* 2013). Tumors arising in the head and neck region constitute approximately 2% of all GCT with the majority occurring in the sphenoid, ethmoid or temporal bones. Involvement of other bones of the craniomaxillofacial region has been reported including the bones of the orbit or of the sella turcica (Yilmazlar *et al.* 2004).

A case of a brown tumor of parieto-occipital region with numerous osteolytic lesions in the skull and multifocal bone injuries as the presenting symptom of primary hyperparathyroidism is reported.

CASE REPORT

In February 2011, 41-years old woman was operated because of a cyst/tumor of the proximal phalanx of third left digit. The tumor was the result of small trauma, which took place when she was playing with her child. The histopathological diagnosis was the giant cell reparative granuloma. The pathomorfologist suggested determination of serum calcium and phosphorus levels for exclusion of brown tumor because of age of patient and tumor localisation. Examination of serum calcium level was done at that time, and it was within normal range. Then, the woman had a 5-months history of severe headache (from July 2011), nausea, vomiting, vertigo and paraparesis of lower legs from November 2011. Physically, the tumor in parieto-occipital region was present. Computed tomography (CT) showed the presence of an expansive, osteolytic lesion in the parieto-occipito-temporal region $73 \times 52 \times 78$ mm with injury of external bone lamina, growing into the scull cavity and compressing such structures as occipital, parietal and cerebellar right lobes with infiltration of the pyramis of temporal bone. Numerous osteolytic lesions in the skull skeleton were observed also (Figure 1). After one month, in the magnetic resonance imaging (MRI), the diameter of the lesion had grown up to $93 \times 80 \times 45$ mm. The bone mass was suspected being a neoplastic lesion. Right parieto-occipital craniotomy

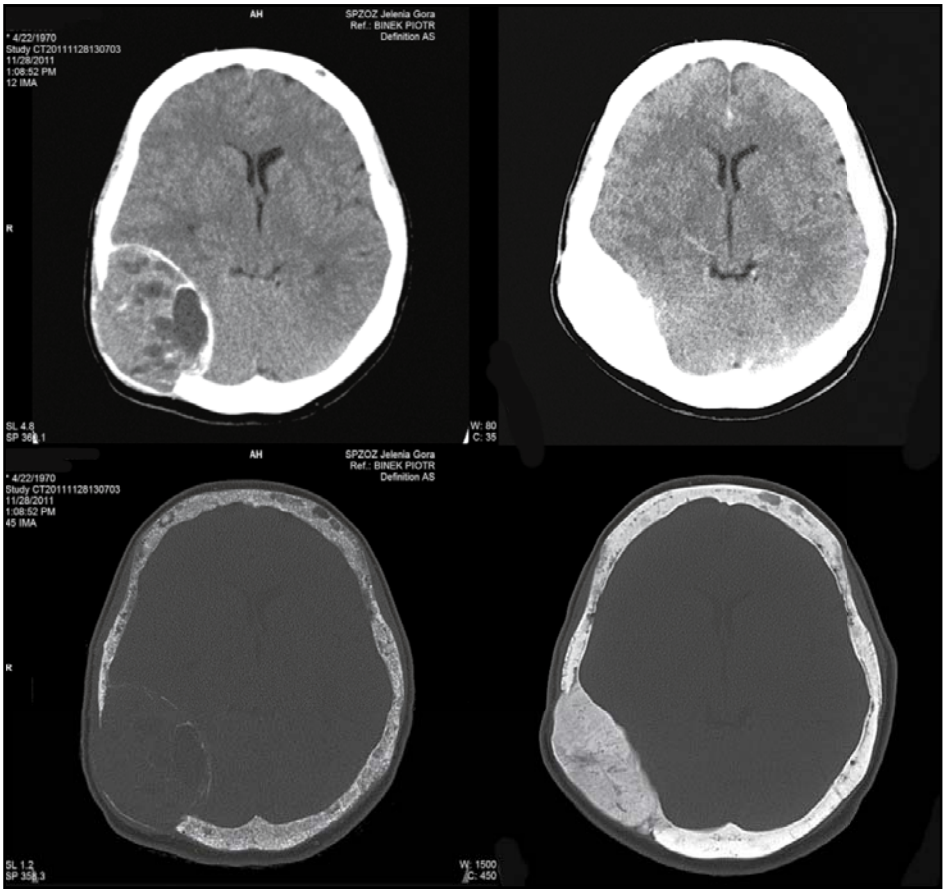

Fig. 1. Brown tumor of the skull with injury of external bone lamina, growing into the skull cavity and compressing neighbouring structures, before and 6 months after parathyroidectomy. Visible numerous osteolytic lesions in the skull skeleton.

Tab. 1. Biochemical parameters before, immediately after surgical treatment of parathyroid adenoma, and one year follow up.

Parameter	before surgery	after surgery	6 mo after surgery	12 mo after surgery	normal ranges
PTH (ng/mL)	1188	9.78	40	60	11–67
serum calcium (mEq/L)	5.91	3.52-4.58	4.54	5.0	4.2–5.15
phosphate (mg/dL)	1.4–1.7	1.15–2.17	3.05	2.9	2.7–4.5
urinary calcium (mEq/24h)	46–52	5.3	23	5.2	5–15
alkaline phosphatase (U/L)	1642	1969	329	167	42–128

Tab. 2. Bone mineral density before surgical treatment of parathyroid adenoma and one year follow up.

Region	Z-score before surgery	Z-score 6 mo after surgery	Z-score 12 mo after surgery	% gain
L2-L4 lumbar spine	(–) 2.42	(–) 1.46	(–) 0.72	34.2
femoral neck	(–) 4.67	(–) 1.21	0.09	171.4
ultradistal forearm	(–) 3.72	(–) 0.91	(–) 0.81	42.1
1/3 radius forearm	(–) 5.38	(–) 3.72	(–) 3.43	44.0

and surgical resection of part of the tumor (because of massive haemorrhage) was undertaken. The diagnosis after histopathology examination was giant cell tumor G1 (tumor gigantocellularis G1). Two weeks after surgery in the end of December 2011, pathological fracture of right femur bone, and then after 2 months pathological fractures of left tibia and ulna occurred. These fractures occurred in The Oncology Center where the patient waited for the palliative radiations due to suspicion of spreading neoplasm process. Then, the patient was admitted to the Orthopedic Department where the fractures were surgically treated. Biochemical investigations showed high plasma parathormone and extremely high serum calcium levels. Patient was referred to our Department with suspected diagnosis of primary hyperparathyroidism. Biochemical evaluation confirmed the diagnosis (Table 1). The patient showed evident signs and symptoms of hypercalcemia: constipation, polydypsia, nausea and vomiting, loss of appetite. An ultrasound of the thyroid showed a 3×3 cm, partially cystic mass at the inferior pole of the left thyroid. Persistent concentration of radiotracer in the inferior aspect of the left thyroid by technetium Tc99m sestamibi scan suggested a left inferior parathyroid adenoma. A bone scan revealed other multiple areas of increased uptake involving the skull (in right parieto-occipital bone where the tumor was located), sternum and both the femurs. Patient was operated and parathyroidectomy and left thyroid lobe excision were undertaken. Pathologic examination of the left inferior parathyroid gland revealed an encapsulated solid and cystic mass 3×2 cm. Based on the pathological and clinical findings a diagnosis of brown tumor secondary to PHPT was made. Postoperatively, the patient recovered without complication but calcium administration because of hungry bones syndrome was needed. Laboratory analysis from both the immediate postoperative period and 6 and 12 months later revealed that patient had attained normal calcium and PTH levels (Table 1). Dual energy X-ray absorptiometry (DXA) performed 6 and 12 months after surgery has shown that the bone mineral density of our patient has markedly improved (Table 2).

DISCUSSION

Primary hyperparathyroidism (PHPT) is caused by solitary adenoma in 80% of the cases and by glandular hyperplasia in about 20%. The diagnosis of PHPT has classically been based on the demonstration of increased serum level of parathormone, hypercalcemia, hypophosphatemia, hypercalciuria and hyperphosphaturia. About 80% of cases of PHPT are diagnosed when a routine assay shows hypercalcemia in patient who is asymptomatic or during evaluation of osteoporosis. In recent years, however, it has been recognized that patients with PHPT may present normal range of plasma calcium concentrations (Emin *et al.* 2004; Meydan *et al.* 2006; Vera *et al.* 2011). Because the disease is commonly diagnosed and treated before bone lesions develop they are nowadays uncommon. Classical skeletal lesions of brown tumor – subperiosteal cortical bone erosions, generalized deossification and local destructive lesions occur in fewer than 3–5% of the PHPT cases and in 1.5–1.7% of those with secondary disease (Etemadi *et al.* 2009; Vera *et al.* 2011). Persistent hyperparathyroidism (HP) leads to altered osseous metabolism involving bone resorption known as oste-

itis fibrosa cystica (OFC). Brown tumor is an extremely rare osseous lesion that constitutes a focal manifestation of OFC induced by HP, independently of its cause. The differential diagnosis of an expansive skull tumor includes metastatic carcinoma, sarcoidosis, fibrous dysplasia or giant cell reparative granuloma (Sanroman *et al.* 2005). In the case of skull tumor with subperiosteal bone resorption, hyperparathyroidism should be considered in the differential diagnosis (Emin *et al.* 2004; Su *et al.* 2010; Park *et al.* 2011). It is especially rare for advanced bone disease, such as brown tumor, to present in the absence of other symptoms of hypercalcemia. Our patient present the giant cell tumor/brown tumor of phalanx and the parieto-occipital region of the skull as the first symptoms of the disease. Clinically brown tumors can manifest as slowly growing, painful masses. Tumors can behave aggressively and be destructive, rarely associated with complications but occasionally may compress neural structures (Yamazaki *et al.* 2003; Yilmazlar *et al.* 2004; Vera *et al.* 2011). The skull tumor in our patient grew into the skull cavity and compressed structures as occipital, parietal and cerebellar right lobes with infiltration of the pyramis of temporal bone. Symptoms depended on the size and location of the lesion. In the other cases, lesions have been asymptomatic, the diagnosis following incidental radiological detection. High serum level of PTH, hypercalcemia and the presence of bone lesions indicate of PHPT in our patient. Diagnosis of HP and brown tumor should be considered in any patient with hypercalcemia and a destructive and expansible bone mass. Due to the radiographic and histologic similarities between brown tumors, reparative granulomas and true giant cell tumors diagnosis of brown tumor relies on finding evidence of HP (Merz *et al.* 2003; Ciorba *et al.* 2004; Sanroman *et al.* 2005). Brown tumors frequently show regression after normocalcemia is achieved what we observed in our case, but surgical resection is necessary in some patients (Martinez-Gavidia *et al.* 2000). The duration of time for bony regeneration varies from several months in young patients to several years in older ones (Vikram *et al.* 2000). In our patient the skull tumor mass distinctly diminished six months after parathyroadenomectomy. This condition was observed after 12 months of surgery equally and surgical treatment was not required. Excision of a parathyroid adenoma normalizes the metabolic state. In our case PTH level returned to normal range just after surgical treatment. After successful ablative parathyroid surgery, hypocalcemia may develop as rapid remineralization of extensive bone destruction occurs. The initial process of demineralization and hypercalcemia caused by high levels of PTH, observed in our patient, suddenly reversed and remineralization proceeds rapidly at the expense of serum calcium. Known as hungry bone disease, this is most likely to occur if bone lesions are present and may produce severe hypocalcemia that requires calcium infusions actually and then chronic treatment with oral calcium and vitamin D. We observed these changes in our patient, she required intensive chronic treatment with calcium and vitamin D in a period of twelve months after surgery. Before surgical treatment the bone density assessed by DXA was decreased especially in femur and forearm – 1/3 distal radius, location were cortical bone predominated. The cortical bone loss is typical for HPT. Poor bone density restored and more than 170% gain in femoral neck and 42–44% gain in forearm was observed (Table 2). Extremely high level of alkaline phosphatase (Table 1) decreased but it is above upper range still now, what shows high bone turnover maintenance.

We report the case of 41-year-old woman with the association of brown tumor and a single parathyroid adenoma, in whom a tumor of cerebri and disseminate neoplasm process was first suspected. The mass, suspected of being neoplastic histopathology, was compatible with a giant cell tumor of bone. The proper diagnosis was reached later despite many clinical manifestations.

Conflict of Interest Disclosure: *there is nothing to disclose.*

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