



A rare cause of primary hyperparathyroidism presented with giant adenoma, multiple brown tumors and end stage renal failure

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Abstract

Single gland adenoma is the most common cause of primary hyperparathyroidism (PHPT). Although PHPT is generally an asymptomatic disease detected by an incidental finding of hypercalcemia, overt skeletal disease, renal failure and huge adenoma that cause local pressure can be seen seldomly in neglected cases. We report a case of a parathyroid adenoma weighing 116 g (normal weight 25 - 40 mgs) causing multiple brown tumors, renal failure and refractory anemia.

Key Words: Giant parathyroid adenoma, primary hyperparathyroidism, brown tumor, chronic renal failure

(Rec.Date: Aug 17, 2013 Accept Date: Sep 17, 2013)

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Introduction

Bone and stone diseases are the most important complications of primary hyperparathyroidism (PHPT). Although clinical parathyroid bone disease and renal failure are rarely seen, nephrolithiasis occurs in approximately 15 to 20 percent of patients with PHPT [1]. The development of renal insufficiency in PHPT is related to the degree and duration of hypercalcemia. PHPT that is commonly caused by a parathyroid adenoma rarely attain huge proportions. We report a patient, previously undiagnosed PHPT presented with an end stage renal disease (ESRD) and multiple brown tumors of the bone, due to a giant parathyroid adenoma with one of the largest mass documented in the literature.

Case report

A 46-year-old woman who had diffuse bone pain was diagnosed as having chronic kidney disease on the basis of laboratory tests (serum creatinine of 2.3 mg/dL, calcium 10.5 mg/dl, phosphorus 2 mg/dL, chloride 103 mg/dL, hemoglobin 9.9 g/dL) in 2006. She was presented with worsening of symptoms in this period, and developed a progressive paraplegia. She used to use a wheel chair for ambulating. A platin on femur head was placed in 2007 for closed femoral shaft fracture. In 2008, she had a complaint of pain in her left arm and right leg without a history of trauma. The radiographs showed marked pathologic fracture of the proximal femur and humerus. In January 2009, hemodialysis treatment had been started in another hospital because of ESRD. She was referred to our clinic for the evaluation of weakness in the lower limbs and diffuse pain and tenderness in bones in April 2009.



Figure 1. Physical examination revealed a large retrosternal goiter and muscle strength of lower extremity 1 out of 5.

She was confinement to her bed. Laboratory tests showed serum creatinine 2.7 mg/dL, calcium 9.9 mg/dL, phosphorus 6.6 mg/dL, chloride 107 mEq/L, albumin 3.5 g/dL, 25-OH-vitamin D3 12 ng/mL and intact parathyroid hormone (PTH) 4583 pg/mL. She had a normochromic normocytic anemia (hemoglobin 7.2 g/dL and ferritin 1200 mg/dL) despite treatment with 150 U/kg erythropoietin alpha. Bone mineral density measured by dual x-ray absorptiometry was indicated a marked reduction in bone mass at the lumbar spine (L1-L4) with total T score of -6. Radiographs of the hands showed a radiolucency in accordance with osteoporosis and subperiosteal bone resorption in her 3rd middle phalanx. Radial and ulnar bones had prominent cortical thinning. Radiographs of the skull showed profound osteopenia with numerous patchy lesion that filled the distance of diploe. Radiographs of the hips and pelvis showed the presence of orthopedic hardware in the right femoral neck.



Figure 2. Computed tomography (CT) of spine revealed an expansive osteolytic lesion and 3.5x 4cm mass in accordance with a brown tumor at the level of thoracal vertebra (T9) compressing spinal canal and neural foramen.

CT of the abdomen revealed kidney stones in both kidneys, and a small left kidney consistent with scarring. CT of the neck region showed 8.5x6x6.5 cm mass lesion on the left thyroid area compressing vascular structures and trachea with retrosternal spreading.

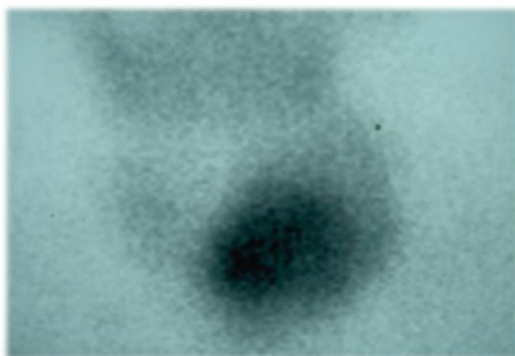


Figure 3. Parathyroid ^{99m}Tc-sestamibi (MIBI) scintigraphy revealed a solitary nodule with a delayed radiopharmaceutical wash-out at the left pole of the thyroid gland.

She got the diagnosis of PHPT due to single parathyroid adenoma. The patient underwent surgery and the large neck mass was resected. The mass was measuring 10 cm and weighing 116 gr.



Figure 4. Pathology showed a benign parathyroid adenoma.

Postoperatively, the serum calcium level was decreased to 5.4 mg/dL and the PTH to 6 pg/mL. She was treated with intravenous calcium gluconate and with calcitriol at the dose of 1 µg/day. Ten days after parathyroidectomy, serum calcium was 8 mg/dL on average, and she was discharged on 3 gr supplemental oral calcium and 1 µg/day active vitamin D3 with chronic dialysis programme. In December 2009, she admitted to our University's Infectious Diseases department due to high fever. Unfortunately, she died because of disseminated urogenital infection that did not respond to medical treatment.

Discussion

There is a great variation in the manifestations of PHPT. The most common clinical presentation of PHPT is asymptomatic hypercalcemia with an elevated or high-normal intact parathormon level, although the presentation may sometimes be atypical. Parathyroid adenomas are rarely palpable. The mass effect of adenoma on neck region was prominent in our patient. The diagnosis of PHPT was delayed because of serum PTH level was not measured until she admitted to our outpatient clinic. Nowadays, the diagnosis is frequently made in the early phase of the disease with screening tests. In our patient, it was not easy to distinguish whether the hyperparathyroidism was primary or secondary to chronic renal failure. Secondary hyperparathyroidism (SHPT) generally is seen in long-standing ESRD patients. Several factors contribute to SHPT including increased phosphorus retention causing decreased calcium, bone

resistance to PTH, malabsorption of calcium in the gut, and inhibition of $1,25(\text{OH})_2\text{D}$ production by increased phosphorous [2]. The short duration of dialysis, presence of an extremely high level of intact PTH, severe bone and kidney diseases may be attributable to PHPT. Additionally, her first laboratory tests were more consistent with PHPT (chloride/phosphate ratio, hypercalcemia and hypophosphatemia in the presence of renal failure). The chloride-to-phosphate ratio is a good marker of PHPT especially when it is above 33 [3], as in our patient. Furthermore, localization of adenoma in our patient at the lower pole of the gland supported the diagnosis of PHPT [2]. A recent study examined the weights of 34 histologically normal parathyroid glands that were removed from 29 patients with PHPT [4]. The average weights of normal glands and adenomas were 62.4 ± 31.6 mg (range: 18-161 mg, 15 weighed ≥ 60 mg) and 553.7 ± 520.5 mg (range: 66-2536 mg), respectively. Although the usual weight of a parathyroid adenoma ranges from 70 mg to 1 g, it has been reported giant parathyroid adenomas weighing 70 g and 110 g in the literature [5,6]. While a 56-year-old woman with resected tumor which weighed approximately 70 g presented hip joint pain and gait disturbance [5], another 85-year-old woman had an anterior neck swelling, intermittent dysphagia and sporadic episodes of dyspnea on exertion with moderately elevated PTH (138.5 ng/L) and calcium (12.8 mg/dL) [6]. In the latter case, the low PTH level was explained with the major proportion of this enlarged gland was probably underactive because of its substantial cystic component and reduced cellularity [6]. In our patient, since the rest of the parathyroid glands seemed to be normal and PTH level decreased rapidly to 1077 pg/mL intraoperatively and 87.6 pg/mL postoperatively after the resection, we thought that this situation was due to a solitary adenoma. Our patient may have more than one condition leading to increased PTH secretion and huge adenoma. Since vitamin D insufficiency is not uncommon in our region, it is possible that it may affect the clinical presentation of our patient. If PHPT and vitamin D deficiency co-exists [7], the serum calcium levels may be within the normal range due to vitamin D deficiency which could be the case in our patient.

Hyperparathyroidism results in disorders of bone and mineral metabolism. Diffuse and focal lesions may arise in multiple bones. The skeletal effects include massive bone resorption, bone fractures, and bone pain, as well as diffuse osteopenia, or circumscribed lytic lesions. Brown tumors commonly occur in the mandible, maxillary sinus, sternum, pelvis and femur. PHPT is known to be a more frequent etiologic factor than the SHPT in the development of brown

tumors. The tumors may be asymptomatic or cause pain and/or fractures depending their sizes and locations. Only a few cases of spinal brown tumor have been reported in the literature[8, 9]. A history of multiple fractures in different bones and distributions of brown tumors in different parts of the skeleton in our patient as seen generally in long-standing PHPT cases [2]. Also her marked bone loss could be a sign of the severity of hyperparathyroidism.

The most important renal manifestations of PHPT are nephrolithiasis, hypercalciuria, several abnormalities in renal tubular function, nephrocalcinosis and chronic renal insufficiency[10]. Among normocalcemic patients with nephrolithiasis, PHPT should be suspected if the serum calcium concentration is in the high-normal range, because hypercalcemia may be intermittent and detected only by multiple measurements. SHPT is usually asymptomatic during the predialysis period or soon after the start of dialysis. Severe bone changes, both radiologic and histologic, necessitating a parathyroidectomy are often found in patients who have been on longterm dialysis for over 10 years. Mizumoto et al [11] reported 5 patients with PHPT and ESRD. In a 79-year-old Japanese woman who had PHPT with ESRD and severe bone changes including multiple fractures of the pelvic bones and lumbar spine, osteoporosis, and subperiosteal bone resorption, histomorphometric analysis of the cancellous bone indicated a diagnosis of osteitis fibrosa [12]. After total parathyroidectomy, her pain subsided completely. It is known that when a patient with PHPT develops renal insufficiency, bone changes can progress rapidly, even during the predialysis period.

In conclusion, we reported an unusual case of severe PHPT originated from a huge single adenoma associated with multiple brown tumors one atypically located in the lumbar spine leading to compression symptoms and ESRD.

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