

## Case Report

# Huge juxtacortical brown tumor in two patients with secondary hyper-parathyroidism due to chronic renal failure

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**Abstract:** The brown tumor of the skeletal system is mainly caused by hyperparathyroidism (HPT), and HPT is divided into three categories according to its causes: primary, secondary and tertiary HPT. The secondary HPT patients with brown tumor caused by chronic renal insufficiency are rarely reported. The tumor occurs mostly in the bones such as metacarpals, phalanges, skull, pelvis, clavicle, ribs, femur and spine. We reported two cases of juxtacortical brown tumor in patients with HPT secondary to chronic renal insufficiency which has never been reported previously.

**Keywords:** Hyperparathyroidism, brown tumor

### Introduction

Brown tumor is due to various reasons lead to local osteolysis absorption, replaced by fibrous tissue hyperplasia and reparative granulation tissue containing giant multinucleated cells. The main reason is hyperparathyroidism (HPT). Parathyroid hormone (PTH) secretion is mainly regulated by the concentration of plasma Calcium. Chronic renal failure with hypocalcemia leads to increased secretion of parathyroid. This will break the bone osteoblast and osteoclast balance, and increase osteoclast activity.

### Report of two cases

Patient 1 was a 37-year-old male. He received hemodialysis for 3 years, twice weekly, for end stage renal disease (ESRD). A gradually enlarging mass was present in the lateral side of left shoulder joint for 10 months. It was 11 cm in diameter, had bone-like density and painless at palpation, and was covered with normal skin. The results from blood tests are shown in **Table 1**.

Plain film and spiral computed-tomography of the left shoulder joint and humerus without amplification showed a huge mass with bone-

like density close to the proximal humerus. It was 10×11 cm, and there were multilocular cystic areas with low density in the mass and the capsule had a high density (**Figure 1**).

Surgical treatment was performed under general anaesthesia. A defined ovoid mass was raised from the thinned cortical bone plate and the underlying soft tissues. Although there was mild bleeding, the porous surface was separated from the proximal humerus. The surgical wound closed favorably after surgery. Histological findings showed fibrous and bone tissues with cystic and degenerative changes, multinucleated giant cells and bleeding (**Figure 2**).

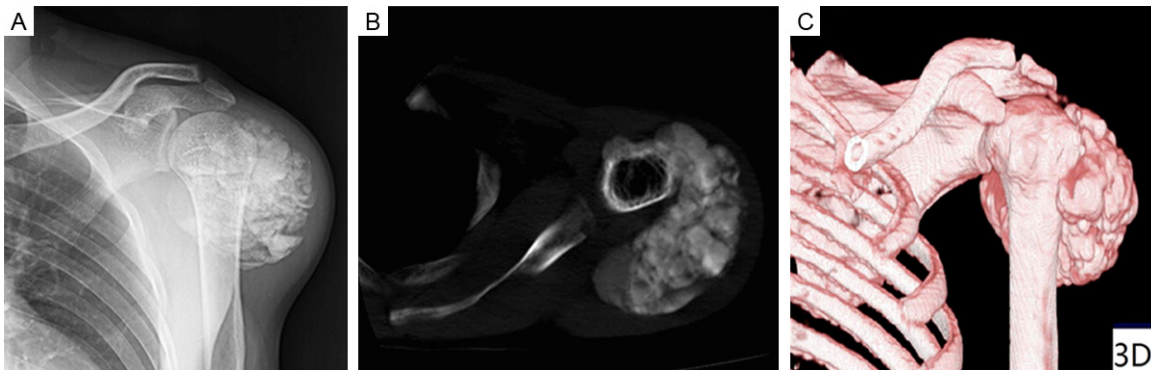
Patient 2 was a 54-year old male. He received hemodialysis due to ESRD for 2 years thrice weekly. A gradually enlarging mass was present in the anterior side of the right pubis for 8 months. Local examination showed the mass had bone-like density and pain at palpation, and was covered with brown skin.

CT and MR of the pubis showed the right pubis had been destroyed, a huge mass with bone-like density was connected to the right pubis with a thin neck and it was 10×11 cm. There were multilocular cystic areas with low density

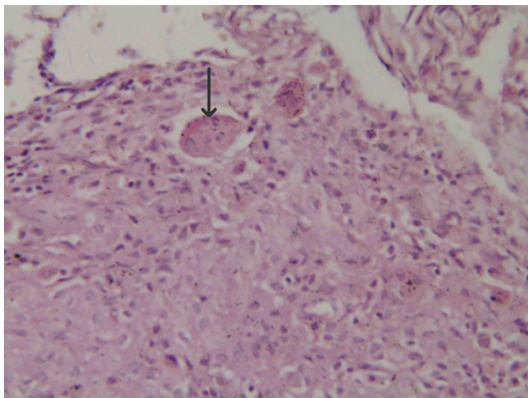
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**Table 1.** Abnormal findings from blood tests

Variables	Patient 1	Patient 2	Normal range	
			Males	Females
Hemoglobin	109 g/L	117 g/L	140-180 g/L	120-160 g/L
Red blood cells	$3.25 \times 10^{12}/L$	$3.57 \times 10^{12}/L$	$4.5-6.0 \times 10^{12}/L$	$3.9-5.3 \times 10^{12}/L$
Urea	9.7 mmol/L	14.9 mmol/L	3.2-8.2 mmol/L	2.6-7.2 mmol/L
Creatinine	459 $\mu\text{mol}/L$	305 $\mu\text{mol}/L$	74-134 $\mu\text{mol}/L$	44-96 $\mu\text{mol}/L$
Alkaline phosphatase	1213 U/L	2297 U/L	98-279 U/L	
Intact Parathormone	2051 pg/ml	1537 pg/ml	12-88 pg/mL	



**Figure 1.** A: Plain film of the left shoulder joint and humerus; B: Spiral computed-tomography scan-bone window; C: 3D reconstruction.



**Figure 2.** Histology showed fibrous and bone tissues with cystic and degenerative changes, multinucleated giant cells (black arrow) and bleeding.

in the mass and the capsule had a high density (**Figure 3**). The results from blood tests are shown in **Table 1**.

## Discussion

ESRD patients often develop injured exocrine and endocrine function of the kidney, which results in decreased 1, 25-dihydroxyvitamin D

synthesis in the kidney leading to a decreased calcium absorption by the gut. Consequently, an increase in serum phosphate is present. Phosphate is a driving force of bone mineralization, and excess phosphate tends to cause the deposition of serum calcium in bones, leading to a decrease in serum calcium and structural deficit in bones. In response to low serum calcium, the parathyroid glands are stimulated to secrete parathyroid hormone (PTH), resulting in secondary HPT [1]. Thus, the patients become hypocalcemic and hyperphosphatemic.

Primary HPT is caused by the hypersecretion of PTH, usually due to hyperplastic or tumoral changes in one of four parathyroid glands. This may cause hypercalcemia. Secondary HPT is usually caused by ESRD which may cause renal loss of calcium. In the presence of normal parathyroid glands, elevation of PTH occurs in response to the hypocalcemia. Tertiary HPT often occurs in patients with longstanding secondary diseases, as hyperplasia of parathyroid glands and loss of response to the serum calcium. PTH (parathyrin) exerts significant effects to maintain the optimal calcium concentration. PTH can raise the serum calcium through direct

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**Figure 3.** Plain film of CT and MR scanning of the pubis showed the right pubis had been destroyed and a huge mass with bone-like density was connected to the right pubis with a thin neck, the mass was 10×11 cm, there were multilocular cystic areas with low density in the mass and the capsule had a high density. A: Plain film; B: CT-soft tissue window; C: Bone window; D: FSE-T2WI.

action on the bone and kidneys: it increases the rate of calcium flowing from the bone to the extracellular fluid, and elevates both the renal tubular reabsorption of calcium and the renal excretion of phosphate. Calcium exerts a negative feedback effect on the PTH secretion. Chronic renal insufficiency in patients with hypocalcemia, hyperphosphatemia and 1,25 (OH) 2D3 deficiency may lead to increase in PTH secretion. Chronic kidney failure (CKF) and consequently chronic hyperparathyroidism are more prevalent [2-4].

Brown tumors are unusual bone lesions that represent a localized manifestation of osteitis fibrosa cystica (OFC) induced by hyperparathyroidism, regardless of its causes. Increased

PTH level and locally produced tumor necrosis factor  $\alpha$  and interleukin 1 (IL-1) by marrow monocytes may induce the proliferation and differentiation of pluripotent bone-marrow cells into osteoblasts. These cells secrete granulocyte macrophage colony stimulating factors, IL-6, IL-11 and stem cell factors which induce the migration and differentiation of monocytes into osteoclasts, thus increase the osteoclasts in bones. Enhanced activity of osteoclasts and osteoblasts leads to bone resorption and a reduction in bone mineral density with an increase in fibrous tissues and extracellular matrix [5]. Brown tumors are present in 3% to 4% of patients with primary hyperparathyroidism and in 1.5% to 1.7% of patients with secondary causes of hyperparathyroidism [6].

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However, around half of patients with CKF may develop OFC due to secondary HPT making brown tumors more common in these patients.

The radiographic findings of brown tumor are generalized osteoporosis; subperiosteal cortical bone resorption and cystic change (important signs of this disease); bone sclerosis and extraskeletal calcification. X-ray characteristics of bone pathology in renal osteodystrophy are associated with demineralization, loss of lamina dura, and trabecular pattern with a "ground-glass" appearance.

Clinically, patients with renal insufficiency complicated with SHPT disease may present pain, proximal muscle weakness, skin itching, ectopic calcification, and increased risk of fracture. The biochemical indexes include serum calcium concentration (decreased or normal), blood phosphorus concentration, blood iPTH level (increased).

### Conclusion

CRF is a kind of complicated refractory clinical syndrome. It can induce a series of pathological and physiological changes (such as HPT) and has several manifestations that can be identified in clinical and radiographic exams. Clinicians should be aware of the clinical manifestations and radiographic appearances of these lesions to avoid the misdiagnosis and improve the prognosis of these patients.

### Disclosure of conflict of interest

None.

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