

## BROWN TUMOR – A RARE MANIFESTATION OF RENAL OSTEODYSTROPHY AND SEVERE SECONDARY HYPERPARATHYROIDISM: CASE REPORT

Neven Baršić<sup>1</sup>, Krešimir Čala<sup>†2</sup> and Draško Pavlović<sup>2</sup>

<sup>1</sup>Department of Gastroenterology, <sup>2</sup>Department of Nephrology and Dialysis, University Department of Medicine, Sestre milosrdnice University Hospital, Zagreb, Croatia

**SUMMARY** – Multifactorial disorders in mineral metabolism and bone structure occur early in the course of chronic kidney disease. The new term of ‘chronic kidney disease – mineral and bone disorders’ has been used to encompass a broad syndrome in which various abnormalities in bone and mineral metabolism are present in patients with chronic kidney disease. Brown tumors are an uncommon type of bone lesions that represent a focal manifestation of high-turnover bone disease. In our report, we describe a patient with chronic kidney disease on chronic hemodialysis that presented with multiple osseous lesions of the right elbow, right scapula and ribs. This case illustrates the importance of taking brown tumor in consideration in differential diagnosis and management of patients with an osseous mass and chronic kidney disease, where a failure to establish an accurate diagnosis can lead to unnecessary further diagnostic procedures and even extensive surgery, increasing the morbidity of these patients. Prevention, early diagnosis and treatment of secondary hyperparathyroidism are important in reducing the prevalence of high-turnover bone disease and consequential bone lesions including brown tumors.

**Key words:** *Renal osteodystrophy – diagnosis; Renal osteodystrophy – complications; Hyperparathyroidism, secondary – diagnosis; Hyperparathyroidism, secondary – prevention; Hyperparathyroidism, secondary – therapy; Case Report*

### Introduction

Multifactorial disorders in mineral metabolism and bone structure occur early in the course of chronic kidney disease. These changes worsen with the progressive course of kidney dysfunction. Since recently, the new term of ‘chronic kidney disease – mineral and bone disorders’ (CKD-MBD) has been used to encompass a broad syndrome in which various abnormalities in bone and mineral metabolism including renal osteodystrophy and extraosseous calcifications

are present in patients with chronic kidney disease<sup>1</sup>. Secondary hyperparathyroidism can be found in over 50% of patients on hemodialysis, and it is associated with significant morbidity<sup>2</sup>. One of the forms of renal osteodystrophy is the high-turnover bone disease (osteitis fibrosa cystica), which is the result of changes in bone metabolism induced by secondary hyperparathyroidism. Secondary hyperparathyroidism is initially present early in the course of chronic kidney disease (often when glomerular filtration rate declines to less than 60 mL/min), and becomes more severe with further deterioration of the renal function, as the result of progressive phosphate retention, decreased calcitriol levels, and hypocalcemia.

Secondary hyperparathyroidism and high-turnover bone disease are radiographically characterized by several types of bone lesions, including subpe-

Correspondence to: *Neven Baršić, MD*, Department of Gastroenterology, University Department of Medicine, Sestre milosrdnice University Hospital, Vinogradska c. 29, HR-10000 Zagreb, Croatia

E-mail: [neven.barsic@gmail.com](mailto:neven.barsic@gmail.com)

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riosteal bone resorption, trabecular bone resorption (giving 'salt and pepper' appearance to the skull), osteosclerosis (resulting in 'rugger jersey spine sign'), bone deformities and fragility fractures<sup>3</sup>.

Brown tumors are an uncommon type of bone lesions that represent a focal manifestation of high-turnover bone disease and a reparative cellular process rather than a neoplastic one. They usually present as unifocal or multifocal well-defined purely lytic bone lesions resulting from rapid osteoclastic activity and peritrabecular fibrosis. Hemorrhages, with accumulation of hemosiderin within the vascularized fibrous tissue, are common and give the lesion its reddish-brown color.

Brown tumors occur in patients with primary hyperparathyroidism with a slightly higher incidence, although most of the cases of primary hyperparathyroidism seen today are diagnosed and managed early in the course of disease, prior to the development of significant bone abnormalities. Because of this and since secondary hyperparathyroidism is much more common than primary, most brown tumors are associated with secondary hyperparathyroidism.

In our report, we present a case of a patient with chronic kidney disease and multiple osseous lesions of the right elbow, right scapula and ribs.

## Case Report

A 60-year-old female patient was admitted to our ward due to persistent cough, occasional dyspnea, and



Fig. 1. Swelling of the right elbow on admission.

pain in her right elbow and shoulder. She also complained of paresthesias in the right hand and noticed a limited motion range and swelling of the right elbow (Fig. 1). Radiograph of the right elbow performed outpatiently prior to hospitalization showed a large cystic formation with destruction of distal humerus (Fig. 2).

The patient had a history of hypertension and chronic renal failure, most probably as the result of hypertensive kidney disease. For the last eight years, she had been on chronic hemodialysis. She was regularly taking antihypertensive therapy, a loop diuretic, analgesics and a phosphate binder sevelamer hydrochloride; she also received epoetin. Elevated parathyroid hormone (PTH) levels were present for more than five years, although the patient was on calcitriol *per os* and paricalcitol *i.v.* for the last six months. Parathyroidectomy was suggested to the patient but she repeatedly refused operative therapy.

Upon admission to the hospital, initial work-up excluded congestive heart failure, pneumonia or other respiratory and heart disorders as the potential cause of cough and dyspnea. In addition to well corrected secondary anemia (hemoglobin levels 109 g/L, normal range 119-157 g/L) and moderately elevated erythrocyte sedimentation rate (65 mm/h, normal range 5-28 mm/3.6 ks), laboratory findings revealed severe secondary hyperparathyroidism with significantly elevated parathyroid hormone level (1779 pg/mL, normal range 15-65 pg/mL), phosphate level (1.50 mmol/L, normal range 0.79-1.42 mmol/L), calcium level 2.47 mmol/L (normal range 2.14-2.53 mmol/L), and el-

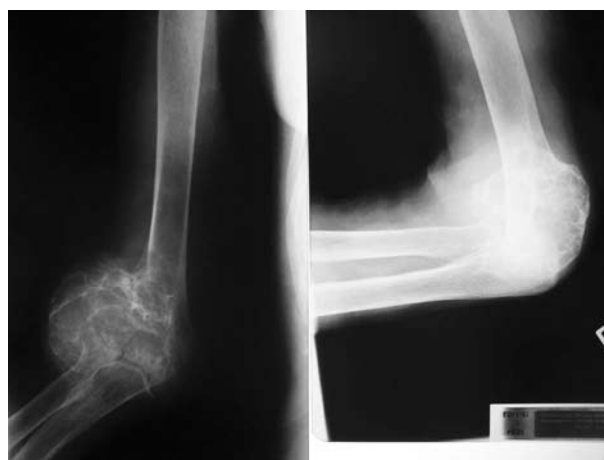


Fig. 2. Radiograph of the right elbow showing a large cystic formation with destruction of distal humerus.



Fig. 3. Chest radiograph showing two masses radiologically characterized as potential metastatic lesions of the ribs or lung parenchyma adjacent to the chest wall.

evated alkaline phosphatase (259 IU/L, normal range 64-153 U/L 37 °C). Chest radiograph revealed two masses, one on each side of the chest, that were radiologically characterized as potential metastatic lesions of the ribs or lung parenchyma adjacent to the chest wall (Fig. 3). Computed tomography scan showed expansive lytic lesions of the 5<sup>th</sup> right rib and 6<sup>th</sup> left rib,



Fig. 4. Computed tomography scan showing expansive lytic lesions of the ribs and a similar lesion of the right scapula.

5 cm and 3 cm in size, and a similar smaller lesion of the right scapula (Fig. 4). Bone scintigraphy was included in the work-up and revealed multiple hypermetabolic lesions at the sites that corresponded to the previously described locations of bone masses (Fig. 5).

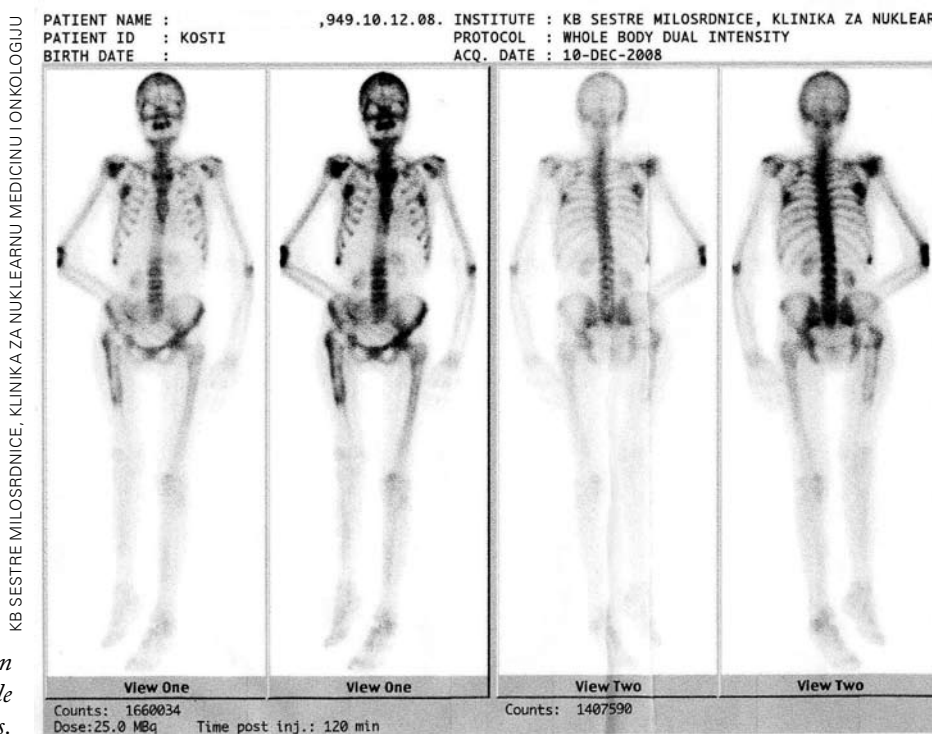


Fig. 5. Full skeleton scintigraphy revealing multiple hypermetabolic lesions.

In order to exclude malignancy, biopsy of the right rib lesion was finally obtained and analysis revealed multinucleated giant cells and reactive fibrous tissue, with no signs of malignancy.

Based on the patient presentation, clinical context and results of the extensive work-up, a diagnosis of multiple brown tumors secondary to renal osteodystrophy and high-turnover bone disease was made, and the patient was discharged from the hospital. During hospitalization and before the time of discharge, almost all of the patient's symptoms had partially regressed. On follow-up, she maintained very high parathyroid hormone levels despite optimal treatment with calcitriol or paricalcitol and phosphate binder sevelamer hydrochloride, and reduced phosphate intake, suggesting the development of parathyroid gland autonomy, i.e. tertiary hyperparathyroidism. Parathyroidectomy was considered, but was not performed due to the patient's preference and general condition. Brown tumors persisted on subsequent follow-ups, although no significant further growth of the lesions was observed.

## Discussion

Renal osteodystrophy as part of the CKD-MBD is one of the most important complications of chronic kidney disease. It represents a spectrum of skeletal disorders ranging from high-turnover bone disease, predominantly due to PTH excess, to low-turnover bone disease very often associated with reduced PTH levels. In both forms, high and low turnover bone disease, soft tissue calcification could be observed<sup>4,5</sup>. Due to persistently high PTH levels in high-turnover bone disease, increased numbers of osteoclasts, osteoblasts and osteocytes are found. Increased bone resorption, accumulation of fibrous tissue within the marrow space and cystic lesions (osteitis fibrosa cystica) are the most common high turnover lesions of renal osteodystrophy<sup>6</sup>.

Brown tumors represent a reparative bone process rather than true neoplasia. They result from localized replacement of normal marrow with reparative granulation tissue and highly vascular proliferating fibrous tissue in the areas of bone where increased parathormone levels lead to particularly rapid osteoclastic bone turnover<sup>7</sup>. Brown tumors are usually painless, slowly

growing masses that are discovered incidentally, but they can cause pathological fractures, compressive syndromes due to nerve or spinal cord compression<sup>8</sup>, difficulties in breathing, eating and phonation, or face deformation<sup>9,10</sup>. Radiologically, they present as well-defined lytic bone lesions with thinned cortical bone without cortex disruption or periosteal reaction. Most common locations of brown tumors are the pelvis, ribs, clavicles, mandible and extremities<sup>3</sup>. In most cases, histopathologic analysis of the lesion is performed in order to confirm the diagnosis. Histology usually reveals numerous multinucleated giant cells, dense fibroblasts and fibrous tissue, osteoid, hemosiderin deposits within macrophages, small microhemorrhages, and areas of cystic degeneration and necrosis<sup>11</sup>. Hemorrhages and hemosiderin confer the characteristic color of the lesion. Histologic differentiation between brown tumor and other lesions that share similar features like giant-cell tumors, reparative granulomas, fibrous dysplasia or giant-cell granulomas can be very difficult. Definitive diagnosis is therefore usually established only by consideration of all clinical, laboratory, radiologic and histologic data, as in our patient. Bone scintigraphy is not necessary in diagnostic work-up, but if done it reveals isolated hypermetabolic lesions. We performed bone scintigraphy in our patient to further characterize the lesions and to exclude bone lesions in other locations.

Treatment of brown tumors consists of the treatment of secondary hyperparathyroidism, which includes prevention and treatment of hyperphosphatemia and administration of vitamin D analogs and calcimimetic agent. In refractory cases in which tertiary hyperparathyroidism develops, parathyroidectomy may be necessary. With the fall in PTH levels, cessation of tumor growth and reduction in lesion size is observed, with subsequent ossification and no further complications. Parathyroidectomy was considered in our patient, but was postponed and eventually abandoned due to the patient's condition and preferences. Surgical extirpation of brown tumor may be required in patients with tumors causing compressive neurological syndromes, high risk of fracture, significant deformity impeding normal functions such as mastication or breathing, or persistence of pain or other symptoms despite adequate hyperparathyroidism control. In our patient, brown tumors caused no significant function-

al impairment except for the somewhat limited motion range in the elbow. Furthermore, occasional paresthesias in the hand that were probably the result of nerve compression were not severe enough to warrant surgery. Mild pain caused directly by the presence of tumor mass was adequately regulated with low-dose combined analgesic therapy.

Our case illustrates the importance of brown tumor consideration in differential diagnosis and management of patients with an osseous mass and chronic kidney disease, where failure to establish the correct diagnosis can lead to unnecessary further diagnostic procedures and even extensive surgery, increasing the morbidity of these patients<sup>12</sup>. Prevention, early diagnosis and treatment of secondary hyperparathyroidism are important in reducing the prevalence of high-turnover bone disease and consequential bone lesions including brown tumors<sup>13</sup>.

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## Sažetak

### SMEDI TUMOR – RIJETKA MANIFESTACIJA BUBREŽNE OSTEODISTROFIJE I TEŠKOG SEKUNDARNOG HIPERPARATIROIDIZMA: PRIKAZ SLUČAJA

*N. Baršić, K. Čala<sup>†</sup> i D. Pavlović*

Multifaktorijski poremećaji mineralnog metabolizma i koštane strukture javljaju se rano u razvoju kronične bubrežne bolesti. Novi pojam „kronična bubrežna bolest – mineralni i koštani poremećaji“ rabi se kako bi obuhvatio širok sindrom različitih abnormalnosti mineralnog i koštanog metabolizma koje nalazimo kod bolesnika s kroničnom bubrežnom bolešću. Smeđi tumori su rijetki koštani poremećaji koji predstavljaju žarišnu manifestaciju bolesti prekomjerne koštane pregradnje. Prikazan je slučaj bolesnice s kroničnom bubrežnom bolešću na programu kronične hemodijalize, koja je primljena s višestrukim koštanim lezijama u području desnog lakta, desne lopatice i rebra. Rad ukazuje na važnost razmatranja smeđeg tumora u diferencijalnoj dijagnostici bolesnika s koštanim masama i kroničnom bubrežnom bolešću, kada propust u postavljanju ispravne dijagnoze može dovesti do nepotrebnih dodatnih dijagnostičkih postupaka, pa čak i do opsežnih operativnih zahvata, povećavajući tako pobol. Prevencija, rana dijagnostika i liječenje sekundarnog hiperparatiroidizma je važno za smanjivanje učestalosti bolesti pretjerane koštane pregradnje i posljedičnih koštanih bolesti uključujući smeđi tumor.

*Ključne riječi: Bubrežna osteodistrofija – dijagnostika; Bubrežna osteodistrofija – komplikacije; Hiperparatiroidizam, sekundarni – dijagnostika; Hiperparatiroidizam, sekundarni – prevencija; Hiperparatiroidizam, sekundarni – terapija; Prikaz slučaja*