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A case of brown tumor mimicking fibrous dysplasia in a patient with chronic renal failure

Kronik böbrek yetersizliği olan bir hastada fibröz displaziye benzeyen kahverengi (brown) tümör

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Renal osteodistrofi, böbrek yetersizliği nedeniyle uzun süre diyalize giren hastalarda ve transplantasyon sonrasında morbiditenin en önemli nedenlerinden biridir. Klinik olarak yüksek döngülü kemik hastalığı, düşük döngülü kemik hastalığı, osteomalazi, osteoskleroz ve osteoporoz görülebilir. Renal yetersizlik nedeniyle diyaliz tedavisi görmekte olan 13 yaşında bir erkek çocuğu, hafif travma sonrası gelişen patolojik sol suprakondiler femur kırığı ile başvurdu. Radyolojik incelemelerde suprakondiler femurda, sol asetabulum tavanı ve sağ tibia proksimal ve distal bölgelerinde kistik kitleler görüldü. Lezyonların radyolojik görüntüleri ve sağ tibia distalinden çıkarılan lezyonun histopatolojik özellikleri göz önüne alınarak, ayırıcı tanıda kahverengi (brown) tümör ve fibröz displazi düşünüldü. Hastanın ilk serum paratiroid hormon düzeyi hafif yüksek, kalsiyum düzeyi normaldi. Takiplerinde serum paratiroid hormon düzeyi belirgin yükselme gösterdi. Böylece, hastaya kahverengi tümör tanısı kondu.

Anahtar sözcükler: Kemik neoplazileri/patoloji/radyografi; tanı, ayırıcı; hiperparatiroidizm, sekonder/komplikasyon; böbrek yetersizliği, kronik/komplikasyon; paratiroid neoplazileri/tanı; renal osteodistrofi.

Renal osteodystrophy is one of the major causes of morbidity in patients receiving long-term dialysis treatment for renal failure and after transplantation. Its clinical implications include high-turnover bone disease, low-turnover bone disease, osteomalacia, osteosclerosis, and osteoporosis. A 13-year-old boy who had been on dialysis treatment for renal failure was admitted with a pathologic supracondylar femur fracture after a minor trauma. Radiological studies showed cystic lesions in the femoral supracondyle, left acetabular roof, and right proximal and distal tibia. Based on radiologic appearances of the lesions and on histopathologic findings of the lesion excised from the right distal tibia, brown tumor and fibrous dysplasia were considered in the differential diagnosis. Initially, serum parathyroid hormone level was slightly increased and calcium level was normal, but during follow-up, serum parathyroid hormone level increased significantly, enabling the diagnosis of brown tumor.

Key words: Bone neoplasms/pathology/radiography; diagnosis, differential; hyperparathyroidism, secondary/complications; kidney failure, chronic/complications; parathyroid neoplasms/diagnosis; renal osteodystrophy.

One of the major causes of morbidity in chronic renal failure patients is metabolic bone diseases. In this disorder, also known as osteodystrophy, clinical indications are high-turnover bone disease, low-turnover bone disease, osteomalacia, osteosclerosis, and osteoporosis. Due to secondary hyperparathyroidism, osteit fibrosa cystica and brown tumors may also be encountered.[1]

Osteit fibrosa cystica is characterized by widespread osteopenia, increased bone resorption and cysts or cyst-like areas called brown tumor or osteoclastoma.[2,3] Osteit fibrosa cystica is the indication of hyperparathyroidism and is seen in varying degrees in approximately 50% of predialytic uremic patients or those who have just started receiving dialysis. In serious cases of osteit fibrosa, the bone cortex conta-

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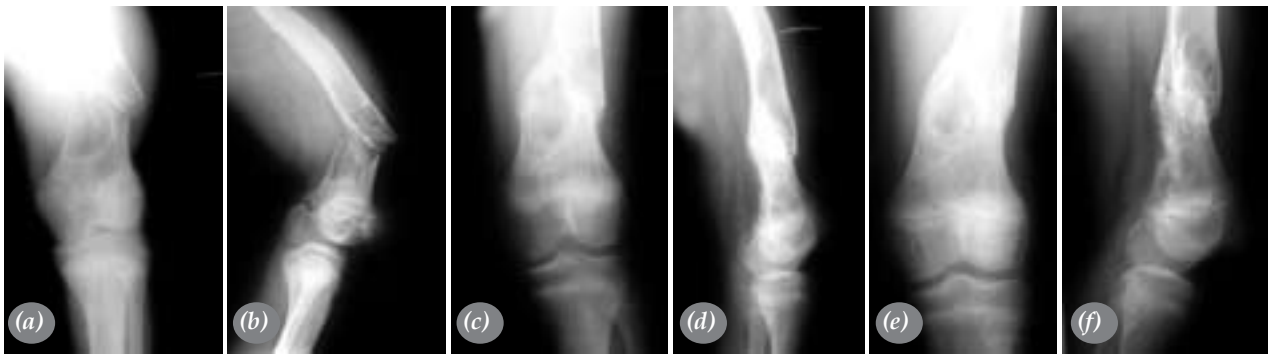

Figure 1. The patient's left femur front-back and side graphics in **(a, b)** November, 2006 (first presentation), **(c, d)** December, 2006 and **(e, f)** May, 2007.

ins large porous areas, mainly due to increased bone resorption. This alteration of the cortical bone structure increases the risk of fracture.[4]

Brown tumor develops in the metaepiphyses of long bones, the pelvis and the diaphyses. It can be seen in the jawbone, the cranium, the costas, the hands, and very rarely, the vertebrae.[5]

In this article, a case of brown tumor mimicking fibrous dysplasia in a patient with chronic renal failure has been presented.

Case presentation

O13-year old male patient. Applied to a hospital with pain in left leg after a minor trauma, where a pathologic fracture was observed in the left supracondylar femur, and he was transferred to our clinic with a splint (Fig. 1). The patient was admitted with a view to further examination and treatment. He was placed in a pelvipedal cast. X-rays of all long bones were taken during the examinations. The right cruris and the left femur were examined by magnetic resonance imaging (MRI) and computerized tomography (CT), and a whole body bone scintigraphy was carried out. In addition to the lesion in the left supracondylar femur, radiologically similar, asymptomatic cystic masses were observed in the left acetabular roof and right proximal and distal tibia (Fig. 2).

From the patient's history, it has been discovered that a blockage of the artery in the left lower extremity was observed two weeks after normal birth and eliminated through medical treatment; at seven years of age he was admitted to hospital with nausea, vomiting and diarrhea, and was diagnosed with right renal agenesis, narrowness of the left ureter, cystic growth in the left kidney and renal failure; was operated for the narrowness of the ureter; received medical treatment for two years afterwards; started hemodialysis

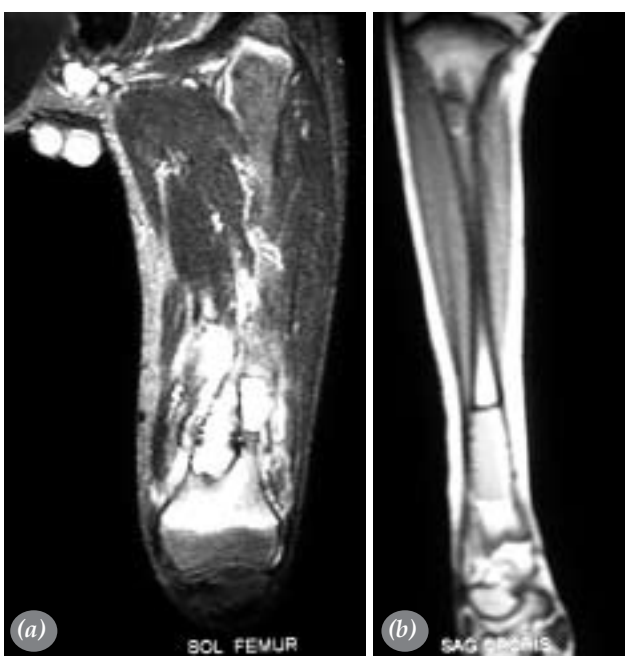

Figure 2. The magnetic resonance images of the lesions in **(a)** the left distal femur and, **(b)** right distal tibia.

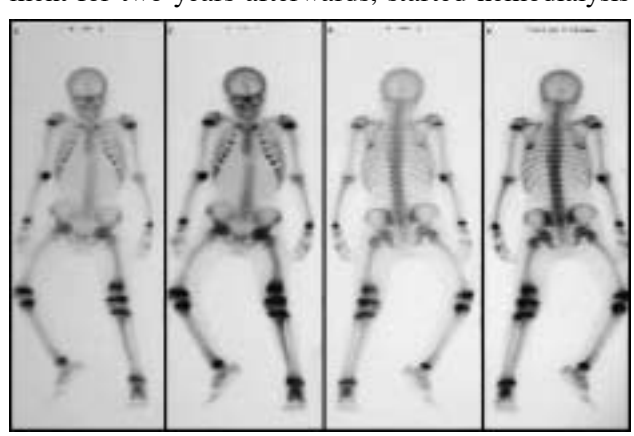

Figure 3. The increased activity involvement in the left distal femur seen In the entire body three phase dynamic bone scintigraphy.

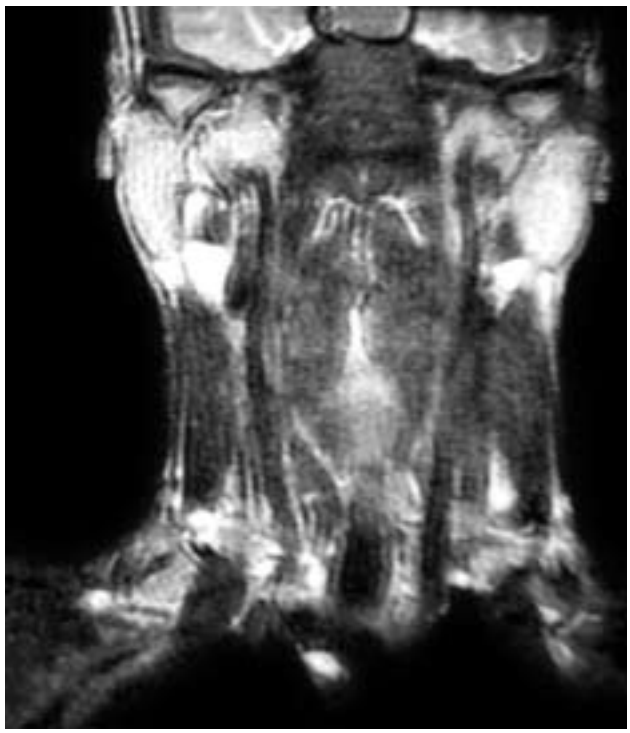

Figure 4. The appearance of adenomas in the magnetic resonance imaging.

treatment in 2003; after receiving hemodialysis for two years, started receiving peritoneum dialysis due to shunt problems. The patient had been receiving peritoneum dialysis through the foot continuously, four times a day for the past two years. The patient had been using calcium acetate (P binder) (250 mg, 4x1 tablets, Phos-Ex, Say) and calcityrol (0.25 _gr 1x2 capsules, Rocaltrol, Roche) when the patient presented at our hospital. The transplant scheduled for November, 2006, was postponed due to the development of the pathologic fracture.

Furthermore, the patient had been evaluated at the Istanbul Medical School Orthopedics and Traumatology Department due to a limp, and two sided flat graphics of the pelvis and left femur from the time were available.

The patient had a 10-year old brother. The brother had been diagnosed with achalasia at age 6 months. The mother had a history of a stillbirth two years ago. The parents, who were healthy, were second degree relatives.

On the examination of the CT and MRI of the patient's left femur and right cruris, a septal lesion of 9x4 cm dimensions, with iso-hypointense characteristics at the T_1- weighted crosscut, and heterogenic hyperintense characteristics at the T_2- weighted crosscut of the left femur; 4.5 cm hypodense lesion at the left acetabular roof; a 7x2 cm lesion causing expansion of the bone in the right distal tibia diaphysis; and similar, 4.5x1.5 cm lesions with hypointense characteristics at the T_1- weighted crosscut, and hyperintense characteristics at the T_2- weighted crosscut of the right proximal tibia diaphysis were observed. These lesions were evaluated as primarily fibrous dysplasia, and a low probability of multi-locational brown tumors.

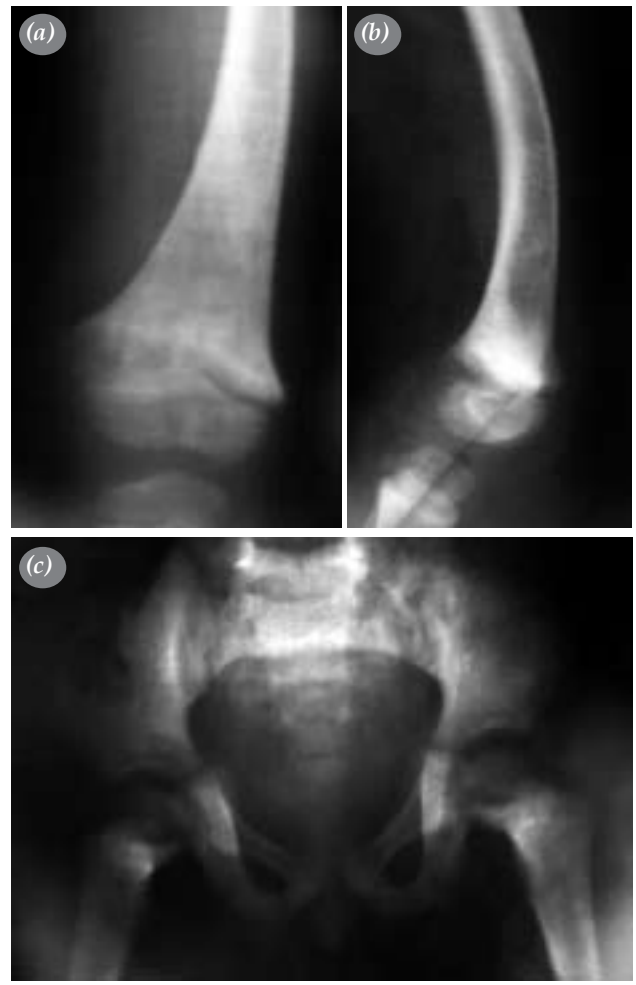

Figure 5. The patient's **(a)** left femur front-back, **(b)** left femur side,and **(c)** pelvis front-back images taken in 1999.

During the entire body three phase dynamic bone scintigraphy carried out with T-99, in the angiogram and blood pool phases, irregularly increased activity involvement was observed in the left distal femur. During the late static and entire body images taken three hours later, a dense lesion with irregular outli-

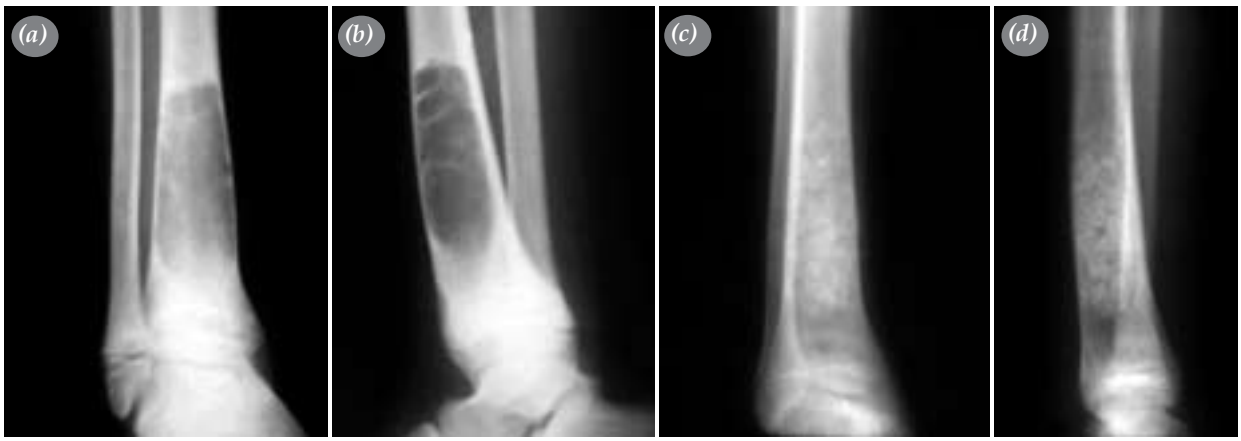

Figure 6. The front-back and side x-rays of the lesion in the left distal tibia **(a,b)** before the surgery, and **(c,d)** five months after the surgery.

nes and containing hypoactivity inside in the left femur metaphysial area (Fig. 3).

Primarily, hyperparathyroidism developing due to renal failure, and connected brown tumors were considered for the patient. Blood analyses showed parathyroid hormone (PHT) value to be 82.3 pg/ml (N: 12-72 pg/ml), calcium (Ca) value to be 9.7 ng/dl (N: 8.4-10.5 mg/dl), phosphorus (P) value to be 5.4 mg/dl (N: 2.3-4.7 mg/dl). However, when the Istanbul Medical School, Pediatric Nephrology Department polyclinic records of the patient were studied, it was seen that his PHT levels had been over 800 pg/ml for two years. In an examination of the MRI of the parathyroid, two 5 mm. lesions on the left, and one 1 cm lesion on the right, consistent with hyperplasia or adenoma, were determined (Fig. 4). Furthermore, it was determined that these lesions did not exist in the pelvis and left femur two sided straight images taken because of a limp when the patient was 5 years old (Fig. 5). According to the bone measurement (DEXA) analysis carried out in January 2007, the Z score was found to be +0.97.

The left supracondylar femur fracture of the patient was treated with a pelvipedal cast. He had no complaints in the right distal tibia. During the physical examination, there was no pain from pressure, there was a slight swelling. Movement of the right ankle was free and painless. He was operated for the cystic lesion in the right distal tibia as the mass was in the weight bearing area and there was a risk of a pathologic fracture. Curettage and grafting with spongy allograft was carried out (Fig. 6). Upon the frozen examination of the sample taken during the operation, it was found to be consistent with the lytic phase of fibrous dysplasia. The macroscopic appearance of the curettage material was grey-white colored and

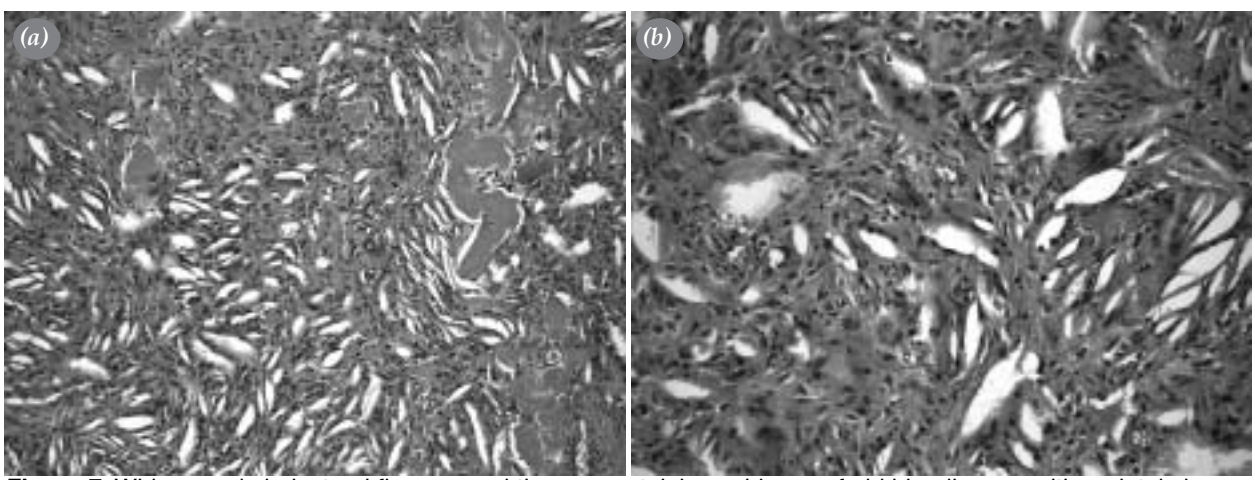

Figure 7. Widespread cholesterol fissures and tissues containing evidence of old bleedings or with parietal characteristics in part, and in between, trabecular, immature bone foci in the histopathological examination **(a)** H-E x 100, **(b)** H-E x 200).

hard. Microscopic examination showed widespread cholesterol fissures and tissues containing evidence of old bleedings or with parietal characteristics in part, and in between, trabecular, immature bone foci. Pathological examination, evaluated together with the clinical and radiological evidence, led to the conclusion of the lytic stage of fibrous dysplasia or brown tumor, although not typical (Fig. 7).

During the follow up examination in the fifth month after the surgery, the patient's left hip movements were free and painless; flexion was 110°, extension full, internal rotation 40°, external rotation 20°, abduction 30° and adduction 45°. The movements of the left knee were free and painless; flexion was 130°, extension was measured as full. Right ankle movements were free and painless. Clinical measurement showed the left lower extremity to be 1 cm shorter. Flat graphics showed the right distal tibia knitted. The fracture of the left supracondylar femur knitted in the cast. The cysts in the right proximal tibia and left acetabular roof, were small, therefore they were tracked and no growth was observed. The patient could walk, putting weight on the affected foot, with one crutch.

Discussion

The concept of renal osteodystrophy covers the changes in bone and mineral metabolism in chronic renal failure. In the last twenty years, developments in the hemodialysis and peritoneal dialysis programs have augmented the application of dialysis, and extended the lives of these patients. Renal osteodystrophy is one of the major morbidity reasons of patients receiving long term dialysis treatment or who have had a transplant.[4]

Brown tumors show a reparatory process more than a neoplastic process. Excess urine and calcium discharge in chronic renal failure can lower serum calcium levels and cause an increase in the secretion of PTH. In such a case, the skeletal calcium passes to the blood to maintain the normal serum calcium levels. This passage takes place through a rapid osteoclastic cycle of the bone. This is the direct effect of PTH on the bone.[6]

Brown tumor is a rare complication, it is more often seen in the metaepiphyses of long bones, pelvis and diaphyses. It can be seen in the jawbone, cranium, costas, hands and rarely, the vertebrae. Hemorrhagic areas, orthoclastic lumps and reactive giant cells may develop masses which may be mistaken for neoplasia. The histological findings of the tumor are similar to those of giant cell tumors, reparative giant cell granuloma and aneurismal bone cyst, and may cause confusion in diagnosis. The increased PTH value is the determinant in diagnosis.[5]

The histopathology of our case had fibro-osseous lesions. Widespread cholesterol fissures and tissues containing evidence of old bleedings or with parietal characteristics in part, and in between, trabecular, immature bone foci were observed. Under the circumstances, it was consistent with neither brown tumor, nor the radiologically primarily evaluated fibrous dysplasia.

In x-rays, brown tumors are seen as lytic lesions with regular borders. The cortex can be seen as narrowed and extended; however, there is no penetration. In CT, they are seen between the blood and fibrous tissue. It is hypervascular in angiography, and intensely active in bone scintigraphy.[6] In our case, apart from the fracture in the left femur, the other three lesions had regular borders. The lesion in the right distal cruris had thinned the cortex. Apart from the fracture in the left femur, the other three lesions were not active in the three phase dynamic bone scintigraphy. For this reason it was evaluated as inconsistent with fibrous dysplasia and with brown tumor, an active involvement is expected for both lesions in scintigraphy.[6-8] However, very rarely, in brown tumors together with hyperparathyroidism, there may be no activity involvement.[9]

When the clinic records of the patient from the Istanbul Medical School, Pediatric Nephrology Department, where he was being treated for chronic renal failure, were examined, it was seen that his PTH levels had been very high for two years. At the time he presented to our hospital due to fracture, his PTH level was borderline high (82.3 pg/ml), and his Ca value was 9.7 mg/dl.

Tertiary hyperparathyroidism was considered after the evaluation of the patient by general surgery and child endocrinology upon admittance to our clinic, in the light of clinical and laboratory findings. There are few presentations of cases in literature announcing brown tumors due to normocalcemic hyperparathyroidism.[10,11] However, the PTH values of those cases at the time they present to a hospital is around 1000

pg/ml. At the last control of our case in May, 2007, when the values of PTH 1238 pg/ml, Ca 8.7 mg/dl, P 5.5 mg/dl, ALP 849 U/L (N: 20-155) were found, the lesions were diagnosed as multi-location brown tumors as a result of an evaluation together with the department of child endocrinology.

The serum PTH level is often used in the diagnosis of hyperparathyroidism which is connected to chronic renal failure, and therefore is compensatory. For dialysis patients, it is recommended to maintain PTH at the 150-300 pg/ml level. It has been shown that the relation between PTH levels and bone histology is variable.[12]

PTH levels being high in spite of normal calcium values is no longer compensatory. We can say that the long present and uncontrolled secondary hyperparathyroidism in our patient has given rise to relative autonomous parathyroid hyperfunction, or in other words, to tertiary hyperparathyroidism.[13,14] In the magnetic resonance examination, the observation of lesions consistent with parathyroid hyperplasia or adenoma support this point of view.

Together with the current developments in medicine, the survival rates of chronic renal failure patients have risen. The renal osteodystrophy seen among these patients is one of the major causes of morbidity. The histological symptoms of brown tumor are similar to the giant cell tumor, reparative giant cell granuloma and aneurismal bone cyst, and may cause confusion in diagnosis. [5] However, as is seen in our case, the fibro-osseous structure of the brown tumor and the findings of the lytic stage of fibrous dysplasia may exhibit histological and radiological similarities, and non-involvement in scintigraphy may further cause confusion. In brown tumors, together with hyperparathyroidism, there may rarely be no activity involvement in scintigraphy. [10]

We believe that the present case will contribute to available knowledge for the differentiative diagnosis and treatment of patients with renal osteodystrophy.

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