Brown tumor of the thoracic spine presenting with paraplegia in a patient with peritoneal dialysis

Eray Eroglu¹ · Mustafa Eymen Kontas² · Ismail Kocyigit¹ · Olgun Kontas³ · Halil Donmez⁴ · Ahmet Kucuk⁵ · Murat Hayri Sipahioglu¹ · Bulent Tokgoz¹ · Oktay Oymak¹

Received: 21 June 2018 / Accepted: 18 April 2019 / Published online: 14 May 2019
© Japanese Society of Nephrology 2019

Abstract

Secondary and tertiary hyperparathyroidism is an important problem of chronic kidney disease. Brown tumor is a benign, unusual, reactive lesion as a result of disturbed bone remodeling, from long-standing increase in parathyroid hormone level. Brown tumors may cause morbidity due to pressure symptoms on neural structures and spontaneous bone fractures. Herein, we presented a peritoneal dialysis patient with tertiary hyperparathyroidism under calcand calcitriol treatment for 4 years due to refusing of the parathyroidectomy operation. She admitted to hospital for sudden onset back pain with difficulty in gait and walking, and imaging studies showed an expansile mass lesion in the thoracic spine. She was operated for mass and diagnosed with brown tumor. After operation, she lost the ability of walking than become paraplegic and she underwent rehabilitation program. Preventive measures including calcitriol and cinacalcet may cause a modest decrease in parathyroid hormone levels but it should be remembered for the development of bone complications such as brown tumor formation in patients with moderate elevated PTH levels, especially those with tertiary hyperparathyroidism. Parathyroidectomy should be performed without delay in these cases.

Keywords Chronic kidney failure · Hyperparathyroidism · Cinacalcet · Brown tumor

Introduction

Renal osteodystrophy (ROD), the skeletal complication of chronic kidney disease (CKD), is a multifactorial disorder of bone remodeling. The term renal osteodystrophy designates the abnormalities in bone and mineral metabolism due to impaired skeletal growth, remodeling and hyperparathyroidism. There are three histological forms of ROD, including predominant osteomalacia, predominant osteitis fibrosa

and, most commonly, a mixed pattern. The classic histological form is osteitis fibrosa cystica (brown tumor), which is attributed to secondary hyperparathyroidism (HPT) [1, 2]. Brown tumor (BT) formation develops only in the osteitis fibrosa cystica form and it is also a benign, unusual, reactive lesion as a result of disturbed bone remodeling, from long-standing increase in parathyroid hormone (PTH) level [3]. BT is a rare benign lesion of the bone, with incidence of less than 5% in primary hyperparathyroidism. It is more common in secondary hyperparathyroidism, with up to 13% of cases [4].

Skeletal involvement such as generalized osteopenia, bone resorption, bone cysts and Brown tumors are seen on the late phase of hyperparathyroidism. The effective control of HPT is crucial to prevent and treat soft tissue calcifications and brown tumors in patients with ROD. Most brown tumors have been treated by parathyroidectomy and rare cases with vitamin D medication [5, 6].

Herein, we reported a peritoneal dialysis patient with secondary HPT under cinacalcet treatment and presented with paraplegia due to brown tumor of the thoracic spine.

✉ Eray Eroglu
drearyeroglu@hotmail.com

¹ Division of Nephrology, Department of Internal Medicine, Erciyes University Medical Faculty, 38039 Kayseri, Turkey

² Department of Internal Medicine, Erciyes University Medical Faculty, Kayseri, Turkey

³ Department of Pathology, Erciyes University Medical Faculty, Kayseri, Turkey

⁴ Department of Radiology, Erciyes University Medical Faculty, Kayseri, Turkey

⁵ Department of Neurosurgery, Erciyes University Medical Faculty, Kayseri, Turkey

Case report

A 26-year-old woman was admitted to our nephrology department with the complaints of difficulty in gait and walking due to weakness in legs for 3 days in August 2017. She also described back pain. Neurological examination demonstrated paraparesis without impaired anal sphincter tonus. She had no history of trauma. She has been diagnosed end stage renal disease (ESRD) in 2007 with unknown etiology and treated with continuous ambulatory peritoneal dialysis (CAPD) during 10 years. Her last weekly K_t/V was 2.52 in May 2017. Patient was anuric; CAPD prescription consisted of four cycles of 2 L exchanges including three cycles with %2.27 glucose solutions and one cycle with icodextrin solution per day. She has no history of diabetes mellitus. She was diagnosed with hypertension after starting of renal replacement therapy. She has been diagnosed with secondary hyperparathyroidism (sHPT) in 2014. Serum intact parathormone (iPTH) level was 1041 pg/mL (15–68.3). Technetium-99 m-pertechnetate (99mTc-MIBI) scintigraphy revealed increased focal metabolic activity in the superior left lobe of the thyroid gland and relatively increased in the inferior lobes of thyroid gland.(parathyroid hyperplasia) (Fig. 1). Parathyroidectomy was proposed to her, but she refused operation; therefore, cinacalcet treatment was started for the sHPT. Patient was followed for 4 years with the cinacalcet medication. Her current medication includes, daily oral calcitriol (0.5 mcg/day), cinacalcet (60 mg/day), sevelamer (2400 mg thrice daily), calcium acetate (2100 mg thrice daily) and amlodipine (10 mg/day). Her current biochemical parameters are shown in Table 1. The levels of iPTH during follow-up from 2013 to 2018 are seen in Fig. 2. She was referred to neurosurgery department due to sudden paraparesia in distal extremities and back pain. Computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated the extradural mass lesion 10×13×19 mm in dimensions compressing to the spinal cord at T10–11

Table 1 Laboratory parameters of the patient on the admission in August 2017

Parameter	Value	Normal range
White blood cell ($10^3/\mu\text{L}$)	7.12	4.8–10.7
Hemoglobin (g/dL)	10.6	12–16
Platelet ($10^3/\mu\text{L}$)	271	130–400
Glucose (mg/dL)	76	74–106
Triglycerides (mg/dL)	181	40–130
Total cholesterol (mg/dL)	212	70–200
HDL-cholesterol (mg/dL)	45	35–55
LDL-cholesterol (mg/dL)	130.8	100–130
BUN (mg/dL)	63.5	6–20
Creatinine (mg/dL)	13.83	0.7–1.20
Calcium (mg/dL)	8.19	8.6–10.2
Phosphorus (mg/dL)	5.24	2.5–4.5
Magnesium (mmol/L)	1.39	0.66–1.77
Sodium (mmol/L)	134	136–145
Potassium (mmol/L)	5.8	3.5–5.1
Clor (mmol/L)	94	98–107
Total bilirubin (mg/dL)	0.51	0.2–1.2
Direct bilirubin (mg/dL)	0.16	0–0.3
GGT (U/L)	9	10–71
LDH (U/L)	219	135–225
AST (U/L)	5	0–40
ALT (U/L)	7	0–41
ALP (U/L)	578	40–130
Total protein (g/dL)	6.97	6.4–8.3
Albumin (g/dL)	4.46	3.5–5.2
Iron ($\mu\text{g/dL}$)	75	70–180
Iron binding ($\mu\text{g/dL}$)	325.5	225–480
Ferritin (ng/mL)	74.47	15–150
iPTH (pg/mL)	400	15–65

HDL high-density lipoprotein, *LDL* low-density lipoprotein, *BUN* blood urea nitrogen, *GGT* gamma-glutamyl transferase, *LDH* lactate dehydrogenase, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *ALP* alkaline phosphatase, *iPTH* intact parathyroid hormone

Fig. 1 The technetium 99 m Sestamibi (Tc-99 m MIBI) dual-phase parathyroid scintigraphy **a** early (15 min.) and **b** delayed images (90 min.), showing, small rounded focus of moderately increased MIBI uptake adjacent to superior pole of left lobe of thyroid gland (arrow) (**a**), with persistent tracer retention in this lesion in delayed images but normal washout from thyroid gland (**b**), suggestive of left superior parathyroid adenoma

Fig. 2 The levels of iPTH during follow-up from 2013 to 2018. (D₃: treated with calcitriol, Ci: treated with cinacalcet, D₃ + Ci: treated with calcitriol and cinacalcet)

vertebra levels (Fig. 3). She was operated for spinal decompression by neurosurgery. In the operation, T10–11 partial hemilaminectomy and flavectomy were performed. Total excision of the lesion was performed at the spinal epidural space. The cord and roots were decompressed on both sides. Pathologic examination of the material showed giant cell bone lesion (Fig. 4). These findings were considered as to be brown tumor of the spine. She has become paraplegic and referred to physical therapy and rehabilitation after surgery. Surgical parathyroidectomy was proposed repeatedly as medical therapy had failed to control serum iPTH levels and brown tumor occurrence. She accepted operation after rehabilitation program was completed.

Discussion

The brown tumor is a benign lesion, characterized by the presence of hemosiderin pigment deposits and osteoclastic giant cells arranged in groups, separated by richly vascularized fibrous tissue. It occurs most often in the long bones, ribs and pelvis, but can be found in any bone and soft tissue

[7]. The name “brown tumor” comes from the accumulation of hemosiderin that gives the surrounding stroma a brown color. BTs histologically resemble to the other giant cell lesions such as giant cell tumor or aneurysmal bone cyst [8]. Elevated PTH levels lead to increased osteoclastic activity, with reactive fibroblastic proliferation of the involved bone, that results in a loss of the bone trabeculae [9]. It predisposes to microfractures and secondary hemorrhage that cause bone pain. Invasion of macrophages or giant osteoclastic cells with reparative fibrous tissue results as a reactive tissue mass known as brown tumor. This lesion may disrupt neuronal structures may lead to neuropathy and/or muscle weakness, as in our case. Only the clinical manifestation and endocrinologic status help to differentiate BTs from other giant cell lesions. BTs usually develop in the third or fourth decades of life [5]. The symptoms of spinal BTs include pain, radiculopathy, myelopathy and myeloradiculopathy according to their locations [10].

In our case, the patient was presented with complaints of difficulty in walking and standing due to weakness in legs for 3 days. She also described back pain. Neurological examination demonstrated paraparesis without impaired

Fig. 3 CT illustrates a lytic lesion (arrow) in the right lamina of the T11 vertebra, which disrupts the cortical integrity in axial images (a). MRI illustrates a cystic mass lesion in the right lamina of the T11 vertebra (arrow) that compresses the spinal canal and spinal cord to

the anterior. MRI demonstrates the lesion as isointense in fat-suppressed T1-weighted sagittal images (b), as hyperintense smooth shaped mass in T2-weighted axial images (c) and T2-weighted sagittal images (d)

anal sphincter tonus. Pain may be explained by the both pressure of the tumor to the neural structures in the spine and pathophysiology of BT. However, the tumor was localized in the thoracic spine, and there are few reports with atypical localization in the literature. Sonmez et al. recently reported a case with primary hyperparathyroidism and brown tumor in the thoracic spine that was successfully treated by surgical decompression of the tumor [8]. Additionally, Noman Zaheer et al. reported a renal transplant patient with brown tumor on the thoracic spine and treated with decompression without post-operative complication and sequelae [11]. Tayfun et al. also presented a 26-year-old female hemodialysis patient with difficulty in gait and back pain diagnosed with BT in thoracic spine and mandible due to sHPT. Patients' walking ability improved after surgical decompression [12]. However, these three cases were not treated with cinacalcet and timing of the surgery was earlier as preventing irreversible neural damage.

Treatment of BTs involve both the management of hyperparathyroidism and neural decompression [8, 11, 12]. Preventive measures is the most important issue for the occurrence of sHPT in the management of ESRD patients. Parathyroidectomy is the gold standard treatment of secondary or tertiary HPT (tHPT) in patients with ESRD [2]. There are different parathyroidectomy modalities and the most preferred method is total parathyroidectomy with auto-transplantation. Patients with increased level of PTH over 1000 pg/mL are the candidates for operation. If muscle pain, weakness, bone pain, resistant pruritus and anemia were occurred, operation should be considered for HPT [2]. Parathyroidectomy is, most effective treatment method of sHPT/tHPT, vitamin D based treatment options including calcitriol, calcidiol, paricalcetriol and/or calcium receptor against including cinacalcet could be a medical treatment option especially patients with high operative risk. However, the effect of these medical agents on BT formation has not been well studied. Only few reports showed that the calcidiol and cinacalcet provided

Fig. 4 This figure illustrates the histopathological view of the brown tumor specimen. **a** There are hemorrhagic and solid areas in the panoramic view of the specimen (H-E, $\times 10$). **b** There are lots of multinucleated giant cells in the lesion (H-E, $\times 40$). **c** Multinucleated giant

cells observed in all areas in the bone trabeculae (H-E, $\times 100$). **d** The demonstration of the Hemosiderin-loaded macrophages in the lesion (H-E, $\times 400$)

regression of BT lesions in patients with sHPT. Mourad et al. reported a hemodialysis patient with sHPT and BT in mandibula and treated with high-dose alfacalcidol during 1 year after initial diagnosis [5]. In that case, BT developed in the absence of preventive treatment, and the medical control of PTH was achieved. Subsequently, BT lesion was improved. However, our case was under both calcitriol and cinacalcet treatment for 4 years and iPTH levels were not controlled well by medical treatment option. Otherwise, craniofacial hypertrophy has been reported in a patient with tHPT under high-dose cinacalcet treatment [13]. The effect of cinacalcet in bone formation remains to be elucidated in severe HPT cases. On the other hand, Resic et al. used cinacalcet in a patient with BT and severe tHPT after the recurrence of HPT. Cinacalcet decreased PTH levels to 450 pg/ml levels after 6 months [14]. However, they reported that cinacalcet is effective in short period, and long-term results should be monitored. Also our patient

PTH levels were within 400–500 pg/mL levels, but BT developed after 4 years of the cinacalcet initiation. We speculate that cinacalcet may control the PTH secretion at mild to moderate levels but long duration of PTH exposure in that levels may result in BT formation.

In conclusion, BT due to secondary HPT is an important clinical problem in patients with CKD. Thoracic spine involvement by brown tumor is a rare condition in sHPT. Physicians should be aware of complications of secondary/tertiary HPT, since late referral and delayed parathyroidectomy may increase the morbidity of the patients.

Funding There is no funding for the study.

Compliance with ethical standards

Conflict of interest All authors declare that there is no conflict of interest.

Research involving Human Participants and/or Animals This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from the patient included in the case report.

References

1. Malluche H, Faugere MC. Renal bone disease: an unmet challenge for the nephrologists. *Kidney Int.* 1990;38:193–211.
2. Moe S, Drüeke T, Cunningham J, Goodman W, Martin K, Olgaard K, Ott S, Sprague S, Lameire N, Eknoyan G, Kidney Disease: Improving Global Outcomes (KDIGO). Definition, evaluation, and classification of renal osteodystrophy: a position statement from kidney disease: improving global outcomes (KDIGO). *Kidney Int.* 2006;69(11):1945–53.
3. Hoshi M, Takami M, Kajikawa M, et al. A case of multiple skeletal lesions of brown tumors, mimicking carcinoma metastases. *Arch Orthop Trauma Surg.* 2008;128:149–54.
4. Alfawareh MD, Halawani MM, Attia WI, Almusrea KN. Brown tumor of the cervical spines: a case report with literature review. *Asian Spine J.* 2015;9(1):110–20.
5. Mourad G, Argiles A, Vela C, Lorho R, Flavier JL, Canaud A, Mion CM. Control of severe hyperparathyroidism and regression of a brown tumor after treatment with i.v. alfacalcidol in a uremic patient. *Nephrol Dial Transpl.* 1995;10:552–4.
6. Graciela GM, Leanza H, Najun ZC, Barreneche M. Medical parathyroidectomy. Its efficacy in treatment of lower maxillary brown tumor. *Medicina (BAires).* 1996;56:59–62.
7. Ayala AG, Ro JY, Raymond AK. Bone tumors. In: Damjanov I, Lindar J, editors. *Anderson's pathology*. 9th ed. St. Louis: Mosby; 1996. p. 2531–73.
8. Sonmez E, Tezcaner T, Coven I, Terzi A. Brown tumor of the thoracic spine: first manifestation of primary hyperparathyroidism. *J Korean Neurosurg Soc.* 2015;58(4):389–92.
9. Marx SJ. Hyperparathyroid and hypoparathyroid disorders. *N Engl J Med.* 2000;343:1863–75.
10. Yokota N, Kuribayashi T, Nagamine M, Tanaka M, Matsukura S, Wakisaka S. paraplegia caused by brown tumor in primary hyperparathyroidism. Case report. *J Neurosurg.* 1989;71:446–8.
11. Noman Zaheer S, Byrne ST, Poonnoose SI, Vrodo NJ. Brown tumour of the spine in a renal transplant patient. *J Clin Neurosci.* 2009;16(9):1230–2.
12. Tayfun H, Metin O, Hakan S, Zafer B, Vardar AF. Brown tumor as an unusual but preventable cause of spinal cord compression: case report and review of the literature. *Asian J Neurosurg.* 2014;9(1):40–4.
13. Hamrahian M, Pitman KT, Csongrádi É, Bain JH, Kanyicska B, Fülöp T. Symmetrical craniofacial hypertrophy in patients with tertiary hyperparathyroidism and high-dose cinacalcet exposure. *Hemodial Int.* 2012;16(4):571–6.
14. Resic H, Masnic F, Kukavica N, Spasovski G. Unusual clinical presentation of brown tumor in hemodialysis patients: two case reports. *Int Urol Nephrol.* 2011;43(2):575–80.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.