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Case Report on Brown Tumor: An Unusual Expression of Renal Osteodystrophy and Secondary Hyperparathyroidism

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

The new term of 'Chronic Kidney Disease- Mineral and Bone Disorders' has been introduced to encompass a wide-ranging syndrome, capturing various abnormalities in bone and mineral metabolism seen in patients with chronic kidney disease. Multifactorial disorders affecting mineral metabolism and bone structure emerge early in the progression of Chronic Kidney Disease. Brown tumors, an uncommon type of bone lesion are distinctive manifestations of high-turnover bone

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disease. In this case, a patient with chronic kidney disease (dialysis dependent) with IgA nephropathy that presented with multiple osseous lesions of bilateral ribs, sternum, scapula, clavicle, mandible and vertebral bodies. The case highlights the significance of considering brown tumors in the differential diagnosis and management of patients with both an osseous mass and chronic kidney disease. Failing to establish an accurate diagnosis may result in unnecessary additional diagnostic procedures and extensive surgery, ultimately increasing patient morbidity. Through this case report, the importance of preventing, early diagnosing, and treating secondary hyperparathyroidism to reduce the prevalence of high-turnover bone disease and associated complications such as brown tumors is emphasized.

Keywords: CKD; renal osteodystrophy; brown tumor; hyperparathyroidism; lesions; PTH.

1. INTRODUCTION

Disorders in mineral metabolism and bone structure, with multifactorial causes, manifest early in chronic kidney disease. These issues intensify as kidney dysfunction progresses [1]. Recently, the term 'chronic kidney disease-mineral and bone disorders' (CKD-MBD) has been adopted to describe a comprehensive syndrome, encompassing diverse abnormalities in bone and mineral metabolism, such as renal osteodystrophy and extra osseous calcifications, seen in patients with CKD [2,3]. In over 50% of hemodialysis patients, secondary hyperparathyroidism is detected and is linked to significant morbidity [4] High-turnover bone disease, a form of renal osteodystrophy, specifically osteitis fibrosa cystica results from alterations in bone metabolism induced by secondary hyperparathyroidism. This condition initially emerges early as CKD, often when the glomerular filtration rate falls below 60 ml/min. Its severity increases with worsening renal function due to progressive phosphate retention, reduced calcitriol levels, and hypocalcemia [5,6].

Secondary hyperparathyroidism and high-turnover bone disease manifest radiographically through various bone lesions. These encompass sub-periosteal bone resorption, trabecular bone resorption that imparts a distinctive 'salt and pepper' appearance to the skull, osteosclerosis leading to the 'rugger jersey spine sign' as well as bone deformities and increased susceptibility to fragility fractures. It is crucial to recognize these imaging characteristics for accurate diagnosis and comprehensive understanding of the impact on skeletal health [7,8].

Brown tumor is a focal, benign bony lesion induced by localized and rapid osteoclastic turnover of bone, a consequence of the direct effects of parathyroid hormone (PTH). Their occurrence has been reported in 1.5% to 4.5% of patients with either primary or secondary hyperparathyroidism [9]. Hemorrhages, accompanied by the accumulation of hemosiderin within the vascularized fibrous tissue, are prevalent and contribute to the reddish-brown color that defines these tumors. Clinically, brown tumors commonly present with swelling, pathological fractures, and bone pain, underscoring the importance of recognizing these manifestations for timely diagnosis and appropriate management [10].

It is noteworthy that the majority of primary hyperparathyroidism cases observed today are identified and addressed early in the disease progression, often before significant bone abnormalities manifest. Due to this trend and the higher prevalence of secondary hyperparathyroidism, most instances of brown tumors are linked to secondary hyperparathyroidism [11]. Here, the case of a patient with chronic kidney disease, IgA nephropathy, renal osteodystrophy and secondary hyperparathyroidism presented with osseous lesions is discussed.

2. CASE PRESENTATION

A 26 year old female patient was admitted with complaints of recurrent fever, shortness of breath accompanied by loss of weight and loss of appetite. The patient had a history of chronic kidney disease with IgA Nephropathy. For the last six years, she had been on hemodialysis. She was regularly taking antihypertensive and also received epoetin. She was with elevated parathyroid hormone (PTH) levels for more than 3 years even though she was on Tab Cinacalcet 30mg.

Upon admission to the hospital, initial work up was done to exclude other diseases like heart failure, pneumonia or other diseases as the

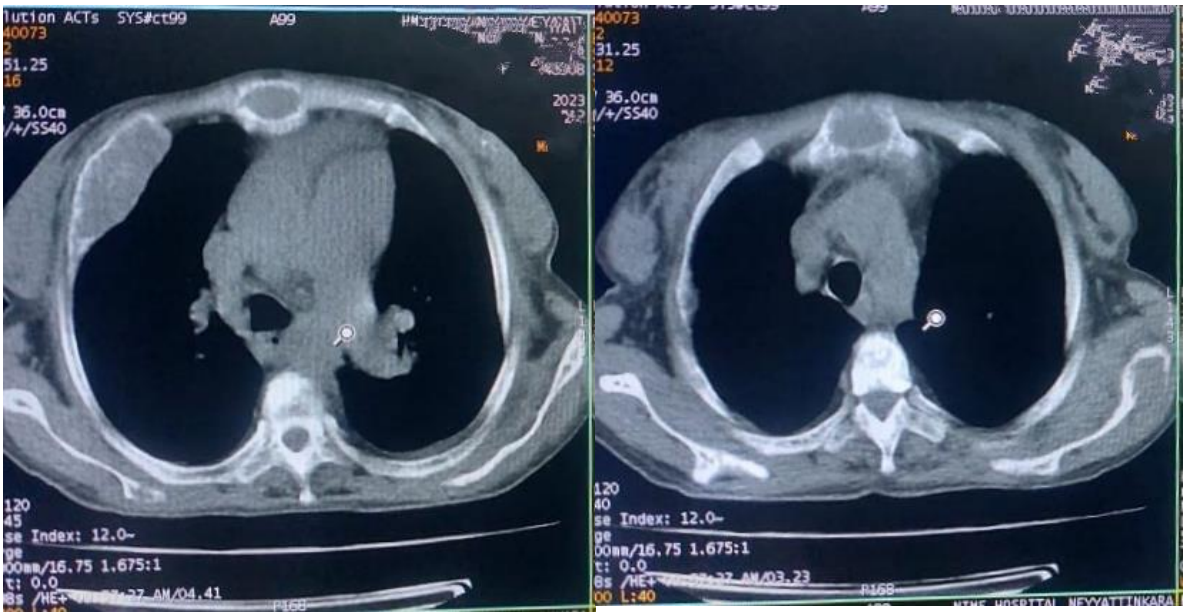

Fig. 1. CT Scan showing expansile lytic lesions in ribs and sternum

potential cause of recurrent fever and shortness of breath. She was with declined Hb levels (8.6 g/dl), moderately elevated CRP (18.4 mg/L) and laboratory findings revealed severe secondary hyperparathyroidism with notably elevated parathyroid hormone level (1166 pg/mL, normal range 15-65 pg/mL), phosphate level (4.3 mg/dL, normal range 2.5 mg/dL), calcium level (7.6 mg/dL, normal range 8.5-10.5 mg/dL) and elevated levels of alkaline phosphatase (1834 U/L, normal range 50-136 U/L). Chest radiograph showed trachea-mediated shift to right side, cardiomegaly, pericardial effusion and perihilar infiltration.

Computed tomography scan showed lytic lesion measuring 3*1.1cms noted in the lateral aspect of right 2nd rib, lesion measuring 7*2.8cms in the antero-lateral aspect of right 3rd rib, 5.6*3.4cms in the antero-lateral aspect of right 6th rib, lesion measuring 7.5*2.9cms in the lateral aspect of right 7th rib, multiple smaller lytic lesions also noted in right 3rd, 4th, 5th, 6th, 7th, 8th, 9th, 10th ribs, lesion measuring 1.8*0.9cms noted in the lateral aspect of left 2nd rib, lytic lesions measuring 4.3*1.5cms in the postero-lateral aspect of left 7th rib, multiple small lytic lesions also noted in left 5th, 6th, 8th, 9th, 10th ribs and lytic lesions noted in the lateral aspect of left 9th rib with cortical discontinuity and surrounding soft tissue fracture with callus formation. It was also evident from CT scan with expansile lytic lesions in the body of sternum measuring 6.6*1.8cms, multiple bilateral scapular lesions measuring 7.5*3.5cms involving the body of left scapula, lytic lesion measuring 3.5*1.1cms involving the mid third of left clavicle, multiple lytic lesions noted involving the body and posterior elements of visualized cervical and thoracic vertebrae, largest ones are measuring 2.1*1.1cms in the body of D5 vertebrae along with 2*1.2cms in D8 vertebral body and finally with a visualized limited cuts of lower part of mandible showing lytic lesion measuring 1.8*1.5cms. The CT scan also revealed that the vertebral body height is reduced with diffuse sclerosis likely secondary to renal osteodystrophy. The CT impression thus gave the picture of multiple expansible lytic lesions in bilateral ribs, sternum, scapula, clavicle, mandible and vertebral bodies that could represent Brown's tumor (Fig. 1).

The patient's presentation, clinical context, and the outcomes of a thorough examination led to the diagnosis of multiple brown tumors arising from renal osteodystrophy and high turnover bone disease. Subsequently, the patient was discharged from the hospital after treating with Tab Cinacalcet 30mg, Tab Calcium acetate 667mg, Vitamin D supplements and discharged along with an inhaler. She came for follow up and showed the PTH was still high (856 pg/mL) despite of standard treatment with Cinacalcet 30 mg tablet and phosphate binder (calcium acetate 667mg). This shows the occurrence of the autonomy of parathyroid gland that may be a picture of tertiary hyperparathyroidism. Due to patient's preference and overall health condition,

parathyroidectomy could not be put into consideration. During subsequent follow-ups, brown tumors continued to persist, with no notable increase in the size of the lesions.

3. DISCUSSION

Secondary hyperparathyroidism commonly occurs as a complication of CKD [12] The development involves a complex pathogenesis associated with elevated parathyroid hormone (PTH) levels, leading to various disruptions in mineral metabolism such as an increase in fibroblast growth factor-23 (FGF 23), a reduction in active vitamin D and alterations in calcium and phosphorous levels [6,13]. Renal osteodystrophy, a component of CKD-MBD, stands out as a significant complication in CKD. It encompasses a spectrum of skeletal disorders, spanning from high-turnover bone disease, primarily linked to excess PTH, to low-turnover bone disease, frequently correlated with decreased PTH levels [3,14,15].

Brown tumors are indicative of a reparative bone process rather than genuine neoplasm. They emerge from the localized substitution of normal marrow with reparative granulation tissue and highly vascular proliferating fibrous tissue in bone areas where elevated PTH levels trigger notably rapid osteoclastic bone turnover [16]. Typically painless and gradually expanding, brown tumors are often discovered incidentally. These are affected in axial skeleton, namely jaws, ribs, clavicles and pelvis, but they can affect any human bone [17].

As per the Kidney Disease Improving Global Outcomes (KDIGO) 2017 guidelines on preventing and treating CKD associated mineral and bone disorders, regular assessment of serum calcium, phosphorous, alkaline phosphatase and PTH levels is recommended. This evaluation helps determine the necessity for specific interventions like restricting dietary phosphate, employing phosphate binders, administering active vitamin D, calcimimetics or even considering renal replacement therapies. These strategies aim to lower PTH levels and calcium burden, ultimately enhancing quality of life [18]. Surgical removal of brown tumor may be necessary in cases where the tumor induces compressive neurological syndromes, poses a high risk of fracture, results in significant deformity affecting normal functions like mastication or breathing, or persists with pain or other symptoms despite effective control of hyperparathyroidism. Bone scintigraphy can be done in order to characterize the lesions [19].

In this case, the patient is treated according to standard treatment guidelines which aimed at reducing PTH levels, administration of vitamin D analogs and calcimimetic agents. The case report underscores the significance of considering brown tumors in the differential diagnosis and management of patients with an osseous mass and CKD. Failure to establish the correct diagnosis can result in unnecessary additional diagnostic procedures and even extensive surgery, escalating the morbidity in these patients. Emphasizing prevention, early diagnosis and treatment of secondary hyperparathyroidism is crucial to reduce the prevalence of these high turnover bone disease and associated complications like brown tumors.

4. CONCLUSION

With early-stage treatment becoming more prevalent, severe complications of CKD are becoming increasingly rare. CKD-MBD including the occurrence of brown tumors is one of the potential complications that may be mitigated through timely intervention. In summary, the case report underscores the significance of vigilance for brown tumors in individuals with CKD, emphasizing that early detection and intervention are pivotal in averting unnecessary procedures and mitigating the complications.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Waziri B, Duarte R, Naicker S. Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD): Current Perspectives. Int J Nephrol Renovasc Dis. 2019 Dec;12:263-276.

2. Lewis R. Mineral and bone disorders in chronic kidney disease: New insights into mechanism and management. Annals of Clinical Biochemistry. 2012;49(5):432-440.
3. Goto NA, Weststrate ACG, Oosterlaan FM, Verhaar MC, Willems HC. The association between chronic kidney disease, falls, and fractures: A systematic review and meta-analysis. Osteoporos Int. 2020 Jan;31 (1):13-29.
4. Simeoni M, Perna AF, Fuiano G. Secondary hyperparathyroidism and hypertension: An Intriguing Couple. J Clin Med. 2020 Feb 27;9(3):629.
5. Allen MR, Swallow EA, Metzger CE. Kidney disease and bone: Changing the way we look at skeletal health. Curr Osteoporos Rep. 2020 Jun;18(3):242-246.
6. Brandenburg V, Ketteler M. Vitamin D and secondary hyperparathyroidism in chronic kidney disease: A critical appraisal of the past, present, and the future. Nutrients. 2022 Jul 22;14(15): 3009.
7. Pazianas M, Miller PD. Current understanding of mineral and bone disorders of chronic kidney disease and the scientific grounds on the use of exogenous parathyroid hormone in its management. J Bone Metab. 2020 Feb;27 (1):1-13.
8. Rodriguez-Ortiz ME, Rodriguez M. Recent advances in understanding and managing secondary hyperparathyroidism in chronic kidney disease. F1000Res. 2020 Sep 1;9.
9. Shavlokhova V, Goeppert B, Gaida MM. Mandibular brown tumor as a result of secondary hyperparathyroidism: A case report with 5 years follow up and review of literature. Int J Environ Res Public Health. 2021 Jul 9;18(14):7370.
10. Zhong Y, Huang Y, Luo J, Ye Y. Misdiagnosis of brown tumor caused by primary hyperparathyroidism: A case report with literature review. BMC Endocr Disord. 2022 Mar 14; 22(1):66.
11. Santoso D, Thaha M, Empitu MA, Kadariswantiningsih IN, Suryantoro SD. Brown tumour in chronic kidney disease: Revisiting an old disease with a new perspective. Cancers (Basel). 2023 Aug 15;15(16):4107.
12. Kilav-Levin R, Hassan A, Nechama M, Shilo V, Silver J, Ben-Dov IZ, Naveh-Many T. Post-transcriptional mechanisms regulating parathyroid hormone gene expression in secondary hyperparathyroidism. FEBS J. 2020 Jul; 287(14):2903-2913.
13. Duque EJ, Elias RM, Moyses RMA. Parathyroid hormone: A uremic toxin. Toxins (Basel). 2020 Mar 17;12(3):189.
14. Machuca-Gayet I, Quinaux T, Bertholet-Thomas A, Gaillard S, Claramunt-Taberner D, Acquaviva-Bourdain C. Bone disease in nephropathic cystinosis: Beyond renal osteodystrophy. Int J Mol Sci. 2020 Apr 28;21(9):3109.
15. Pimentel A, Urena-Torres P, Bover J, Luis Fernandez-Martin J, Cohen-Solal M. Bone fragility fractures in CKD patients. Calcif Tissue Int. 2021 Apr;108(4):539-550.
16. LiU Z, Yang H, Tan H, Song R, Zhang Y, Zhao L. Brown tumor of the cervical spine with primary hyperparathyroidism: A case report and literature review. Medicine (Baltimore). 2023 Feb 10;102(6): e32768.
17. Lessa MM, Sakae FA, Tsuji RK, Filho BCA, Voegels RL, Butugan O. Brown tumor of the facial bones: Case report and literature review. Ear, Nose & Throat Journal. 2005;84(7):432-434.
18. Wiederkehr M. Brown tumor complicating end-stage kidney disease. Clin Nephrol Case Stud. 2020 Oct 12;8:72-79.
19. De La Flor Merino JC, Justo P, Dominguez JJ. Mutliple brown tumors-forgotten pathology in times of calcimimetics: A case report and literature review. SAGE Open Medical Case Reports. 2021;9.

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