Case Report

Oncogenic osteomalacia diagnosed by blood pool scintigraphy

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ABSTRACT

Oncogenic osteomalacia is a rare metabolic bone disease characterized by phosphaturia and hypophosphatemia. Certain tumors secrete a phosphaturic factor, which results in this metabolic abnormality; this factor called as phosphatonin, is in fact a fibroblast growth factor 23 (FGF-23) involved closely in phosphate homeostasis and skeletogenesis. Complete excision of these tumors facilitates reversal of the problem. We have reported here the case of a patient who was crippled with this disease and on thorough investigation revealed an oncogenic osteomalacia with tumor focus in the right tibia. The tumor was identified as a mesenchymal tumor, i.e., hemangiopericytoma. Tumor excision alleviated patient symptoms with rapid symptomatic and biochemical improvement.

Keywords: Hemangiopericytoma, oncogenic osteomalacia, reb blood cell blood pool scan, Tc 99m MDP bone scan

INTRODUCTION

Tumors responsible for oncogenic osteomalacia are usually benign mesenchymal tumors. They cause generalized, debilitating osteomalacia and rickets, which are important clinical problems for the patient. Haemangiopericytoma (HPC) is one of the most important soft tissue neoplasm causing this problem. However, it involves lot of diagnostic dilemmas, for example, it exhibits a characteristic well-developed "staghorn" branching vascular pattern histologically. But this pattern is non-specific and can be shared both by benign and malignant tumors. Thus, these tumors need special reference as they show a questionable prognosis and, by histological investigations, it cannot be decided if we are dealing with a benign or malignant tumor growth. Also, it can exist anywhere in the body, thus, whole body screening is imperative.

Wide surgical excision is the mainstay of treatment. HPC are poorly radiosensitive, while both primary and metastases respond well to chemotherapy. However, adjuvant radiotherapy and chemotherapy are desirable because the malignant nature of this tumor is frequently unpredictable. Adjuvant therapy is recommended for metastases, recurrence, and incomplete resection. Long-term follow-up is advisable as recurrence can occur many years later. In this scenario of very little or no experience in managing these tumor, it is important for us to be aware of its clinical presentation, biochemical derangements, tumor behavior, and the treatment options; hence, we are presenting this case report.

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CASE REPORT

A 56-year-old male presented with progressive lower limb weakness and inability to walk with generalized body pains. Magnetic resonance imaging (MRI) reported lumbar canal stenosis. The patient gradually became wheel chair bound with severe body aches for more than 3 years. As his MRI brain was normal, tropical spastic paraparesis was suspected.

The patient later presented to our hospital, where he was thoroughly evaluated. Biochemically, serum alkaline phosphatase was raised in the presence of normal serum calcium, parathormone (PTH), reduced vitamin D3, and serum phosphorus. Urinary calcium excretion (24 h) was normal, but with hyperphosphaturia. X-ray pelvis suggested severe osteoporosis, while a whole body Tc 99m methylene diphosphonate (MDP) skeletal scintigraphy showed features of metabolic bone disease.

Based on this, a diagnosis of hypophosphatemic osteomalacia was made and the patient was started on oral phosphate replacement.

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While all other causes of hypophosphaturia were ruled out, tumor induced osteomalacia had to be investigated.

RESULTS

Biochemically, serum alkaline phosphatase was raised in the presence of normal serum calcium, parathyroid hormone (PTH), reduced vitamin D3, and serum phosphorus. Urinary calcium excretion (24 h) was normal, but with hyperphosphaturia. Venous sampling was used to confirm local FGF-23 production and was found to be 389 kRU/l, normal range 5-210 kRU/l. X-ray of the pelvis suggested severe osteoporosis, while a whole body Tc 99m MDP skeletal scintigraphy showed features of metabolic bone disease with costochondral beading, increased periarticular tracer uptake, hot spots in bilateral posterior ribs (pseudofractures), and "superscan appearance" [Figure 1]. Based on this, a diagnosis of hypophosphatemic osteomalacia was made and the patient was started on oral phosphate replacement. On trying to evaluate causes of hypophosphaturia, a provisional diagnosis of tumor-induced osteomalacia was also believed.

In this line, a whole body Tc 99m Red blood cell (RBC) blood pool scintigraphy was performed as a screening procedure, and an abnormal focus of RBC accumulation was found in the right tibia [Figures 2 and 3]. An MRI of lower limb further confirmed the above finding, which showed two elongated tumors in the right tibial shaft [Figure 4]. The patient underwent a complete tumor excision, and histopathology was reported to be hemangiopericytoma [Figure 5]. Postoperatively, there was a dramatical improvement in the general condition (the patient started walking within 6 weeks) and his serum phosphorous became normal.

DISCUSSION

Tumor-induced osteomalacia is typically caused by benign mesenchymal tumors of vascular or skeletal origin, comprising of pericytes as first described by Stout and Murray in 1942.[1] The tumor can occur anywhere in the body, reported sites are lungs,[1] thyroid,[2] extremities, pelvis,[3] orbit,[4] head and neck, retroperitoneum, and abdomen.[5] Primary central nervous system

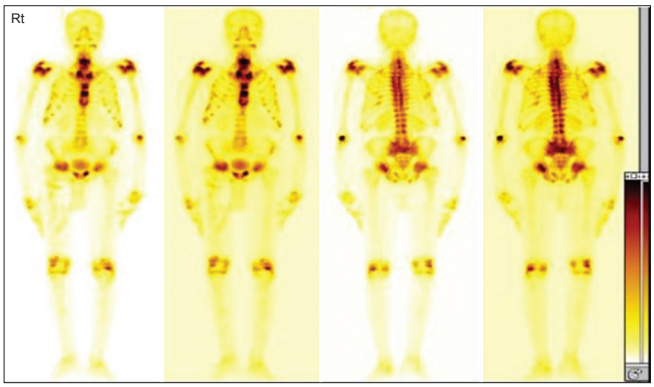

Figure 1: Tc 99m MDP whole body scintigraphy in dual intensity showing scintigraphic picture of metabolic bone disease

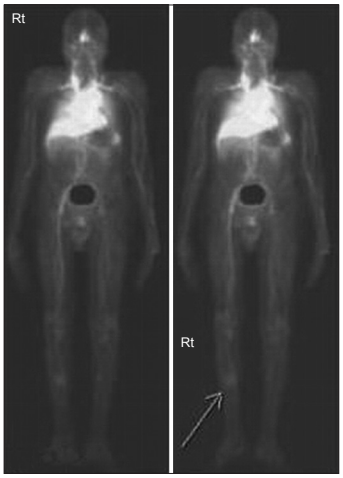

Figure 2: Tc 99m RBC blood pool whole body scintigraphy in anterior projection (dual intensity)

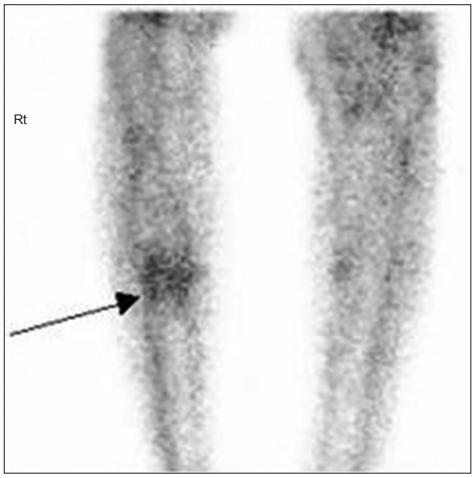

Figure 3: Anterior static Tc 99m RBC blood pool scintigraphy—high resolution static image of the right tibial shaft showing focal abnormal RBC accumulation at the site of tumor

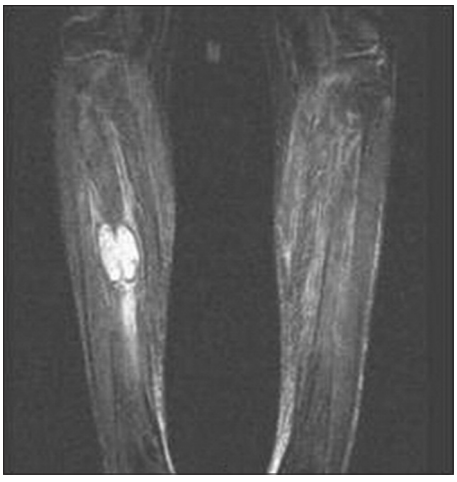

Figure 4: MRI of both lower limbs showed two elongated tumors corresponding to the site of abnormal RBC accumulation in the right tibial shaft

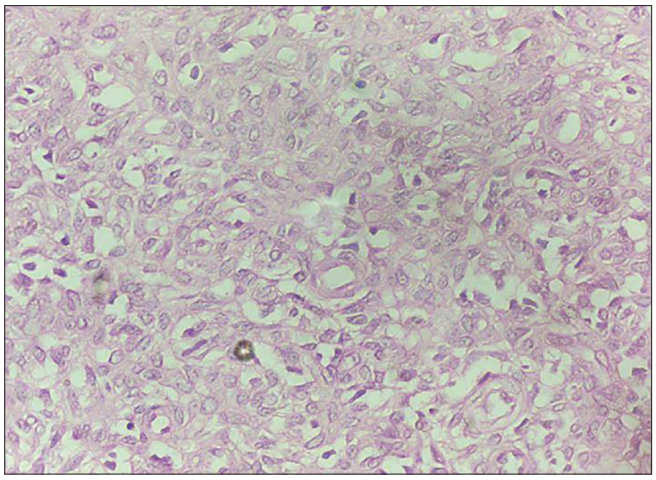

Figure 5: Histopathology of the right tibial tumor—phosphaturic mesenchymal tumor showing round to oval, spindle-shaped cells in a vascular background having a Hemangio pericytoma-like pattern. Presence of myxoid matrix around vascular channels and multi-nucleated giant cells

occurrence has also been reported.[5] Manifestation in bone is extremely rare, but has been reported in tarsal bones also.

Weidner and Santa Cruz[6] classified this heterogeneous group of tumors into four types: Phosphaturic mesenchymal tumor, mixed connective tissue type, osteoblastoma-like tumors; ossifying fibrous-like tumors; and nonossifying fibrous-like tumors. HPC is found to be one of the most frequent causes of tumor-induced osteomalacia.

The main mechanism underlying this disease condition is a circulating phosphaturic factor called phosphatonin, which is in fact, a fibroblast growth factor 23 (FGF-23) intricately involved in phosphate homeostasis and skeletogenesis. It is a 30 kD secreted protein that inhibits renal tubular reabsorption of phosphate and renal conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D.

FGF-23 secretion in the body produces muscle weakness, bone pain, and osteomalacia due to markedly reduced serum phosphorus and renal phosphate. When serum phosphate concentration is < 0.3 mmol/l, symptoms become apparent.[7] The other most frequent underlying abnormality is severe 25-OH vitamin D (25-D) deficiency with secondary hyperparathyroidism and PTH-dependent renal phosphate loss. Serum calcium and PTH levels were normal and 1,25-dihydroxyvitamin D was low in these cases.

Other benign mesenchymal tumors producing oncogenic osteomalacia are fibromas or giant cell tumors, often of the skeletal extremities or skull. It has also been described in sarcomas and in patients with prostate and lung cancer. Resection of the tumor reverses the disorder, confirming its humoral basis.

FGF-23 levels are increased in some, but not in all patients with osteogenic osteomalacia Three possible mechanisms of FGF 23 overexpression can be postulated in these patients, leading to their characteristic presentations.[7] First, increased levels of FGF-23 lead to renal tubular dysfunction and skeletal effects as in our patient. The second plausible explanations after doing genetic studies have been linked to specific mutations of arginine residues at position 176 or 179 of FGF-23, which disrupts the sequence motif recognized by furin proteases, presumably leading to alterations in processing or decreased degradation of the protein—the mechanism being autosomal dominant hypophosphatemic rickets. The next cause may be the loss of function of phosphate-regulating gene with homologies to endopeptidases on the X chromosome (PHEX), which occurs in X-linked hypophosphatemia, resulting in increased circulating levels of FGF-23.

CONCLUSIONS

Localization and resection of the FGF-23-secreting tumor offers the best chance of cure. Final diagnosis in our patient is phosphaturic mesenchymal tumor in the right tibia—hemangiopericytoma-induced osteomalacia with vitamin D deficiency.

We deduced the following points from our case:

Occult vascular bone lesions can be conveniently screened with either a whole body bone scan or more precisely with Tc 99m labeled RBC blood pool scan in patients with high clinical suspicion.

Oncogenic osteomalacia presents as a tetrad of very low serum phosphate level, increased urinary phosphate excretion, inappropriately low to low-normal 1,25-dihydroxy vitamin D levels, and elevated serum FGF-23.

Increased FGF-23 is a useful tumor marker in identification of these tumors as evident in our case.

Many tumors are small and asymptomatic, extensive imaging studies may be required to identify the source. Tc MDP whole body bone scan and RBC labelled scintigraphy are useful, non-invasive, whole body screening investigation, which can be used in any age group to identify occult vascular tumors.

REFERENCES

1. Stout AP, Murray MR. Hemangiopericytoma: Vascular tumour featuring Zimmerman's pericytes. Ann Surg 1942;116:26-33.
2. Hansen T, Gaumann A, Ghalibafian M, Hoferlin A, Heintz A, Kirkpatrick CJ. Haemangiopericytoma of the thyroid gland in combination with Hashimoto's disease. Virchows Arch 2004;445:315-9.
3. Ahmad GF, Athavale R, Hamid BN, Davies-Humphreys J. Pelvic malignant hemangiopericytoma mimicking an ovarian neoplasm; A case report. J Reprod Med 2004;49:404-7.
4. Alhassan MB, Kyari F, Mohammed A. Haemangiopericytoma of the eyelid and orbit: Report of cases. Nigerian Journal of Surgical Research 2003;5:166-70.
5. Pitluk HC, Conn J, Jr. Hemangiopericytoma. Literature review and clinical presentations. Am J Surg 1979;137:413-6.

6. Weidner N, Santa Cruz D. Phosphaturic mesenchymal tumors. A polymorphous group causing osteomalacia or rickets. Cancer 1987;59:1442-54.
7. Knochel JP. The pathophysiology and clinical characteristics of severe hypophosphatemia. Arch Intern Med 1977;137:203-20.

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