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CASE REPORT

Phosphaturic mesenchymal tumour in the temporal bone – A rare presentation

Gaurav Ashish [a,*], John Mathew [b], Nihal Thomas [c], Nitin Kapoor [c], S. Elanthenral [d]

[a] *Christian Medical College, Vellore, India*
[b] *Department of ENT, Christian Medical College, Vellore, India*
[c] *Department of Endocrinology, Diabetes and Metabolism, Christian Medical College, Vellore, India*
[d] *Department of Pathology, Christian Medical College, Vellore, Tamil Nadu, India*

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KEYWORDS

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Abstract *Background:* Tumour-induced osteomalacia (TIO) is a rare clinical entity in which secondary osteomalacia is induced by tumour-related products. There is impaired reabsorption of phosphorus in the renal tubules and hypophosphatemia as a result of over expression of FGF-23 mRNA. Treatment of choice is considered to be total or near total resection of the tumour.

Methods and results: A 49-year-old man had experienced systemic bone pain and bilateral limb weakness for several months. He had refractory hypophosphatemia and marked elevation of serum FGF-23 level. Magnetic resonance imaging (MRI) of the lumbar spine showed a focal lesion in the left temporal bone which was hyper metabolic on positron emission tomography (PET) scan, leading to a diagnosis of TIO. He underwent lateral skull-base surgery after thorough evaluation of the tumour. After the en bloc resection, FGF-23 became gradually undetectable, phosphate reabsorption normalised, and all symptoms were resolved.

Conclusions: We present the clinical features and treatment options for this most unusual manifestation of phosphaturic mesenchymal tumour in the temporal bone.

1. Introduction

Impaired mineralization of osteoid matrix in mature bone leads to a metabolic disorder known as Osteomalacia. Fanconi's syndrome and FGF-23 secreting mesenchymal tumours are acquired causes of Osteomalacia; the latter referred to as TIO or oncogenic osteomalacia.[1]

Last member of FGF family was identified as the Fibroblast growth factor 23 (FGF23). It is produced by bone and reduces serum phosphate level by suppressing phosphate reabsorption in proximal tubules and intestinal

* Corresponding author. Address: PG Registrar, Room No 304, Department Of ENT, CMC Vellore, Vellore 632004, Tamil Nadu, India. Tel.: +91 9626731659.
E-mail address: gauravashish05@gmail.com (G. Ashish).

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phosphate absorption through lowering 1,25-dihydroxy vitamin D level. It has been shown that excess levels of FGF23 result in hypophosphatemic rickets/osteomalacia.[2]

A rare para neoplastic form of renal phosphate wasting which results in phosphaturia, due to defect in vitamin D metabolism, and osteomalacia is known as TIO (Tumour-induced osteomalacia).[3,1,4]

Tumour induced osteomalacia (TIO) is a rare and often unrecognised cause of hypophosphatemia in subjects with adult onset osteomalacia.

We report a case of a 49-year-old man with TIO caused by a FGF-23 secreting mesenchymal tumour localised in the left temporal bone. Confirmation of the diagnosis was obtained by biopsy which revealed a phosphaturic mesenchymal tumour secreting FGF 23. The patient subsequently underwent surgery with en bloc removal of the tumour and subsequent normalisation of biochemical abnormalities.

To our knowledge, this paper represents the first documented case of a phosphaturic mesenchymal tumour secreting FGF 23 located in the temporal bone from India. Our case also highlights the importance of considering TIO when assessing patients with low serum phosphate.

2. Case report

A 49 year old gentleman, presented with the history of pain in bilateral lower limb for 3 years and difficulty in walking for 1 year. Initially it started with pain in right knee, which gradually progressed with involvement of left knee and bilateral hip and whole of lower limb. Initially he had difficulty in getting up from floor and climbing stairs which progressed to need support to get up and use walker for ambulation. He also complained of decreased hearing and intermittent low intensity tinnitus in left ear for the last 1 year.

Ear examination suggested a fleshy mass occluding the left external ear. Bilateral facial nerve was intact on clinical examination. A MR-CT (Fig. 4) revealed a fairly well defined heterogeneous mass in the left temporal bone, showing iso-intensity on T1-weighted images (T1WI) (Figs. 1 and 2), high-intensity on T2WI (Fig. 3), and enhancement with gadolinium in left jugular foramen extending into middle ear cavity and external ear .The lesion caused erosion of middle ear ossicles, bony labyrinth, and facial nerve canal along with moth eaten pattern of bony destruction in the adjacent skull base.

On evaluation patient was found to have hypophosphatemia (1.7 mg %) with Tmp GFR < 0.9, normal serum calcium level (Ca: 9.4 mg/dL) and low serum 1, 25(OH) 2D.

Pure tone audiogram suggested moderate degree of conductive hearing loss in the left ear.

A biopsy of the fleshy mass was done which confirmed a FGF 23 secreting mesenchymal tumour. He was posted for enbloc excision of the tumour via a lateral skull base approach.

Per op findings suggested that tumour was filling the mastoid antrum, aditus, epitympanum, and mesotympanum and hypo tympanum. Sinus plate and dural plate thinned out. Lateral semicircular canal and tympanic segment of the facial nerve eroded. Ossicles were intact but encased in the tumour. Malleus and incus had to be removed along with the tumour tissue in the middle ear. Anterior part of the superior semicircular canal eroded. Facial bridge removed and ridge lowered. Middle ear and mastoid obliterated with fat and lined with fascia lata and temporalis fascia. En bloc excision of the tumour was done with Cul-de-sac closure of the external auditory canal.

Histopathological examination was consistent with FGF 23 secreting mesenchymal tumour.

Immuno histochemistry suggested that the tumour cells were immunopositive for vimentin but negative for SMA, S-100 and CD34 (Figs. 5–7).

He had a high FGF 23 pre operatively and his phosphate levels stabilised after surgery. He had been on Neutral phosphate for 6 weeks. By post-operative week 4, the FGF-23 level was undetectable (preoperative value was 449 RU/mL, and the value on postoperative 6th week was 37 RU/mL) Thereafter, phosphate reabsorption (Tmp/GFR) normalised and all his symptoms improved gradually. Post operative review Computerised tomography shows soft tissue density in the external auditory canal signifying fat and soft tissue as a result of cul-de-sac closure with complete resolution of the pathology

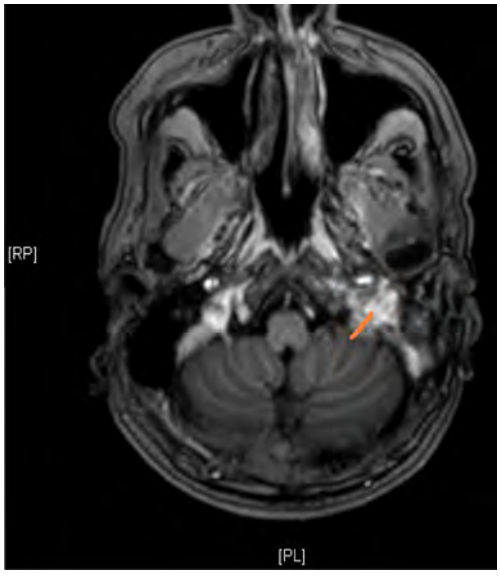

Figure 1 T1W1: Line pointing towards lesion in the left temporal bone.

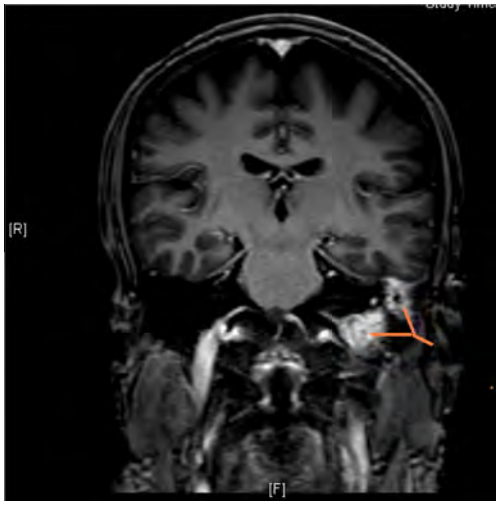

Figure 2 T1W1 coronal view.

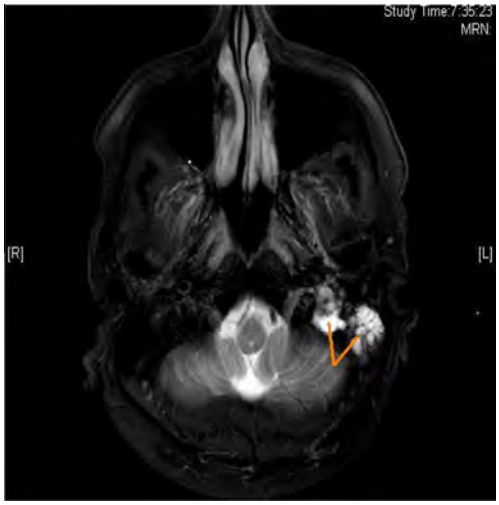

Figure 3 T2W1: Line pointing towards the lesion.

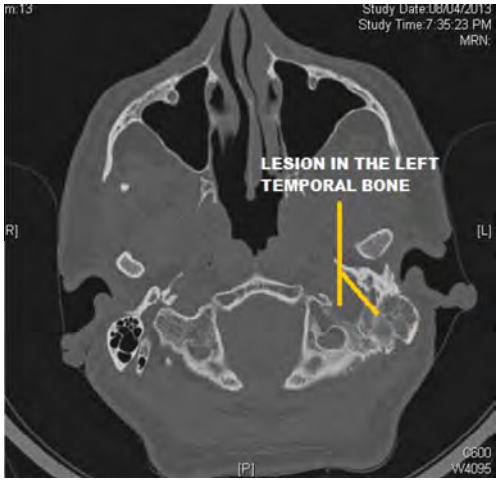

Figure 4 CT Scan image.

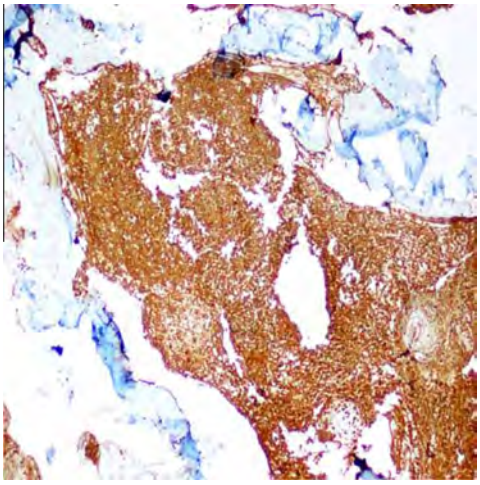

Figure 5 Vimentin positive.

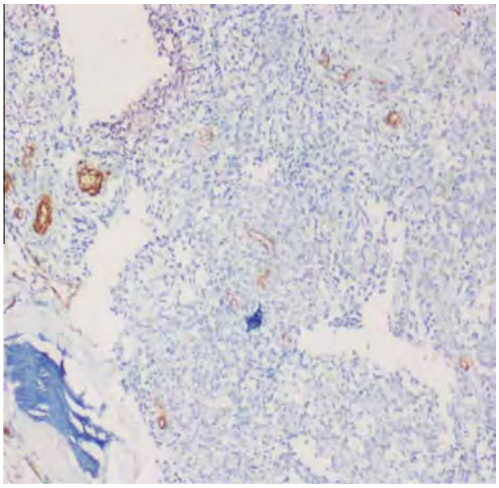

Figure 6 SMA negative.

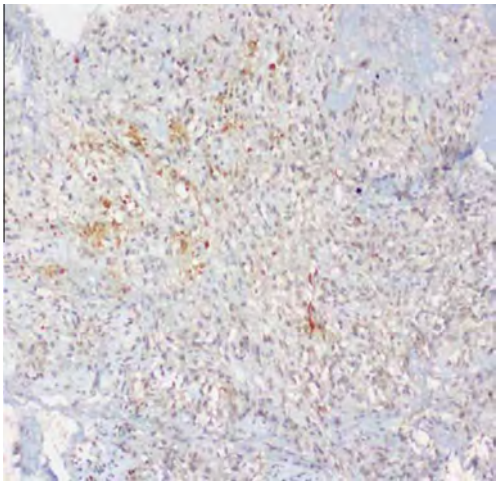

Figure 7 S 100 negative.

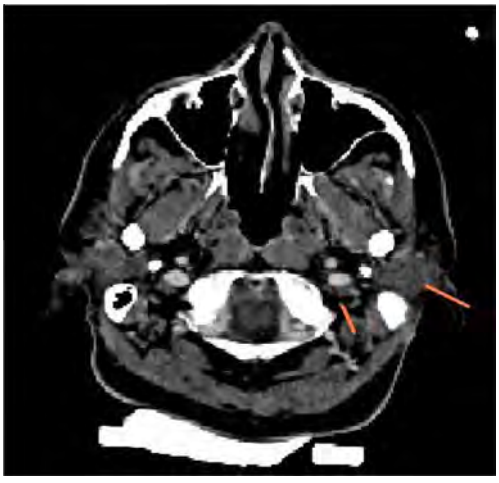

Figure 8 Post op CT scan: line pointing to cul-de-sac closure with fat and soft tissue and another line suggesting resolution of tumour in the left temporal bone area.

from the left temporal region (Fig. 8). He has been followed-up in our outpatient clinic without recurrence for 8 months.

3. Discussion

TIO was first recognised as a disease by Prader *et al* in 1959.[5]

Tumour induced osteomalacia (TIO) is a rare para neoplastic syndrome characterised by hypophosphatemia and abnormal vitamin D metabolism. Usually small tumours that secrete the phosphaturic hormone fibroblast growth factor 23 (FGF23) cause this entity.[6]

Clinicians are often unaware of the existence of TIO, and even if TIO is recognised as a possible diagnosis, localising the instigating tumour may be very difficult .Most patients with TIO can have symptoms for up to 10 years before a definitive diagnosis is made.[7] This was indeed the case for the present patient, for whom it took 3 years to find a primary lesion.

Symptoms of hypophosphatemia include fatigue, weakness, bone pain and occasionally fractures. About 2/3 of dietary phosphate is absorbed in the proximal part of the intestine (duodenum and ileum). The circulating phosphate is filtered by the glomerulus and 85–95% of filtered phosphate is reabsorbed in the proximal tubule of the kidney. Renal phosphate reabsorption can only increase up to a threshold and thereafter phosphate is excreted in the urine.[8]

FGF23 regulates the phosphate homeostasis via 2 mechanisms. First, FGF23 binds to FGF receptor 1c and its co receptor known as klotho, and activation of this receptor complex inhibits reabsorption of phosphate by down expression of sodium-phosphate transporters in the proximal tubule. Secondly, it also decreases the synthesis of 1,25-dihydroxy vitamin D [1,25(OH)2D] in the renal proximal tubules. Both of these effects serve to lower serum phosphate levels.[9,10].

Battery of tests recruited for diagnosing TIO should include serum measurements for phosphate, calcium, alkaline phosphatase, creatinine, PTH and 1,25(OH)D and a fasting 2-h urine for the measurement of phosphate, creatinine, calcium, amino acids and glucose. In addition, the tubular reabsorption of phosphate (TmP/GFR) should be calculated: 1 − urine phosphorous × serum creatinine/urine creatinine × serum phosphorus (milligrams per deciliter), as was done in our case.

Assays for FGF23 have become available which has increased chances of diagnosing FGF23-related hypophosphatemia drastically.[11]

As TIO can be totally cured by complete surgical resection, localising the tumour is critical. These tumours are often found in the unexpected anatomical regions. Thus, a careful physical examination should be focused in these areas. Imaging techniques like MRI, CT or PET scans can be used to image areas of clinical suspicion.[12,13]

This patient's tumour originated in the temporal bone, with erosion of the jugular foramen, which is commonly seen with a glomus jugulare tumour. Glomus tumours are the most commonly diagnosed tumours of this region[14] Differential diagnosis includes meningioma, neural lesion, carcinoma, and occasionally cholesteatoma. Patients with glomus jugulare tumours present with pulsatile tinnitus and hearing loss, as their main complaints were consistent with the patient's clinical history. However Glomus jugulare tumours, histologically, have characteristic clusters (zellballen) of epitheliod chief cells and sustentacular cells with multiple small blood vessels which were inconsistent with our histopathological study.[15]

TIO-associated mesenchymal tumours are generally considered a heterogeneous population; however, roughly 90% represent phosphaturic mesenchymal tumours of mixed connective tissue type as per recent studies.[16–18]

Surgical treatment with en bloc excision of the primary lesion is by far the treatment of choice. Medical treatment of TIO is mainly symptomatic and includes phosphate supplements and calcitriol.[19]The most common side effect of phosphate supplementation is diarrhoea. Patients should be carefully monitored for hypercalciuria and nephrocalcinosis. Cinacalet (a calcium-sensing receptor agonist) can be used as an adjunct to induce hypoparathyroidism. This helps due to the fact that full phosphaturic effect of FGF23 is dependent on PTH.[20]

The tumour may arise from any mesenchymal tissue, including bone and soft tissue. In head and neck, only few documented cases have been found in sinonasal area, mandible, nasopharynx, skull base, and gingiva.[21]

Tumour origin in the temporal bone, as in the present case, appears to be extremely rare; to our knowledge the literature contains only two other similar cases.[22,23].However this seems to be the first such case report from India.

4. Conclusion

In conclusion, we investigated and managed a 49-year-old man with TIO in whom the primary lesion was in the left temporal bone. Although this is a rare site for the primary lesion, clinical features and pathologic findings were typical. Along with specific laboratory tests, serum level of FGF-23 aided the diagnostic process and also helped in periodic assessment of the patient.

Other possible causes of renal phosphate wasting with elevated FGF23 were ruled out due to the fact that our patient was well until the age of 49 years with no family history of bone disease or hypophosphatemia. Moresoever biopsy proved the pathology in the left temporal bone to be FGF 23 secreting mesenchymal tumour which was removed by lateral skull approach in toto. After complete resection, all symptoms were resolved and he has remained free of recurrence for 8 months. Our patient's clinical course highlights both the difficulty in diagnosing TIO and the rapid clinical improvement when the tumour is removed.

Competing interests

None.

Sponsorships

None.

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