Tumour-induced Osteomalacia Secondary to Intracranial Tumours – Report of 2 Cases

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Abstract

Tumor-induced osteomalacia (TIO) is a paraneoplastic syndrome which is mostly caused by a phosphaturic mesenchymal tumour mixed connective tissue variant (PMTMCT). These tumours do not have any specific site predilection but their presence in cranial compartment is very rare. Two cases of TIO secondary to phosphaturic mesenchymal tumour at the skull base are described ahead, one of which was in the posterior fossa and the other in middle cranial fossa. Early diagnosis and complete excision of PMT is essential in preventing morbidity secondary to osteomalacia. This case report stands distinct in highlighting a rare site of a phosphaturic mesenchymal tumour and the need to keep a high index of suspicion in cases of TIO especially wherein localization of the tumour is unsuccessful.

Case Summary 1

A 53-year-old female presented with longstanding history of bilateral hip and knee joint pain, along with low backache. Though she took symptomatic treatment for 5 years, she never had satisfactory relief. She had started developing proximal muscle weakness along with walking difficulty. Biochemical tests showed low level of serum phosphorus. Bone densitometry showed osteopenia and two MRI scans of bilateral hip joints done over a period of one year showed nonspecific osteoporotic changes and pathological fracture of neck of femur. Serum fibroblast growth factor-23 (FGF-23) level was 725 RU/ml, which was high compared to reference value of 180. High FGF-23 was suggestive of tumour induced osteomalacia but tumour was not evident on MRI of the neck, chest, abdomen and pelvis. To help in localization, a Somatostatin receptor positron emission tomography PET-CT scan was done and it revealed a tumour in the left jugular foramen region involving posterior skull base and part of occipital condyle (Figure 1). Contrast enhanced MRI of the brain showed an homogenously enhancing extraaxial tumor in the region of jugular bulb (Figure 2). Surgical excision of tumor was necessary to reverse the symptoms of osteopenia and in view of the subtle neurological deficits. Preoperative embolisation of feeders from ascending pharyngeal and occipital artery was performed and surgical excision of tumor was carried out with retromastoid craniotomy. A completely extradural bony tumour was seen in the jugular region with occasional involvement of outer dural surface. Total excision of tumour was possible.

Histopathological examination revealed neoplastic tissue containing giant tumor cells composed of oval to short fusiform cells arranged in sheets and fascicles within a vascularised stroma. The neoplastic cells contained scant cytoplasm and uniform bland appearing nuclei. It also showed trabeculated osteoid and reactive fibroblast proliferation without evidence of sarcomatous change. Diagnosis of phosphaturic mesenchymal tumor of skull base was made.

Post-operative dynamic CT scan of cervico-vertebral junction showed no instability. Patient’s serum phosphorus level started improving. At last follow-up after 6 months, serum phosphorous was 2.7 mg/dl and FGF-23 levels were 135 RU/ml.

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These tumours secrete FGF-23, which inhibits phosphate reabsorption from renal tubules. This leads to hypophosphatemia, reduced calcitriol production, impaired bone metabolism, osteomalacia and impaired healing of fractures. In contrast to Parathormone (PTH), it has no effect on calcium metabolism, its action is not blocked by a PTH antagonist, and its effects do not appear to be mediated by cyclic AMP. Often such patients have long history of nonspecific symptoms of bone pain, weakness, fatigue or pathological fracture due to osteomalacia. Diagnosis of PMT is often delayed. The 2 cases reported here too had long history of bilateral hip and knee joint pain. Old age and menopause were considered causative reasons for symptoms before detailed investigations lead to final diagnosis. The diagnosis of TIO should be suspected from the clinical picture of an acquired hypophosphatemia and osteomalacia/rickets in association with renal phosphate wasting, absence of proximal tubular defects and an inappropriately low plasma calcitriol concentration. Serum levels of FGF-23 are elevated in PMT. However localisation of tumor is challenging. They are generally located in appendicular skeleton or sino-nasal region. Intracranial location of PMT/MCT is uncommon and intracranial tumors are unlikely to manifest as paraneoplastic syndrome. Therefore cranial compartment is often excluded from screening for tumor localisation leading to delayed diagnosis.

Recent studies have tested and defined a systematic approach to tumor localisation in patients, in whom there was a failure of initial localization of the tumor or in cases wherein re-localization was needed viz. recurrence or metastases. A multimodality approach was employed. Functional imaging studies included whole body 111In-octreotide single photon emission computed tomography (SPECT) and, if necessary, whole body 18-fluorodeoxyglucose PET/CT and anatomic imaging i.e. CT, MRI. Selective venous sampling was performed to discriminate a functional mass when multiple suspicious lesions were discovered.

Mathis et al. reviewed intracranial PMTs and found that all 8 reported cases of intracranial PMT were in the anterior cranial fossa except one case where tumor was in cavernous sinus. No case report in present literature describes occurrence of PMT in posterior fossa. Histologically these tumors are of mesenchymal origin with or without aggressive sarcomatous change.

Intracranial PMTs are often confused with meningioma, hemangiopericytoma and esthesioneuroblastoma on imaging. They are often neurologically silent so correlation between tumor and osteomalacia should be established before surgery.

After surgical excision of tumour, serum phosphate levels should normalize within a week. Serum FGF-23 level rapidly falls down after excision of tumor however it does not normalize and achieves a level which is just above normal. Complete excision of PMTs is the treatment of choice whenever feasible. Stereotactic radiotherapy may represent a viable treatment option for patients who are not ideal candidates for surgery or refuse surgery. However the effects manifest in a delayed phase and the pros and cons of radiation must be taken into account prior to initiation.

**Conclusion**

Early diagnosis and complete excision of PMTs is necessary for avoiding morbid effects of TIO. There has been a better understanding of this condition in recent years leading to fairly early diagnosis and effective treatment. Clinicians must be aware of cranial location of PMTs as well and should include skull base and brain imaging in evaluation of a patient with TIO.

**References**