case report

Perioperative concerns in patients with tumor-induced osteomalacia for surgical excision of tumor

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Ann Saudi Med 2012; 32(6): 656-658

DOI: 10.51444/0256-4947.2012.26.5.1113

Tumor-induced osteomalacia (TIO) or oncogenic osteomalacia is a paraneoplastic syndrome, usually associated with mesenchymal tumors. TIO is probably an underreported entity owing to diagnostic and localizing limitations. With improvement in such modalities, patients with TIO are likely to be encountered more frequently in future anesthetic practice. It does not respond to conservative medical management; thus surgical resection of the lesion is the treatment of choice. Anesthetic management of such cases has not been reported in published studies and thus we report two such cases of hypophosphatemia, induced by frontoethmoidal tumors and the anesthetic implications and challenges of such a rare entity. Surgical excision of the causative lesion results in dramatic resolution of symptoms. Vigilant adherence to the pertinent perioperative concerns related to severe hypophosphatemia is crucial to a favorable surgical outcome in these patients.

Tumor-induced osteomalacia (TIO) or oncogenic osteomalacia is a paraneoplastic syndrome characterized by hypophosphatemia, hyperphosphaturia, and a low 1,25-dihydroxy vitamin D level resulting in multisystemic manifestations.[1] It is usually associated with mesenchymal tumors secreting a humoral factor (FGF-23), a member of fibroblast growth factor family, which inhibits reabsorption of phosphate through the proximal renal tubule by down-regulation of type IIA sodium phosphate cotransporter.[2,3] TIO is commonly associated with tumors that are located in the craniofacial region and in the extremities; hence localization can be done with the help of a CT scan, MRI, octreotide scan, and positron emission tomography (PET) scan.[4-6] A mixed connective tissue-type phosphaturic mesenchymal tumor comprises approximately 70% to 80% of the tumors associated with TIO and reportedly involves the paranasal sinuses in 6.2% of cases.[7] It does not respond to conservative medical management; thus surgical resection of the lesion is the treatment of choice.[4-6] We tried to focus on the anesthetic concerns in patients with TIO based on our recent experience of two such cases.

CASE 1

A 51-year-old Indian male presented to the department of endocrinology and metabolic diseases at our institute with complaints of generalized body ache and muscle weakness for the past 2 years. The progressive muscle weakness was more in the proximal muscles and gradually led to an inability to bear weight. Serum biochemistry revealed normal calcium and parathormone levels with severe hypophosphatemia (phospahate, PO4 level 1.2 mg/dL) and a high level of serum alkaline phosphatase (770 IU/L [normal range - 20 to 140 IU/L]). Renal parameters were within normal limits. He was started on oral phosphate supplementation (3 g/day), but without significant clinical and biochemical improvement even after 2 weeks. Renal parameters were within normal limits. A CT scan of the thorax and abdomen were normal while MRI of the whole spine revealed a diffuse bulge of the disk annulus at L4-5 and L5-S1 levels with minimal thecal indentation. The PET scan using 18F-FDG (fluoro-deoxyglucose) revealed active uptake by a soft-tissue mass lesion in the left anterior ethmoidal sinus. A provisional diagnosis of tumor-induced osteomalacia was established. Hence

ethmoidectomy was planned for this patient. We reviewed the history and tests and focused on manifestations of hypophosphatemia perioperatively. The patient had severe proximal myopathy and respiratory muscle weakness manifested by poor coughing ability and decreased breath holding time of 11 seconds. There was no cardiovascular or neurological involvement. Airway examination was within normal limits. Based on severe restrictive pulmonary disease based on clinical findings and a pulmonary function test, the possibility of postoperative ventilatory support was explained to the patient and consent was taken. Oral phosphate supplementation was continued until the day of surgery. On the day of surgery the patient was shifted in the operating room and monitors including electrocardiography (ECG), pulse oxymetry, noninvasive blood pressure, end-tidal carbon dioxide, and a neuromuscular monitor were attached. Temperature and urine output were also monitored. Anesthesia was induced with intravenous thiopentone 200 mg and fentanyl 100 μg, and endotracheal intubation was facilitated by administering atracurium 25 mg. Anesthesia was maintained with isoflurane 1% in O2/N2O (50:50) (MAC 1–1.2), fentanyl [1 μg/(kg/hour)], and neuromuscular monitor-guided atracurium boluses. The surgery lasted for 3 hours with a blood loss of approximately 600 mL, which was replaced with a balanced salt solution. At the end of the surgery, residual neuromuscular block was reversed and the trachea was extubated after the TOF ratio exceeded 0.9. The patient was conscious, pain-free, and normothermic, and was monitored overnight in the high-dependency unit. In the first postoperative week, clinical symptoms and serum biochemistry improved dramatically-serum PO4 levels became 2 .8 mg/dL (normal, 2.5-4.5 mg/dL) on the postoperative day 2 itself, and muscle weakness gradually resolved.

CASE 2

A 45-year-old Indian male presented with bone pain, nasal obstruction, and proximal muscle weakness for 7 years, which progressively worsened and he was almost bedridden for the last 1 year. He was operated on for suspected rhinosporidosis of the left nostril 8 years back, which on histopathologic examination revealed hemangiopericytoma. He also had a history of pathological fractures of the right humerus and left femur following trivial trauma. He was receiving oral phosphate supplementation (NaH2PO4 + Na2HPO4) 3 g/day with no symptomatic improvement. The biochemical investigation revealed a low serum PO4 (1.4 mg/dL), a decreased ratio of maximum rate of renal tubular reabsorption of phosphate to glomerular filtration rate (TmPO4/GFR), similar to that in the previous case, and a high level of serum alkaline phosphatase (480 IU/L [normal range: 20-140 IU/L]). MRI revealed a recurrent mass in the left nasal cavity with intracranial extradural extension into the frontal and sphenoid sinus. A pulmonary function test revealed a combined restrictive and obstructive pulmonary disorder (FVC [forced vital capacity) 49%, FEV1 [forced expiratory volume in second] 50%, PEFR [peak expiratory flow rate] 65% of predicted value). A similar anesthetic technique as that of case 1 was followed in this patient with a special emphasis on careful positioning during induction and while shifting him postoperatively.

DISCUSSION

In both our patients, TIO was associated with mesenchymal tumors of the paranasal sinuses. Increased renal excretion of phosphorus was noted based on the decreased value of the maximum transport of PO4 in the renal tubules relative to the glomerular filtration rate (TmPO4/GFR) (0.5 mmol/L, normal range 0.8-1.4 mmol/L). Parathyroid hormone (PTH) being the chief physiologic regulator of renal reabsorption of phosphate, the detection of normal PTH levels with decreased tubular reabsorption of phosphorus prompted the search for ectopic causes. A skeletal survey and bone scan suggested a metabolic bone disease with multiple pseudofractures in ribs and bilateral subtrochanteric regions.

Moderate-to-severe hypophosphatemia is the hallmark of TIO and can potentially result in multiple organ dysfunction primarily because of a decrease in intracellular adenosine triphosphate and 2,3-diphophoglycerate.[8] These changes are of great concern in the perioperative management of these patients for any surgical procedures. Hypophosphatemia has been implicated as a cause of rhabdomyolysis, chronic myopathy, respiratory failure, hemolysis, osteomalacia, and left ventricular dysfunction. Untreated severe osteomalacia may lead to pathological fractures of the vertebrae and ribs, resultant chest wall deformity, and respiratory compromise.[1] Decreased diaphragmatic contractility, low maximal inspiratory pressure, or low maximal expiratory pressure and failure in weaning from ventilatory support has been attributed to hypophosphatemia.[9] Also, hyperventilation with resultant respiratory alkalosis and infusion of dextrose-containing fluid exacerbates hypophosphatemia by stimulating movement of phosphorus into cells. It also leads to reversible cardiomyopathy and ventricular arrhythmias, and may also induce an impaired response to vasopressor agents.[10] Hypophosphatemia is associated with impaired glucose metabolism in both

hyperglycemic and euglycemic states. This effect is primarily a reflection of decreased tissue sensitivity to insulin. Hemolytic anemia and reduced chemotaxis and leukocytic bactericidal activity have also been reported in hypophosphatemia.[10] The neurologic sequelae of severe hypophosphatemia include central and peripheral neuropathy, central pontine myelinolysis, seizures, and coma. A severe neuropathy resembling Guillain-Barré syndrome has also been reported recently.[11] TIO is characterized clinically by adult-onset bone pain, muscular weakness, and multiple fractures with dramatic recovery after complete resection. All these manifestations of hypophosphatemia and possible complications from phosphate supplementation are of concern to anaesthesiologists when a patient with TIO presents for surgical resection.[9] Positioning of the patient during movement to the operating room and induction of anesthesia in the perioperative period should be done with utmost caution because of severe osteomalacia, the risk of pathological fractures, and skeletal deformities. This is also implicated during positioning for regional anesthetic techniques and hence feasibility should be assessed in the preanaesthetic evaluation. Based on the severity of respiratory compromise, postoperative ventilatory assistance should be anticipated. However, both our cases could be extubated in the operating room. Features of cardiomyopathy and ECG changes suggestive of arrhythmias should be noted preoperatively, and the need for invasive monitoring may be anticipated. These were not present in our cases. Peripheral neuropathy should also be documented prior to regional anesthetic procedures.

TIO is probably an underreported entity owing to diagnostic and localizing limitations. With improvement in such modalities, patients with TIO are likely to be encountered more frequently in future anesthetic practice. Vigilant adherence to the pertinent perioperative concerns related to severe hypophosphatemia is crucial to the favorable surgical outcome in these patients.

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