Tumor-induced osteomalacia with IgG4-related lymph node disease

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To the Editor: A 60-year-old man presented with progressively worsened limb weakness of 4 years duration, which had rendered him wheelchair-bound since May 2018. The patient also had muscle and joint pain and numbness. He had a history of type 2 diabetes, hypertension, and gout, no family history of bone disease. He took diabetic peripheral neuropathy treatment but the symptoms kept progressing. On admission, the patient was well developed and in normal body shape. Physical examination was unremarkable except for all-sided weakness. Laboratory evaluation showed hypophosphatemia with notable elevated vitamin D status, and mild elevated parathyroid hormone. Other laboratory abnormalities were elevated alkaline phosphatase levels, mild insufficient urinary phosphorus loss. He reported normal serum phosphorous level of 2.75 mg/dL (normal: 2.5-4.5 mg/dL), and abnormal urinary phosphate wasting. The increased urinary phosphorus loss. The increased phosphaturic hormone produced by tumors leads to decreased renal phosphate reabsorption through reduction of the sodium-phosphate co-transporter expression in the proximal renal tubule. Clinically, patients suffering from TIO may develop weakness, fatigue, bone, muscle pain, and fractures.

Tumors resulting in TIO are often too small to localize by conventional radiologic methods. In the case that an anatomical imaging (CT or magnetic resonance imaging) fail to detect the tumors, scintigraphy with a radiolabeled somatostatin analog or 18F-DOTATATE were performed to make clear diagnosis of oncocytic hypophosphatemic osteomalacia. Both of the examinations revealed a suspicious mass in subcutaneous tissue around the umbilicus and enlarged right axillary lymph nodes [Figure 1A and 1B].

The patient was subjected to surgery for resection of the subcutaneous mass and enlarged right axillary lymph nodes after obtaining written informed consent. The subcutaneous mass was red, round-shaped without necrosis. It displayed spindle-shaped cells with oval nuclear and eosinophilic cytoplasm, and characteristic scattered cloud-like calcium deposits under histologic examination. No atypical cells, abnormal mitotic activity, or necrosis were observed [Figure 1C]. On the basis of its morphologic and immunohistochemical features, the tumor was diagnosed as a phosphaturic mesenchymal tumor. Interestingly, histologic examination of lymph nodes revealed immunoglobulin G (IgG) 4-positive plasma cells >100 cells per high-power field, and the IgG4-positive rate was up to 70% of IgG-positive plasma cells in intrafollicular zones [Figure 1D]. Supplemental laboratory testing demonstrated elevated IgG4/IgG ratio, thus an IgG4 lymph node disease could be diagnosed.

The patient was released from the hospital after a rapid recovery of serum phosphorous [Figure 1E] and urinary phosphorus loss. He reported normal serum phosphorus and significantly improved symptoms during our one and a half months follow-up.

IgG4-related diseases (IgG4-RD) is a fibro-inflammatory condition involving multiple organs characterized by storiform fibrosis, increased serum IgG4 level, and inflammatory infiltrate with IgG4-rich plasma cells. It was reported that patients with IgG4-RD had higher risks of solid and hematologic malignancies than the general population.[1,2] Furthermore, history of malignancy may be related to subsequent IgG4-RD development.[3] However, the connection between IgG4-RD and malignancy...
still remains unclear. Some studies claimed no connection between IgG4-RD and malignancy. A Japanese prospective study found that the incidence of total malignancies in IgG4-RD patients was similar to that in the general population[4]. Pathogenesis of IgG4-RD and TIO are totally different as immunity-related and FGF-23 related. We speculate that there is no association between TIO and IgG4-RD in this patient.

Here, we presented a 60-year-old man who had suffered from severe clinical manifestations of TIO due to a mesenchymal tumor in the umbilicus and was discovered an IgG4 lymph node disease accidentally. In this case, the tumor was identified by 68Ga-DOTATATE PET/CT and surgical removal of the tumor resulted in significant relief of symptoms and hypophosphoremia. When meeting with unexplained bone pain and fatigue, TIO should always be taken into consideration and scintigraphy with a radiolabeled somatostatin analog should be applied early when routine examination failed to detect tumors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the article. The patient understands that his name and initial will not be published and due efforts will be made to conceal the identity of the patient, although anonymity cannot be guaranteed.

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Conflicts of interest

None.

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