Osteomalacia revealing a Synovial Sarcoma of the Nasal Cavity


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ABSTRACT
Oncogenic osteomalacia is an acquired, rare paraneoplastic syndrome characterized by renal phosphate wasting and subsequent hypophosphatemic osteomalacia. We report a case of oncogenic osteomalacia associated with phosphaturic mesenchymal tumor in a 41-year-old woman. She presented with pelvicrural pain. There was also a lateral-left nasal swelling 3 cm in diameter with no other symptoms. BMD revealed a remarkable decrease in lumbar spine BMD (Tscore to -5.2 DS). Radiologic examination showed multiple pathologic fractures of the pelvis. Severe hypophosphatemia, hyperphosphaturia, low plasma 1,25-dihydroxyvitamin D3 level were disclosed at presentation. Computed tomography of the facial bones showed a large tumor formation of the left nasal cavity in connection with a synovial sarcoma (SyS) confirmed by immunohistochemistry. After removal of the tumor, biochemical and hormonal abnormalities disappeared with remarkable symptomatic improvement. In conclusion, although an extremely rare disease, clinicians and pathologists should be aware of the existence of Tumor induced osteomalacia.

KEYWORDS: oncogenic osteomalacia; tumor induced osteomalacia; causes of osteoporosis; causes of low BMD; mesenchymal tumor; synovialosarcoma.

BACKGROUND
The oncogenic osteomalacia (OO) is a rare paraneoplastic syndrome associating hypophosphatemia, hyperphosphaturia, a low concentration of 1,25- (OH) 2 vitamin D and severe osteomalacia.[1,2] The initial abnormality is unregulated secretion of fibroblast growth factor 23 (FGF 23) by mesenchymal slow-growing tumors.[3] The association of OO with synovial sarcoma (SyS) is exceptional. We report a case of SyS of the nasal cavity revealed by osteomalacia.

OBSERVATION
A 41 years old, from Mauritania, with repeated history of epistaxis, consulted for pelvicrural pain with a progressive worsening of her general condition for the past 18 months. The spine, hips and sacroiliac joints were normal. Furthermore, there was a lateral-left nasal swelling of 3 cm in diameter. Radiographs revealed malunion at the ischiopubic branches with a washed out aspect of the lumbar spine without vertebral fractures. Bone densitometry showed severe osteoporosis profile with a T-score -5.2 SD at the lumbar spine and -5.1 at the proximal femur (corresponding respectively to Z score -4.1 and -3.9DS). ESR was 45 mm and CRP 8 mg /l. The protein electrophoresis showed a slightly raised polyclonal gamma globulin. Calcemia was normal (2.24 mmol /l), serum phosphorus was low (0.18 mmol /l compared to laboratory reference range [0.87 - 1.5 mmol/l]) with an elevated alkaline phosphatase to 3 times normal (300 UI/l laboratory normal values: [40 - 98 UI/l]) and hyperphosphaturia (30 mmol / 24 hours, laboratory normal values: 10 - 20 mmol/24h). Glycosuria was negative and chromatography of urinary amino acids was normal. 25-OH vitamin D was normal (32 µg /L with normal range: 30 to 80 µg /L) but the 1, 25 (OH) 2 vitamin D was low (11 pg/ml, laboratory normal values: 20-76 pg/ml). Parathyroid hormone was normal. The determination of fibroblast growth factor 23 (FGF 23) could not be achieved. This measurement is not available in our laboratory. Computed tomography of the facial bones (fig 1) showed a large (30mm *17*12 mm) aggressive highly vascular tumor formation expansive in left nasal cavity. The thoracic, abdominal and pelvic CT scans were normal.
Fig 1: Computed tomography of the facial bones (fig 1): A large tumor formation expansive in the left nasal cavity repressing the nasal septum, the lateral wall of the maxillary sinus and the ipsilateral papery blade that ruptured, and a tumor extension at the orbit, of the side portion of the frontal sinus and facing the left olfactory tract.

Biopsy of the tumor mass (fig2) showed a proliferation of spindle cells with ovoid nuclei without frank atypia and moderate mitotic index, expressing immunohistochemistry, Bcl2 and S100 protein.

**DISCUSSION**

In this observation, the diagnosis of OO was retained after elimination of other causes of hypophosphatemia and regression of biological and clinical picture after removal of SyS.

The OO is a rare paraneoplastic syndrome occur at any age, it is more frequent in adults (160 reported cases in the literature). It affects both sexes equally. The diagnosis is usually delayed for months or years, due to the low prevalence of the OO. In our case the OO presented with In accordance with other severe, painful fractures and a myopathic like picture with hypophosphatemia, hyperphosphaturia and a low 1,25 (OH) 2 vitamin D.

The OO has been reported in benign (and more rarely in malignant) mesenchymal tumors secreting a phosphaturic factor, in particular FGF23 which inhibits tubular phosphorus reabsorption and the 1 alpha hydroxylation of vitamin D.\[14\]

In our case, the OO was associated with SyS of the nasal cavity revealed by nosebleeds, aggressive radiologically and confirmed by immunohistochemistry. In fact, the SyS is a malignant mesenchymal tumor that usually affects the soft tissues of the lower limbs in adolescents and young adults. Its facial location represents 3-5% of soft tissue sarcomas of the head and neck and often interested mandible\[15\] and oro-pharyngeal regions\[5,7\]. The multitude of its histopathological aspects may be the cause of diagnostic confusion. Immunohistochemistry, sometimes aided by cytogenetic examination showing a specific sarcoma translocation, is necessary for the diagnosis.\[8\]

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The association OO with SyS is exceptional. The only case of SyS induced OO reported in the literature was associated with a low grade metatarsal SyS in a 34-year-old male patient.\[9\] Moreover, tumors of the facial cervical region reported as inducing OO were mainly hemangiopericytoma, hemangiomass\[10,11\], and very rarely giant cell tumors.\[12\] Their diagnosis is most often difficult due to the small size of the tumor and its unusual location, requiring in-depth investigations such as whole body MRI\[2\] or whole body PET- CT.\[4\]

Treatment of OO is the removal of the tumor, leading to a biological and clinical normalization, often spectacular, as is the case of our patient. When the tumor can not be located, symptomatic treatment with a phosphate supplementation and calcitriol (1,25 (OH) 2 vitamin D3) may be beneficial. Other treatments are still under consideration including a monoclonal antibody against FGF 23 (anti FGF 23).\[13\]

**CONCLUSION**

OO is a rare, severe and difficult to diagnose condition, imposing a relentless search for the responsible mesenchymal tumor. Thus rare tumors of the facial
cervical region should be sought, even in the absence of clinical symptoms. Recovery is obtained by the resection of the responsible.

REFERENCES