Tumor-induced hypophosphatemic osteomalacia as a rare cause of bone pain

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A 49-year-old female patient in a good general condition was admitted due to pain in the attachments of the lower ribs to the sternum, distal femurs, tibias, and fibulas, as well as lower limb muscles, persisting for 3 years. Medical history revealed hyperthyroidism treated with radiodine therapy a few years earlier. Because of subsequent hypothyroidism, the patient additionally used levothyroxine. Her serum phosphate levels were reduced for the past 2 years (1.17–1.7 mg/dl; reference range, 2.7–4.5 mg/dl). The family history was negative for hypophosphatemia. Based on an interview and clinical data, we had no reason to suspect increased phosphate displacement from the extracellular to intracellular space due to hypophosphatemia.

Because of a suspected phosphorus loss in urine, daily urine collection was performed; a tubular reabsorption of phosphate was 62% (reference range >86%). The ratio of the tubular maximum reabsorption of phosphate was 0.87 mg/dl (reference range, 3.0–5.0 mg/dl). The results confirmed renal phosphate wasting. The serum concentrations of sodium, potassium, calcium, magnesium, parathyroid hormone, alkaline phosphatase, and creatinine were normal. The levels of venous blood gases, 25(OH)D3, 1,25(OH)2D3, as well as the results of complete blood count and urinalysis, were normal.

Considering other causes of hypophosphatemia, we tested the patient for oncogenic hypophosphatemia, using abdominal ultrasound, gastrointestinal endoscopy, mammography, and classic chest X-ray. Skeletal scintigraphy with 99mTc Na2HPO4 and NaH2PO4, and additional calcium phosphate supplementation (a mixture of Na2HPO4 and NaH2PO4, and additional calcium). A gradual clinical improvement and an increase in the phosphate concentration were observed. Skeletal scintigraphy at approximately 2-year follow-up showed significant bone lesions (FIGURE 1B). However, due to persistent hypophosphatemia and elevated FGF-23 concentrations despite the resolution of symptoms, we decided to perform another scintigraphy using somatostatin analogs. Somatostatin receptors type 2 and 5 were clearly visible in the occipital region (FIGURE 1F and 1G), suggesting mesenchymal cancer producing the phosphaturic factor. We performed 18F-fluorodeoxyglucose positron emission tomography/computed tomography, which confirmed the tumor site and its malignant type (FIGURE 1H–1J). Magnetic resonance imaging showed features of pathological tumor vascularization (Supplementary material, FIGURE S1).

Due to the biological behavior of the tumor-induced hypophosphatemic osteomalacia and its rare incidence, a comprehensive evaluation of medical, laboratory, and radiographic findings is crucial for a definitive diagnosis.
**FIGURE 1**

A – skeletal scintigraphy (2013) showing foci of increased osteotropic marker accumulation in the ribs on the front and back sides of the chest, at the lesser trochanter and in the shafts of both femurs, uneven marker collection within vertebrae Th3–Th9 in the spine, diffuse accumulation in sacroiliac joints, large intensive foci in the front and medial condyles of the right tibia (arrows);

B – skeletal scintigraphy (2015) showing a lower uptake of osteotropic marker in the ribs, slightly more intense uptake in the focus at the lesser trochanter and the foci in the shafts of both femurs, uneven and lower uptake in the spine (invisible collection in Th3–Th9), slightly increased accumulation in the sacroiliac joints, lower uptake in the medial condyle of the right tibia; a new focus on the smaller right trochanter of the femur and the lateral femoral condyle (arrows);

C – single-photon emission computed tomography and computed tomography (2013), front projection: increased uptake in the osteotropic marker inside the thickened cortex of femur shafts (arrows);

D – left femur X-ray visible focal Looser–Milkman zone in the thickened cortex of the vertebral body (arrow);

E – chest X-ray: history of broken ribs VI and VII on the right side and rib V on the left side (arrows); visible bone junctions with the local reconstruction of the bone at the site of fracture (arrows)
**REFERENCES**


**SUPPLEMENTARY MATERIAL** Supplementary material is available with the online version of the article at www.pamw.pl.

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