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A Rare Case of Tumor-Induced Osteomalacia Secondary to a Benign Glomangioma

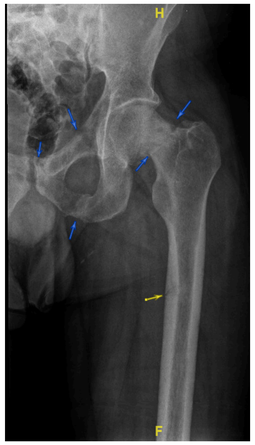
Tiffany Tsang, MD; Rakhee Barai, MD; Lissette Cespedes, MD
Department of Endocrinology, Rutgers New Jersey Medical School

Background

Tumor-induced osteomalacia (TIO), a rare paraneoplastic syndrome, ectopically secretes fibroblast growth factor 23 (FGF23) and prevents phosphate reabsorption by suppressing renal Na/Pi cotransporter and inhibiting 1-α-hydroxylase. Tumor localization can be challenging.

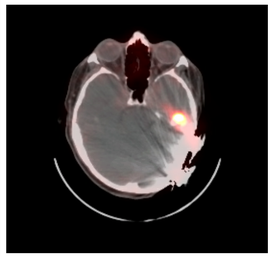
Clinical Case

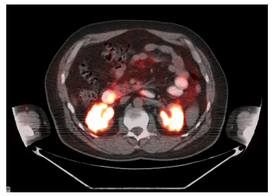
A 42-year-old male with an incompletely resected left mastoid glomangioma presented with widespread, unprovoked fractures for the past four years. He had a DEXA scan which showed low bone mass and a bone scan which showed innumerable foci of increased activity in the axial and appendicular skeleton. Previous workup for multiple myeloma was negative. A phosphorus level was never ordered. On exam, there was tenderness to palpation in his forearms and he ambulated with crutches. A skeletal survey revealed diffuse subacute fractures and impending fractures of the femurs. Labs were obtained (as shown in the tables). Tubular maximum phosphate reabsorption per GFR (TmP/GFR) was low at 0.43mmol/L (0.99-1.34mmol/L) indicating high urinary phosphorus excretion. Intact FGF23 level was elevated to 93pg/mL (<22pg/mL) and genetic testing for hypophosphatemic rickets was negative. A ^{68}Ga-DOTATATE CT/PET scan revealed an intense focal uptake in the left temporal bone (SUV max 19.0) at the site of his glomangioma resection. Laboratory and imaging findings confirm a diagnosis of TIO, secondary to incompletely resected glomangioma. Burosumab was initiated while he awaits radiation therapy to definitively treat the residual tumor, which may lead to cure of TIO.

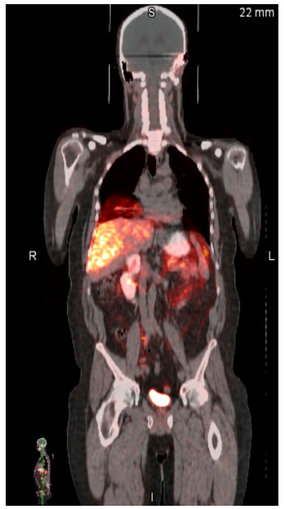


Skeletal survey with diffuse subacute fractures, and impending fractures of the left femoral neck and femoral shaft.

^{68}Ga-DOTATATE CT/PET scan showed a somatostatin receptor-positive lesion in the left temporal bone (SUV max 19.0) which is more intense than the numerous foci of uptake in areas of fractures.







Comprehensive metabolic profile	
Sodium	143 mEq/L (133 - 145 mEq/L)
Potassium	4.1 mEq/L (3.5 - 4.8 mEq/L)
Chloride	108 mEq/L (97 - 110 mEq/L)
Bicarbonate	25 mEq/L (23 - 30 mEq/L)
BUN	18 mg/dL (6 - 20 mg/dL)
Creatinine	0.8 mg/dL (0.7 - 1.2 mg/dL)
Glucose	113 mg/dL (70 - 109 mg/dL)
Calcium	8.8 mg/dL (8.4 - 10.2 mg/dL)
AST	11 U/L (0 - 40 U/L)
ALT	12 U/L (0 - 41 U/L)
Alk Phos	**183 U/L** (40 - 130 U/L)
T. bili	0.2 mg/dL (≤1 mg/dL)
Albumin	4.3 g/dL (3.5 - 5.2 g/dL)
Total Protein	7.2 g/dL (6 - 8.3 g/dL)

Other labs	
Magnesium	2.2 mg/dL (1.6 - 2.5 mg/dL)
Phosphorous	**1.8 mg/dL** (2.5 - 4.5 mg/dL)
Bone alkaline phosphatase	**73%** (12 - 68 %)
25-hydroxyvitamin D	52.2 ng/mL(30 - 100 ng/mL)
1,25-dihydroxyvitamin D	**19.1 pg/mL** (19.9 - 79.3 pg/mL)
PTH intact	**80 pg/mL** (15 - 65 pg/mL)
Testosterone	552 ng/dL (249 - 836 ng/mL)
C-telopeptide	614 pg/mL (34 - 635 pg/mL)
Intact FGF-23	**93 pg/mL** (≤22 pg/mL)
24hr urine calcium	61 mg/24hr (47 - 462 mg/24hr)
24hr urine creatinine	0.5 g/24hr (1.0 - 2.2 g/24hr)
24hr urine volume	300 mL (1 - 10,000 mL)
Random urine phosphorus	68.4 mg/dL
Random urine creatinine	169.0 mg/dL
TmP/GFR	**0.431 mmol/L** (0.90 - 1.35 mmol/L)

Conclusion

TIO is a rare paraneoplastic syndrome. The constellation of findings of unprovoked fractures, hypophosphatemia, urinary phosphate wasting, and a negative genetic evaluation points to a diagnosis of TIO. Measuring phosphorus levels is important in any evaluation for metabolic bone disease. Tumors leading to TIO are often small and difficult to localize using standard imaging studies. ^{68}Ga-DOTATE CT/PET, a somatostatin receptor imaging modality, is emerging as the radiographical study of choice to localize these tumors. It is both highly sensitive and specific since tumors that cause oncogenic osteomalacia have been shown to express somatostatin receptors. Complete surgical resection is the treatment of choice; however, it may not always be feasible. Burosumab, a human anti-FGF-23 monoclonal antibody, is a therapeutic option in cases of unresectable TIO to normalize phosphorus levels and improve fracture-healing. TIO is often undiagnosed for many years, leading to significant patient morbidity. A thorough patient evaluation and high index of suspicion is necessary to accurately make the diagnosis.

References

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