He was diagnosed Fanconi’s syndrome and osteomalacia after taking ADV for 6 years.

ADV was changed to tenofovir disoproxil fumarate 300mg qd (TDF) in Dec 2014. He was given alfacalcidol 1mcg bd and PO4 mixture 1250mg/d. His S PO4 rose to 2.82mg/dL but later dropped to 2.14mg/dL because of poor drug compliance. ALP dropped to 126IU/L. His bone pain improved and could walk with stick. TDF was then switched to tenofovif alafenamide (TAF) 25mg qd in Mar 2019. His S PO4 further normalized to 3.13mg/dL in Jul 2019. His HBV remained suppressed. Alfacalcidol and PO4 solution were stopped.

The patient developed depression since Sep 2017. He had poor short term memory since 2018 and was confirmed mild cognitive impairment in Apr 2019. MRI brain in May 2019 found moderate global cerebral atrophy with bilateral parietal lobes and cerebellar predilection. His cognitive assessment further declined to < 2%ile in Jan 2020. He was admitted for recurrent fall in Sep 2020 and showed Parkinsonism feature. He was given Sinemet 25/100 and rivastigmine by neurologist with some improvement. He now walked with frame.

Nucleotide and nucleoside analogues (NA) can impose long term side effect on kidney. ADV and TDF are excreted from proximal renal tubule and can accumulate in the cytoplasm causing mitochondrial dysfunction. In this patient, hypoPO4 persisted after switching from ADV to TDF. TAF did not enter proximal renal tubular cells and the plasma concentration is lower than TDF and hence less nephrotoxic. The PO4 level in this patient normalized one month after changing to TAF.

Low serum phosphorus level was found to have correlation with cerebral amyloid deposition on Pittsburgh compound B positron tomography in a Korean study. The chronic hypoPO4 may be a contributing factor for the development of dementia in this patient which did not show reversibility. In summary, this case illustrates the nephrotoxicity of NA and importance of multi-disciplinary care as the side effect can be multi-systemic.

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BONE AND MINERAL CASE REPORT

Favorable Effects of Burosumab on Fibroblast Growth Factor 23-Related Osteomalacia: A Case Report
Yuki Oe, MD,1 Hiraku Kameda, MD, PhD,1 Hiroshi Nomoto, MD, PhD,1 Keita Sakamoto, MD, PhD,2 Takeshi Soyama, MD, PhD,2, Kyu Yong Cho, MD, PhD,2 Akinobu Nakamura, MD, PhD,3 Datosuke Abo, MD, PhD,4 Kohsuke Kudo, MD, PhD,4 Tatsuya Atsumi, MD, PhD,4 Hideaki Miyoshi, MD, PhD,4
1Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan, 2Department of Diagnostic and Interventional Radiology, Hokkaido University Hospital, Sapporo, Japan, 3Division of Diabetes and Obesity, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan.

Background: Fibroblast growth factor 23 (FGF23) decreases serum phosphate levels by inhibiting proximal tubular phosphate reabsorption and intestinal phosphate absorption by decreasing serum 1,25-dihydroxyvitamin D level, thereby regulating phosphate metabolism.

Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome caused by FGF23 overproduction by tumor tissue. Resecting the responsible tumor is a radical treatment for TIO. When the responsible tumor is undetectable, phosphate and active vitamin D administration is recommended. However, supplementation alone is frequently insufficient to maintain phosphate levels and it is difficult to prevent the complications associated with medical therapy, including hypercalcemia and nephrocalcinosis. Recently, burosumab, a human monoclonal anti-FGF23 antibody, has been approved in Japan as a therapeutic agent for FGF23-related hypophosphatemia. Here, we present a patient with TIO effectively treated with burosumab in the absence of identification of tumour location. Clinical case: A 47-year-old female developed pain and edema of the feet; however, the cause could not be determined at local hospitals. Afterwards, she developed marked bone atrophy in the feet and was referred to our hospital. Her age at symptom onset, hypophosphatemia (serum P, 1.9 mg/dl, 2.7 mg/dl < n < 4.6 mg/dl), high serum FGF23 level (630 pg/ml, 16 pg/ml < n < 69 pg/ml), and decreased 1,25-dihydroxyvitamin D level (12.9 pg/ml, 20 pg/ml < n < 60 pg/ml) indicated FGF23-related osteomalacia. She was not having any medication at the time of diagnosis, including saccharified iron oxide or iron polymaltose. Urinary phosphate excretion increased without renal tubular defect; therefore, hypophosphatemic osteomalacia was diagnosed. MRI showed high signal intensity in the talus, sacral, and L5 vertebral regions, indicating multiple pseudofractures. Comprehensive imaging studies, including systemic CT scan and 111In-pentetreotide scintigraphy, did not reveal any tumors despite the suspicion of TIO. Next, we performed systemic venous sampling, which revealed high FGF23 level in the left external iliac vein. Second venous sampling limited to the left lower limb exhibited high FGF23 level in the posterior tibial vein. However, an additional imaging study limited to the left foot could not identify any tumors. Genetic variation was negative for potentially responsible genes, including PHEX and FGF23. We decided to administer burosumab to normalize serum phosphate level without phosphate supplementation. Within 2 months, pain was relieved and the visual analog scale scores also improved from 10 to 6. Moreover, bone MRI showed improved pseudofractures. Conclusion: Burosumab administration was effective for TIO of unknown origin, and it improved not only laboratory findings but also clinical symptoms in this case.

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Fix That PHEX Loss
Sonic Sarah Sunny, DO, MS.
University of Arizona College of medicine phoenix, Phoenix, AZ, USA.

Phosphorous has a critical role in multiple biological functions in the body, such as skeletal mineralization, and an imbalance of this can lead to several musculoskeletal disorders. An important regulator of renal phosphate excretion is fibroblast growth factor 23 (FGF23) which is produced by osteocytes and osteoblasts themselves thus
providing a mechanism for the skeletal system to influence its own mineralization needs. PHEX is a gene that regulates FGF23 secretion therefore a loss-of-function mutation in this gene would result in elevated circulating FGF23 and phosphate depletion. This mutation has been identified as a cause for X-linked hypophosphatemia (XLH). Treatment of XLH has been limited and mainly involved phosphorous replacement in combination with 1,25(OH) vitamin D. Antiresorptive osteoporosis treatment can exacerbate the skeletal mineralization process. Here we present a patient with multiple fractures who was on denosumab treatment for presumed osteoporosis before being found to have PHEX mutation. The patient is a 64 year-old female with past medical history of bilateral hip replacement and recurrent femur fractures who was seen in clinic in 2014 due to recurrent fractures and diagnosis of osteoporosis since early 2000s. She had only tried alendronate up until that point. Due to the recurrent fractures she was switched to denosumab therapy while workup was underway for secondary causes. She was found to have low phosphorous levels and elevated FGF23 therefore genetic counseling was pursued and was recommended to check for PHEX mutation. The testing came back positive for loss-of-function mutation in PHEX, and by that point she had received 3 doses of denosumab therapy. She suffered another femoral fracture which was determined to be an atypical fracture, and therefore denosumab treatment was stopped and she was continued on phosphorous replacement as well as 1,25(OH) vitamin D replacement. Most recently her phosphorous levels have been controlled with therapy, and there is current discussion underway to try burosumab, an antibody to FGF23. During evaluation for osteoporosis, it is important to consider phosphorous roles in skeletal mineralization. If recurrent fractures are seen in a patient with low phosphorous levels, especially while they are on conventional antiresorptive osteoporosis medications, genetic testing for PHEX mutations should be considered as well as safely stopping antiresorptive medications.

In 2017, she underwent CT abdomen for suspected appendicitis, which revealed multiple renal cysts and hepatic hemangiomas. In 2019, patient was found to have recurrent parathyroid adenoma and underwent revision parathyroidectomy. Pathology revealed hypercellular parathyroid gland consistent with adenoma. Based on constellation of symptoms, HPT-JT was suspected. Patient was referred to genetic counselor. Detailed family history revealed multiple family members affected by malignancies including melanoma, breast cancer, prostate cancer, liver cancer and two cousins with suspected MEN1. She underwent testing for hereditary hyperparathyroidism and melanoma including CDC73 gene. All genetic testing was surprisingly unrevealing. **Discussion:** CDC73 gene (also known as HRPT2 gene) is responsible for the pathogenesis of HPT-JT. While HPT-JT itself is a rare condition, 60% of patients affected by it, harbor the HRPT2 gene mutation. About 10–15% of these individuals are affected by parathyroid carcinoma. HRPT2 mutated parathyroid adenomas also seem to have some malignant potential. The autosomal dominant inheritance of HPT-JT makes gene testing important since it has implications for other family members and carries weight in clinical management of genetic carriers. Therefore patients with extensive personal or family history of malignancy should be followed closely. Endocrinologists should have a low threshold to refer such patients for genetic counseling and testing. However genetic testing also has its limitations and can only explain 50–75% of cases of HPT-JT syndrome. Hence, even though our patient has a negative genetic screen, the possibility of HPT-JT is not complete ruled out.

**Bone and Mineral Metabolism**

**BONE AND MINERAL CASE REPORT**

**Glomus Tumor: An Unusual Cause of Hypophosphatemic Osteomalacia**

Rishi Raj, MBBS, MD, a Samaneh Hasanazadeh, MD, a Mitra Dastizadeh, MD, a Mohammadreza Kalantarhormozi, MD, a Katayoun Vahdat, MD, a Mohammad Hossein Dabbaghmanesh, MD, a Iraj Nabipour, MD, a Mohammadreza Ravanbod, MD, a Majid Assadi, MD, a Basir Hashemi, MD, a Kamiyar Asadipooya, MD. a PIKEVILLE MEDICAL CENTER, Pikeville, KY, USA. b Bushehr University of Medical Sciences, Bushehr, Iran, Islamic Republic of. c Shiraz University of Medical Sciences, Shiraz, Iran, Islamic Republic of. d University of Kentucky, Lexington, KY, USA.

**Introduction:** Tumor-induced osteomalacia (TIO) is a rare condition resulting in hypophosphatemic osteomalacia. We present a rare case of TIO secondary to glomus tumor. **Clinical Case:** A 39-year-old woman with history of chronic sinusitis presented with progressively worsening generalized body pain and muscle weakness of eight months duration. Examination showed decreased muscle strength in bilateral upper and lower extremities and congenital cleft palate. Laboratory work up revealed elevated alkaline phosphatase 603 U/L (44–147 U/L), low serum phosphorus 1.5 mg/dL (3.5–5.0 mg/dL), normal serum calcium 8.9 mg/dL (8.3–10.4 mg/dL), normal 25-hydroxyvitamin D 32 ng/dL (30–100 ng/dL), elevated 1,25-dihydroxyvitamin D 62 g/mL (20–45 pg/mL), elevated intact PTH level 99.01 pg/mL (8–74 pg/mL), high normal 24 hour urinary phosphate.

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**BONE AND MINERAL CASE REPORT**

**Hyperparathyroidism-Jaw Tumor Syndrome (HPT-JT)**

Fatima M. Kazi, MD, a Sobia Sadiq, MD. a Loyola University Health System, Maywood, IL, USA. b Loyola University Health System, Hinsdale, IL, USA.

**Introduction:** Hyperparathyroidism-jaw tumor syndrome (HPT-JT) is a rare autosomal dominant disorder characterized by parathyroid tumors in association with fibrous-osseous jaw tumors, uterine tumors and renal lesions. We present a case of suspected HPT-JT. **Clinical Case:** A 50-year-old female with suspected HPT-JT was referred for treatment of osteoporosis. Patient was initially diagnosed with osteosarcoma in 1980 at age 10, and underwent resection with leg amputation and chemotherapy. Around 1995, she was found to have primary hyperparathyroidism secondary to a parathyroid adenoma and underwent one gland parathyroidectomy. At age 30, she was then found to have multiple uterine tumors requiring hysterectomy.

**Discussion:** Genetic testing also has its limitations and can only explain 50–75% of cases of HPT-JT syndrome. Hence, even though our patient has a negative genetic screen, the possibility of HPT-JT is not complete ruled out.