2019 Interdisciplinary Symposium on Osteoporosis

Friday, May 17, 2019

7:15 am – 8:00 am

In the Clinic

Treatment and Conundrums

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Treatment Conundrums

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May 17, 2019

Conflict of Interest

National Osteoporosis Foundation: Trustee

Consultant: Health Stream, Viking

Cofounder and Equity Owner: BisCardia, Inc; Faculty Connection, LLC

Co-Inventor US Patent: "Methods for preventing or reducing secondary fractures after hip fracture" Number 20050272707

Inventor US Provisional Patent Application: Compositions and Methods for the Treatment of Infection-Induced Cardiomyopathy

Inventor US Patent: "Medication Kits and Formulations for Preventing, Treating or Reducing Secondary Fractures After Previous Fracture" Number 12532285

Co-Inventor US Patent: "Bisphosphonate Compositions and Methods for Treating Heart Failure" Number 20104717

Co-Inventor of US Patent: "Bisphosphonate Compositions and Methods for Treating and/or Reducing Cardiac Dysfunction" Number 61/560,328

Conundrum

Noun

A confusing and difficult problem or question

A question asked for amusement, typically one with a pun in its answer; a riddle

Google, 4-3-19

Case 1

A 92-year-old woman caring for her demented husband moves to Durham to be close to her daughter. She is referred for evaluation of osteoporosis. She has a history of three new vertebral compression fractures over the last three months occurring with no trauma. For the past 5 years, the patient has been regularly taking oral formulations of elemental calcium, 1500 mg/d; cholecalciferol, 800 U/d; and alendronate, 70 mg once weekly. On physical examination, the patient appears frail. Vital signs are normal, BMI is 19. There is kyphosis. Tenderness in the upper lumbar region over the recent compression fractures is noted. The rest of her exam is unremarkable except for her frailty which her daughter says has progressed over the last 6 months.

Case 1

Initial laboratory studies:

Calcium, 9.5 mg/dL, Phosphorus, 3.8 mg/dL, Parathyroid Hormone, 33 pg/mL, Thyroid Stimulating Hormone, 1.8 microU/mL, 25-Hydroxyvitamin D, 35 ng/mL. Results of a Bone Mineral Density study T-scores of −2.7 in the spine and −2.6 in the hip.

Are there additional studies that should be considered at this initial visit?

Case 1

A serum protein electrophoresis was obtained which showed and IgG spike.

The patient was referred to an Oncologist and died within two months despite treatment of her multiple myeloma.

Case 2

A 54 year old elementary school art teacher is referred for evaluation of osteoporosis, Spine T-score -3.0, Left femoral neck -2.3. At age 18 she weighed 95 pounds, FMP 14; Gr2 P2 A0; LMP 50. No family history of osteoporosis, but positive for nephrolithiasis. Patient has had no fractures, but has had 3 kidney stones, first 16 years ago. Four years ago a 24 hour urine calcium was 337 mg. She was told to drink lots of water. Physical exam was normal except for sun damaged skin of face, neck, arms and back. She weighed 61 kilograms. A repeat 24 hour urine calcium was 365 mg. All other laboratory studies were normal.

Case 2

Patient was instructed to drink three 8 ounce glasses of water daily, one before bedtime. She was prescribed chlorthalidone 25 mg daily and risedronate 35 mg weekly.

In two months a 24 hour urine calcium was 245 mg.

In one year a repeat Bone Mineral Density on a different machine showed Spine T-score -3.0, Left femoral neck T-score -2.2.

Evaluation for osteoporosis

Hypercalcemia

Hyperparathyroidism

Vitamin D deficiency

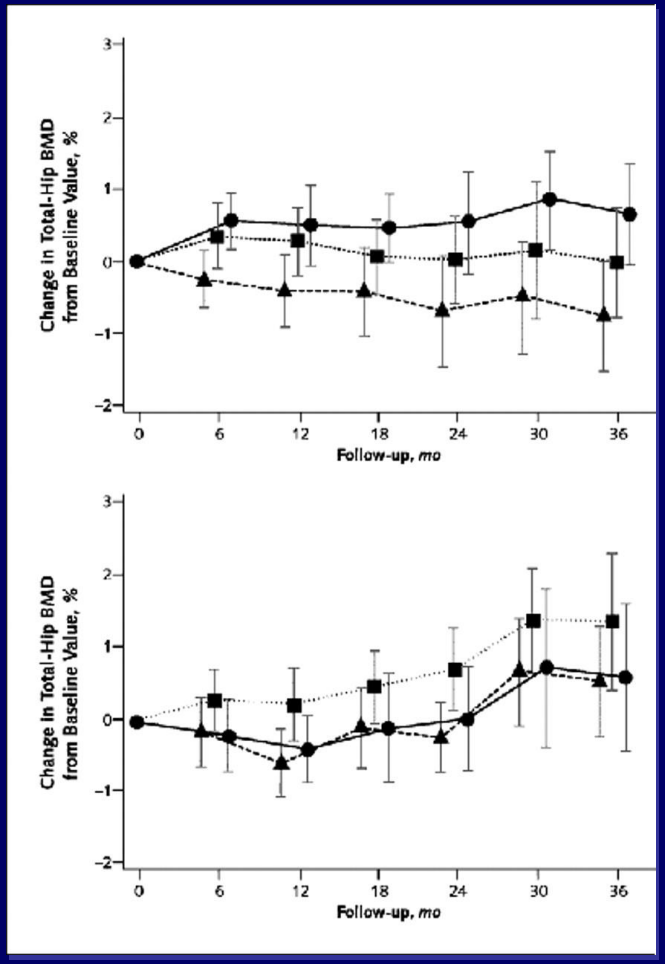
Hyperthyroidism

Hypercalcuria (more than 4 mg/kg)

Additional rarer causes of osteoporosis include male hypgonadism, malabsorption (Celiac Disease), medications (glucocorticoids) multiple myeloma

Vokes, T, *Translational Endocrinology and Metabolism,* 2010

Hydrochlorothiazide Preserves Bone Mineral Density in Older Adults



LaCroix, AZ, *Ann Intern Med* 2000

Case 3

A 71 year old lady returns to be evaluated for her osteoporosis, having been treated with Risedronate for 5 years for vertebral and metatarsal fractures. She has been on not therapy beside calcium and vitamin D for 5 years. Now she has severe depression and GERD. She again is having recurrent metatarsal fractures, her Total hip T-score -1.7. The exam is remarkable for flat affect and kyphosis. She also wears a fracture boot on her left leg. All laboratory studies are normal. It was decided to use intravenous zoledronic acid. She received two doses separated by 16 months. Three months after her last zoledronic acid infusion she had severe pain in her left thigh. A radiograph of the femur confirmed an atypical femur fracture, the right femur is normal.

Case 3

The patient has a rod placed in her left femur. After three months she still have left thigh pain and the fracture shows no healing. It decided to treat her with teriparatide 20 mcg subcutaneously daily. She tolerates the therapy well for two years and the fracture heals. She ambulates without pain and has had no more fractures. A BMD on a different machine shows Total hip T-score -1.4.

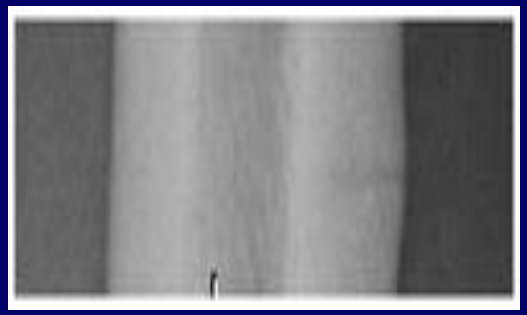
Upon completion of the teriparatide a decision was needed as to the antiresorptive therapy she should receive. After consultation with coleagues it was decided she should be placed on raloxifene for 12 months with a follow-up BMD measurement. Her Framingham Stroke risk was 2% at ten years.

https://www.framinghamheartstudy.org/fhs-risk-functions/stroke/

Atypical Femoral Fractures with Bisphosphonates

Lenart, B, *N Engl J Med,* 358, 1305, 2008

Femoral Subtrochanteric Insufficiency Fractures in Patients on Bisphosphonates



Porrino, JA., *AJR,* 2010

Case 4

A 71 year old lady is referred for management of her osteoporosis. She has retired and enjoys gardening and must care for a husband who has severe dementia, still living in their home. She fractured her right distal tibia after slipping on ice. She had a history of hypertension, CKD 3 (GFR24-34), breast cancer estrogen receptor positive, and aromatase inhibitor use. She previously had a 5 year course of risedronate which ended 4 years previously. Her physical exam is unremarkable. Laboratory studies are normal except for a Creatinine of 1.5. Bone Mineral Density: Spine T-score -1.2, Right femoral neck T-score -2.4, Right total hip T-score -1.2.

It is decided to treat her with denosumab 60 mg subcutaneously every six months.

Case 4

The patient tolerated the denosumab well every six months for 4 years. On month after receiving her eighth denosumab dose she had an episode of sepsis from diverticulitis. This was treated, but recurred two months later. It was decided that since she had a large anterior myocardial infarction two years before her episodes of sepsis, that she was not a candidate for raloxifene therapy. She continues to do well on calcium carbonate 500 mg and vitamin D 1000 IU daily.

Denosumab as a Therapy for Osteoporosis

This antiresorptive agent is an effective agent to reduce the risk of fractures in patients with osteoporosis. In addition to hypocalcemia, allergic reactions, and the rare risks of osteonecrosis of the jaw and atypical femur fractures. There are two other cautions when prescribing it:

1. It is a weak immunosuppressant causing bacterial infections in one in 100 to 1000 patients.
2. Upon discontinuing this drug patients who have had a vertebral fracture have a fourfold increased risk of an additional vertebral fracture. Other patients have rapid bone loss and are at increased risk for fractures.

Crandall, CJ, *Ann Intern Med,* 2017 Cummings, SR *J Bone Mineral Res,* 2017

Case 5

An 80 year old retired dairy farmer was referred for treatment of his osteoporosis. Three months earlier he fell in his home and had a left displaced femoral neck fracture which was repaired. He spent 8 weeks in a rehabilitation facility with a feeding tube for malnutrition. He has had prior vertebral and rib fractures, losing two inches. He also had coronary artery disease with an EF of 35% with a left apical thrombus and significant peripheral arterial disease. On exam he was a cachectic man. His mandible had six teeth fractured at the gum line with no evidence of inflammation, no other oral mucosal lesions. Heart mitral regurgitation murmur, no gallups. He also had a stocking glove peripheral neuropathy. He ambulated with a walker.

Case 5

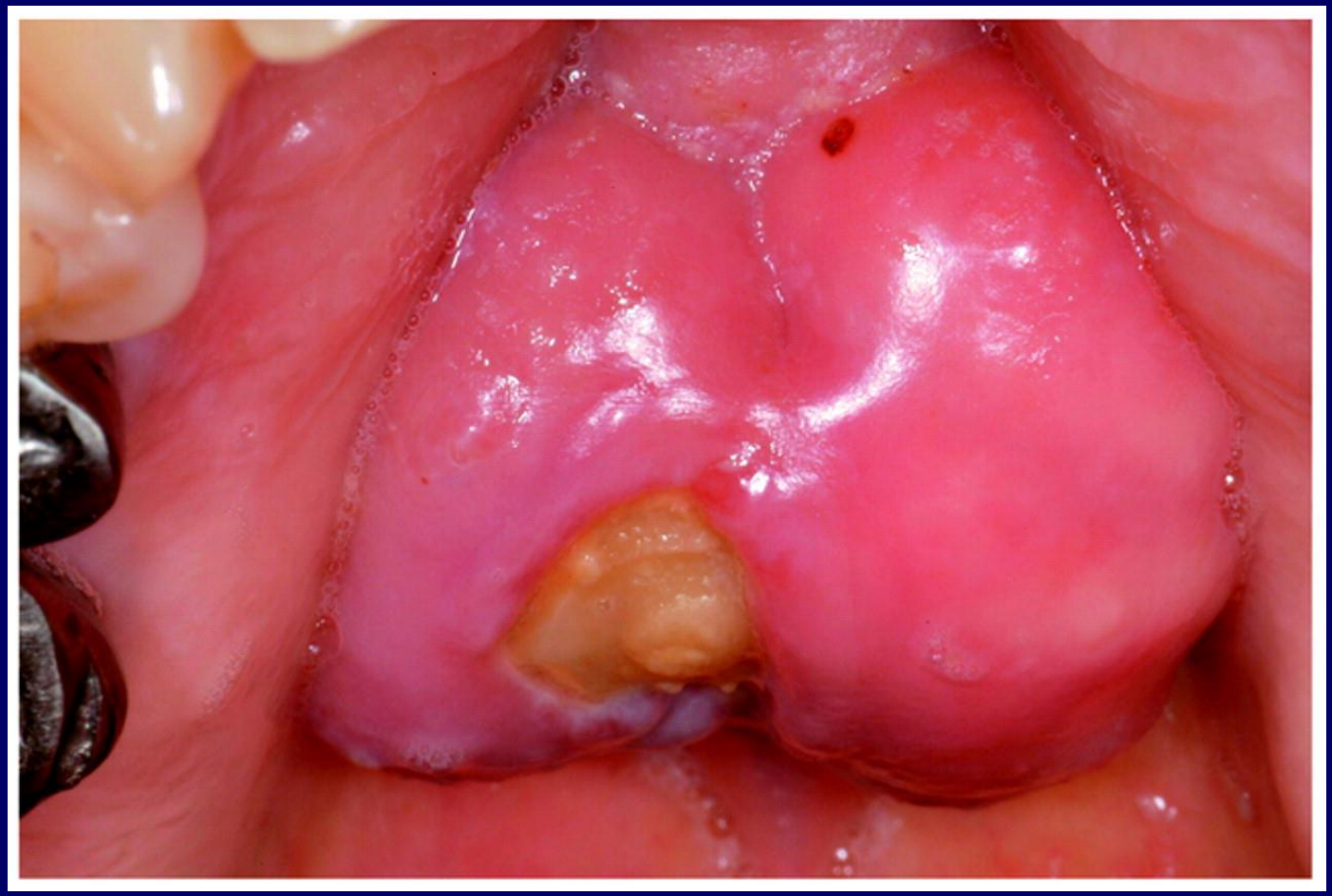
Laboratory studies: Creatinine 0.9mg/dl (MDRD est GFR>60), Calcium 9.8 mg/dl, Albumin 3.8 gm/dl, and 25 (OH) vitamin D 25 ng/ml.

He was started on cholecalciferol 2000 IU daily and calcium carbonate 500 mg twice daily with meals. Two weeks later he received zoledronic acid 5mg IV.

He has subsequently had two more doses of zoledronic acid with no more fractures and no difficulty with his mandible.

Eighteen months ago he developed acute cholecystitis from gall stones. He was deemed not to be a surgical candidate, so he has a percutaneous drainage tube with intermittent antibiotics. He still enjoys living on his 50 acre farm.

Osteonecrosis of the palatal torus in a patient with osteoporosis taking alendronate



Woo, S.-B., *Ann Intern Med ,2006*

Medication-Related Osteonecrosis of the Jaw-2014 Update

For individuals who have taken an oral bisphosphonate for less than four years and have no clinical risk factors, no alteration or delay in the planned surgery is necessary. This includes any and all procedures common to oral and maxillofacial surgeons, periodontists and other dental providers.

Questions and Comments

THANK YOU!