

Osteomalacia Case Studies

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Monday AM, 8:15am

- 42yo WM recently in MVA
- CXR: osteopenia
- No PMHx
- ROS +:
 - Vague sense of weakness
 - Dull achiness of leg bones – inhibited pts ability to go jogging over the past year

Evaluation

- DXA:
 - Lumbar spine L1-L4
 - T-score –1.2
 - Z-score –2.0
 - Total hip
 - T-score –1.7, Z-score –1.9
 - Femoral Neck
 - T-score –2.4

You next step is to:

1. Start Fosamax
2. Order labwork
3. Consult ortho for iliac crest bone biopsy
4. Start testosterone

Initial laboratory evaluation

- Calcium 8.2 mg/dL (8.6 – 10.0)
- Phosphorous 2.1mg/dL (2.6 – 4.0)
- Alk phos 199 ng/mL
- Creatinine 0.8
- PTH 132 pg/mL

What else would best assist you in this patient's evaluation?

1. Testosterone level
2. 1,25(OH)₂vitamin D
3. 25(OH)vitamin D
4. FGF23

Labs

- Calcium – **8.5 mg/dL** (8.6-10)
- Phosphorous – **2.1 mg/dL** (2.7-4.5)
- Alkaline Phosphatase – **199 u/L**
- PTH – **125 pg/mL (9-47)**
- 25(OH)vitamin D – 12 ng/mL (2-44)
- 1,25(OH)₂vitamin D – 26pg/mL (22-67)

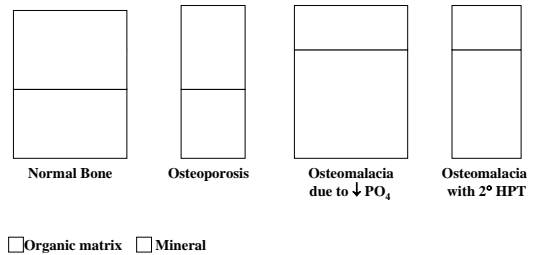
Evaluation

- 24hour urine:
 - Hyperphosphaturia
 - Calcium <100mg/24hr
 - Creatinine WNL for 24hr urine
 - No excess aminoaciduria, glucosuria, uric acid, etc

Osteomalacia

- Disorder of mineralization of newly formed organic matrix
- Occurs after cessation of growth
- Low calcium, phosphate or both in extracellular microenvironment leads to defective hydroxyapatite formation

Osteoporosis and Osteomalacia



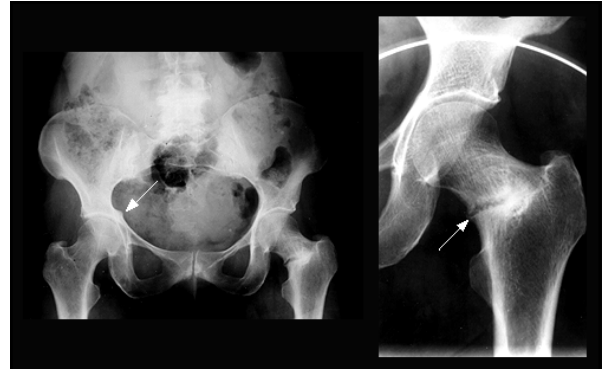
Clinical Presentation *Osteoporosis versus Osteomalacia*

- | | |
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| <ul style="list-style-type: none"> • Osteoporosis <ul style="list-style-type: none"> – Fragility fracture – Normal healing – Local pain at fracture site – No diffuse skeletal tenderness – Progressive kyphosis | <ul style="list-style-type: none"> • Osteomalacia <ul style="list-style-type: none"> – Fragility fracture – Diffuse bone pain (particularly lower extremities or pelvis) – Proximal muscle weakness-waddling gait – Pelvic deformities |
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Clinical Manifestations of Osteomalacia

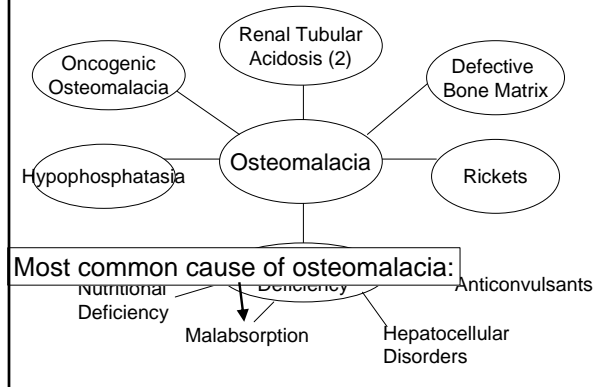
Radiologic Findings

- Radiographs and DEXA cannot differentiate osteoporosis from osteomalacia
 - Both show “osteopenia”
- subperiosteal bone resorption with increased PTH
 - Brown tumors, cartilage calcification and sclerosis less common
- Pseudofractures



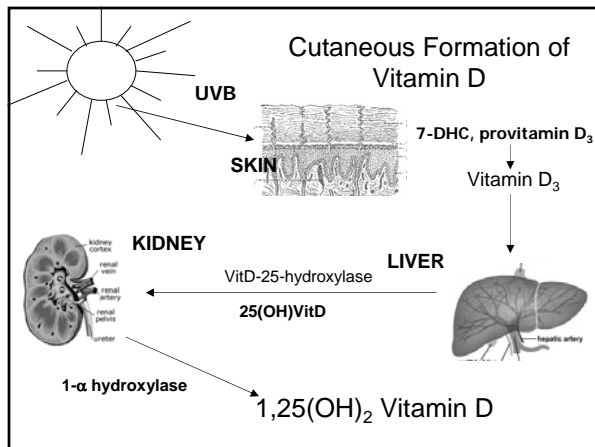
Pseudofractures in osteomalacia Looser-Milkman pseudofractures of the pelvis and left femoral neck (arrows) in a patient with osteomalacia. Courtesy of CJ Menkes, MD.

Etiology of Osteomalacia

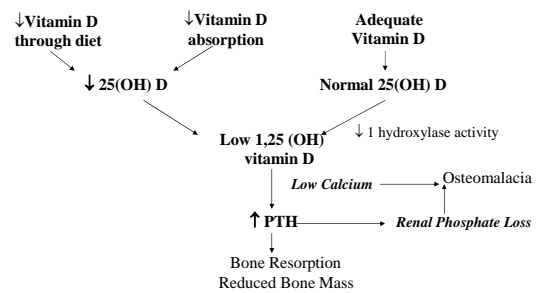


Inadequate serum Calcium and Phosphate

- Vitamin D and Calcium malabsorption
 - Most common cause of osteomalacia
 - Celiac Sprue, gastrectomy, chronic pancreatitis, primary biliary cirrhosis
 - Also described in gastric bypass
- Nutritional Deficiency
 - Most common cause worldwide
 - In US, typically in elderly
 - Subclinical deficiency now recognized



Impact of Vitamin D Deficiency States on Osteomalacia



Laboratory Evaluation

Dx	Ca ²⁺	Phos	PTH	Alk Ph	1,25 D
Vit D Def	Low NL	Low	++	++	"NL"
VDDR	Low	Low	+++	++	High
Hypophosphatasia	NL	NL	NL	LOW	NL
PMO	NL	NL	NL	NL	NL

Case 1

- Diagnosis: Celiac Sprue
- Chronic malabsorption of calcium and Vitamin D
- Secondary hyperparathyroidism
- Hyperphosphaturia with hypophosphatemia
- Undermineralized bone

Case 1 Treatment

- Start Calcium + Vitamin D
 - 1500mg calcium divided into 3 doses/day
 - 800IU vitamin D
- Replace Vitamin D stores
 - 50,000 unit capsules twice a week x 6wks
- Labs every 6-8 weeks
 - Calcium, phosphorous, Alk Phos, PTH
 - Treat to Vitamin D ≥ 32 , and normal PTH

Vitamin D factoids

- Exists as cholecalciferol (D3) or ergocalciferol (D2)
 - Cholecalciferol found to be more efficacious in raising serum vitamin D levels
- With 25(OH)vitamin D levels < 25 , will likely need high dose supplementation
 - 20 - 28 – 50,000 once a week x 6 weeks
 - 12 - 20 – 2x a week
 - < 12 – 3x/week or longer than 6 weeks
- Hypercalciuria and hypercalcemia may occur with 25(OH)D levels $> 90-100$

Case 1 follow up

- You check labs in 6 weeks:
 - Calcium 9.0 mg/dL
 - 25(OH)vitamin D - 42
 - PTH 52 pg/mL
- 4 months later
 - Calcium 8.3 mg/dL
 - 25(OH)vitamin D 18
 - PTH 130 pg/mL

You decide to:

1. Restart high dose vitamin D: 50,000u 2x/week then weekly
2. Add UVB exposure
3. Switch to calcitriol
4. Over the counter vitamin D 2000 units each day

Case 2

- 54 year old female presents with pelvic pain following a fall onto black ice
- PMHx Gastric CA s/p chemo
- Appetite has been poor; 15# weight loss since her last visit
- PE: pain on pelvic rock maneuver; she cannot tolerate passive internal/external rotation of either hip



The most useful next test to order might be:

1. Labwork including calcium, PTH, and vitamin D levels
2. Bone density by DXA
3. Bone turnover markers including Bone specific alkaline phosphatase and serum C-telopeptide
4. Iliac crest bone biopsy

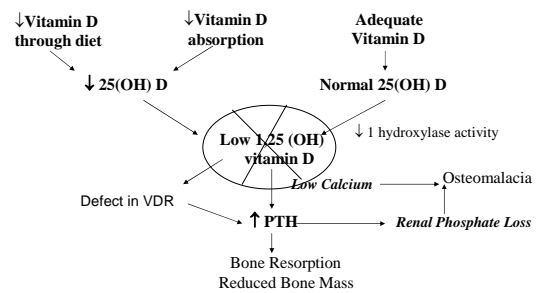
Lab results

- Calcium 7.8 mg/dL
- Phos 1.8 mg/dL
- PTH 325 pg/mL
- 25(OH)vitamin D – 32 (32-100)
- 1,25(OH)₂vitamin D – 112 (22-67)

The most likely diagnosis is:

1. Malabsorption of vitamin D with secondary hyperparathyroidism
2. Tertiary hyperparathyroidism
3. Vitamin D Dependent rickets
4. Idiopathic hypercalciuria

Impact of Vitamin D Deficiency States on Osteomalacia



New consult in NH/AL

- 76 year old WF with T2DM sustains hip fracture after tripping over loose carpet
- Previously independent, living at home
- Chronic renal insufficiency, GFR 42
- Chronic back pain with spinal stenosis
- Has been on calcium + D twice a day plus one centrum silver MVI

Does this patient need a DXA?

1. Yes
2. No

Further evaluation

- DXA
 - LS T-score -1.2 (L₁ – L₄)
 - TH T-score -3.2
- Labs
 - Calcium 8.0 mg/dL
 - 25(OH)vitamin D = 42
 - Phosphorous 2.2
 - PTH 128
 - GFR 45

You order 1,25(OH)₂vitaminD – it is most likely:

1. 110 (22-67)
2. 60 (22-67)
3. 13 (22-67)
4. <4.0

Osteomalacia in setting of Renal insufficiency

- See inability to activate vitamin D due to deficiency of 1- α - hydroxylase in elderly and in those with renal insufficiency
- Won't respond to ergocalciferol
- Start calcitriol
 - Start low at 0.5mcg per day
 - Follow labwork closely, every 3-4 weeks –
 - Hypercalcemia much more common in calcitriol therapy
 - Advance to normal calcium and high normal PTH

Case 4

- 46 year old male presents with fatigue and weakness: "I can't even get out of the car without pulling on the car door!"
- Previously healthy; exercised 3d/week
 - Has been feeling weak, though, for 2 years
- 2 years ago fractured ankle after slipping on wet grass while mowing
- Has lost 2 inches in height since his youth
- Poor libido

You order some labs:

- TSH – 2.2
- Testosterone – 415 (241 – 827 ng/dL)
- 25(OH)vitamin D – 43
- Electrolytes, kidney function, CBC – normal
- Phosphorous – 0.9 mg/dL (2.7 – 4.5)

Further workup:

- PTH – 40
- Alk phos 110 U/L (38-126)
- Calcium 9.0
- 24 hour urine phosphorous, fractional excretion = 20%
- DXA: LS T-score -1.1; TH T-score -0.9

What is your next step?

1. Start phosphorous supplementation: neutraphos packets with each meal
2. Order Bone Biopsy
3. Start Alendronate
4. Order an octreotide scan

Oncogenic Osteomalacia

- Seen in mesenchymal tumors
- Paraneoplastic syndrome: the tumors produce factors that cause phosphate wasting
- Hyperphosphaturia; hypophosphatemia
- Osteomalacia on bone biopsy, but often otherwise normal work up
- Cured with resection of the tumor

In Summary

- Osteomalacia is not uncommon
- It can frequently look like osteoporosis on imaging, but usually is symptomatic
- Making the diagnosis and treating the problem can independently reduce fracture risk – and they feel better!
- Keep in mind with any patients presenting with bone pain or fracture outside the usual demographics of PMO