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Clinical skill update: Unusual cases in osteoporosis*

Grand rounds

Dr Stan Lipschitz
Department of Geriatric Medicine
Faculty of Health Sciences
University of the Witwatersrand

Learning objectives

You will learn:

- To use anonymised case studies to focus on the diagnostic skills needed to diagnose unusual causes of osteoporosis
- The first case with osteoporotic features is the result of undetected coeliac disease in a 50-year-old woman; treatment options are presented for this patient
- The second case tracks a patient over 10 years before a diagnosis of primary hyperparathyroidism is made; an adenoma is identified, resected and effective patient treatment initiated
- The third case describes the sequelae in a 41-year female who had anorexia nervosa in adolescence, options for treatment of the resultant osteoporosis are presented
- The fourth case is an elderly patient with HIV on antiretroviral therapy with chronic kidney disease (CKD), diabetes, Gastroesophageal reflux disease (GORD), depression and severe osteoporosis. The pathophysiology of renal osteodystrophy is discussed, and options for osteoporotic treatment at various CKD stages are presented
- The fifth case is patient with X-linked Hypophosphatemic Rickets, which had been missed in childhood
- The sixth case is of unexplained bone growth due to genetic abnormality

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*This summary report is based on the live webinar held on 13th April 2021. Please also watch the accompanying 35-minute video for details of the case studies as presented by Dr Lipschitz

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Case 1

Clinical notes on Coeliac Disease

- Coeliac disease was confirmed by the presence of positive endomysial antibodies (EMA).
- Osteoporosis is relatively common in coeliac patients
- Diagnosis is important as a gluten-free diet resolves symptoms, improves quality of life and can prevent later complications including osteoporosis
- Many patients with coeliac disease are asymptomatic, but commonly present with diarrhoea without weight loss. Constipation does not however exclude the diagnosis
- Treatment is a strict lifelong gluten-free diet

Additional reading: Leonard MM, *et al*. Celiac Disease and Non-Celiac gluten sensitivity: A review *JAMA* 2017; **318**(7): 647-656.

Case 2

Clinical notes on Primary hyperparathyroidism (PTH) as a cause of osteoporosis

Throughout the course of this patient's10-year evaluation, her calcium was normal, parathyroid hormone levels only slightly raised though at times it would be briefly and significantly raised.

- Bone turnover markers were elevated and Vit D levels low
- A Sestamibi scan was strongly suggestive of parathyroid adenoma; subsequently resected
- Clinician features of Normocalcaemic Primary Hyperparathyroidism are summarised in Table 1

Table 1. Normocalcaemic Primary Hyperparathyroidism

- PTH levels are elevated, Ca levels persistently normal
- Exclude other causes of hyperparathyroidism, such as vitamin D deficiency, hypercalciuria, reduced creatinine clearance
- Some patients become hypercalcaemic with time
- Sestamibi scans are positive in 60% of cases
- Surgical findings may include the presence of a single adenoma, double adenomas & 4-gland hyperplasia
- Patients often develop severe complications requiring surgery
- In asymptomatic patients without osteoporosis – monitor serum and urine biochemistry and BMD
- Indications for surgery:
  - numbers are too small to produce guidelines
  - Clinical decisions based on symptoms, biochemistry, DEXA and history of fractures

Additional reading: Palermo A, *et al*. Clinical biochemical and radiological profile of normocalcaemic primary hyperparathyroidism. *J Clin Endocrinol Metab* 2020.

Case 3

Clinical notes on Anorexia Nervosa: Clinical consequences after many years

- While many of the clinical consequences of anorexia appear to be reversible with recovery, this may not hold true for its impact on the skeleton
- Anorexia Nervosa is an important cause of bone loss in younger patients
- The condition has negative effects on skeletal maturation and growth in adolescent years (Table 2)
- Oral estrogen alone will not improve BMD in adults or in adolescents with anorexia
- Low BMD in an adult is due to uncoupling of bone remodelling
- Strategies to improve BMD in anorexia nervosa (Table 3)

Table 2. Anorexia Nervosa in adolescent years

- Hormonal alterations specific to this time are critical for:
  - Stimulating bone mass accrual
  - The pubertal growth spurt
- These hormonal alterations are essential in establishing:
  - Optimal peak bone mass (PBM)
  - Optimizing final adult stature
- Hormonal alterations include:
  - Rising levels of gonadal steroids in early puberty
  - Increase in Growth Hormone (GH)
  - Increase in IGF-1
- Maximal increases in bone mass
  - 11-14 in girls
  - 13-16 in boys
- Almost 25% of peak bone mass is formed in the 2 years around peak height velocity
- >95% of PBM is achieved by age 18 years
- Failure to achieve this PBM is of grave concern given this narrow window
- Complete catch-up may not be possible
- Residual deficits in bone mass and bone microarchitecture then persist into adult life

Table 3. Anorexia Nervosa – Strategies to improve Bone Mineral Density (BMD)

- Weight gain and resumption of menses
  - Conflicting data
    - » Some studies show no improvement in BMD or BTM
    - » Other studies show restoration of bone formation activity
- Estrogen replacement
  - Multiple studies show that estrogen therapy alone does not have an effect on BMD
  - No basis for prescribing either HT or OC in these patients
- Bisphosphonates
  - Adolescent study with ALN – modest increase in BMD
  - Adults with AN
    - » Risedronate treatment decreases BTM and increases BMD even without weight gain
- Denosumab
  - No data

Additional reading: Robinson L, *et al*. A systematic review and meta-analysis of the association between eating disorders and bone density. *Osteoporosis Int* 2016; **27**: 1953-1966.

Case 4

Clinical notes on renal osteodystrophy

- Fracture risk is twice as high in patients with CKD
- Consequences of CKD-MBD are summarised in Figure 1
- In ageing there is an increased prevalence of both CKD and osteoporosis
- eGFR decreases with age
- When a fracture occurs in the elderly, it can be due to osteoporosis or renal osteodystrophy
- Treatment of osteoporosis in CKD disease should be done according to staging of CKD

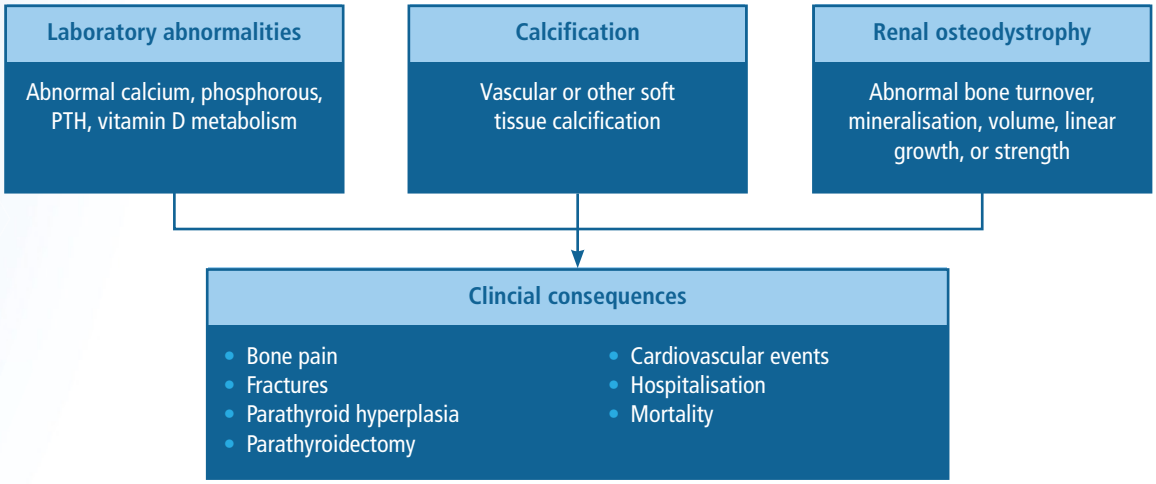

Figure 1. Consequences of CKD-MBD

Table 4: Osteoporosis treatment at CKD stages

- CKD Stages 1-3
  - Choice as usual
- CKD Stage 4
  - Can use BZP slowly (off label)
  - Teriparatide (especially for Adynamic bone disease, ADBD)
  - Denosumab
- CKD Stages 4-5
  - May need bone biopsy
- CKD Stage 5 – do the best you can!
- Denosumab can be safely used for all stages
  - Ensure adequate calcium & vitamin D intake
  - It has no effect on creatinine and vascular calcium

Additional reading: Evenepoel P, Cunningham J, Ferrari S, *et al*. European consensus statement on the diagnosis and management of osteoporosis in chronic kidney disease stage G4-G5D. *Nephrol Dial Transplant* 2012; **36**: 42-59.

Case 5

Clinical notes on X-Linked hypophosphatemic Rickets

- May be missed in childhood
- Bisphosphonates must not be given, rather give phosphate supplements, high dose calcitriol

Case 6

Clinical notes on unexplained bone growth due to genetic sclerostin deficiency

- Genetic testing is helpful
- Occurs in patients of Dutch ancestry in South Africa as a rare recessive disease, <1000 cases in SA

Additional reading: Brunkow ME, *et al. Am J Hum Genet.* 2001;68:577-589. Balemans, *et al. Hum Mol Genet.* 2001;**10**:537-543.

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Reg: 2012/216456/07
70 Arlington Street, Everglen, Cape Town, 7550
Tel: (021) 976 0485 | info@denovomedica.com