IN THE NAME OF GOD

Case presentation

NAHID KORD,MD

Feb 26, 2024

A 30-year-old woman with lactation associated osteoporosis

PATIENT ID

- A 30-year- old woman
- Born and live in Eslamshahr
- Associate degree
- Married and has two children
- Hair stylist
- SOH: patient, reliable
- Cc: severe back pain

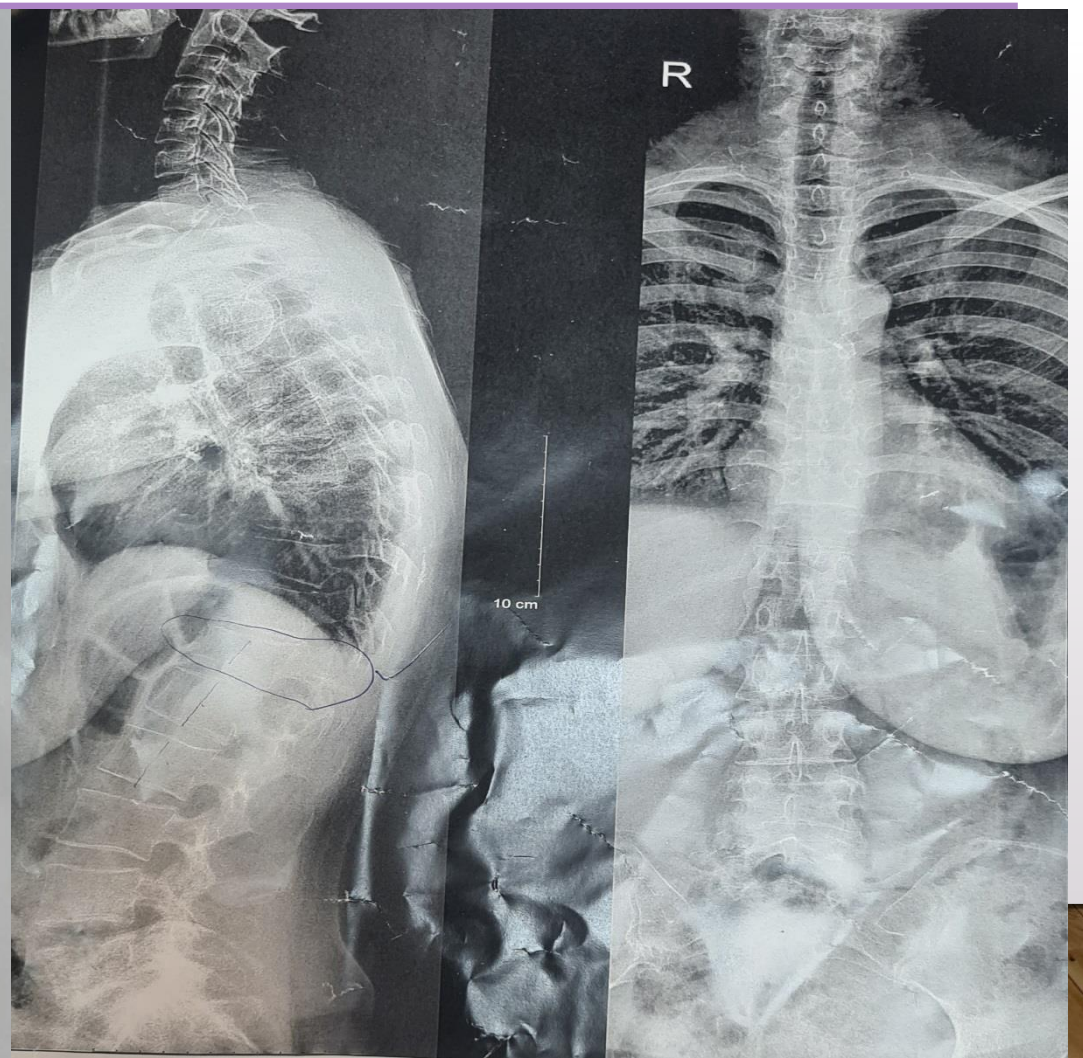
PRESENT ILLNESS

- A 30-year-old woman, G2 P2 L2, at 1402.06.27,when she was 38 W + 4 d, underwent cesarean section under spinal anesthesia.
- A few days after delivery, she had back pain that gradually increased severity until she could not get up and do daily works.
- She went to an orthopedic specialist in Eslamshahr, and prescribed an X-RAY and MRI.

1402. 09.16

On AP and lateral TOTAL spine X-rays;

Cervical lordosis angle: 22 degree
Thoracic kyphosis angle: 55 degree
Lumbar lordosis angle: 55 degree
Mild compression fracture of T12 vertebra is seen.
Other vertebral bodies, posterior elements, spinal canal and intervertebral disc spaces seem to be normal.
Bone density appears normal and there is not any evidence of focal lesion within the bones.



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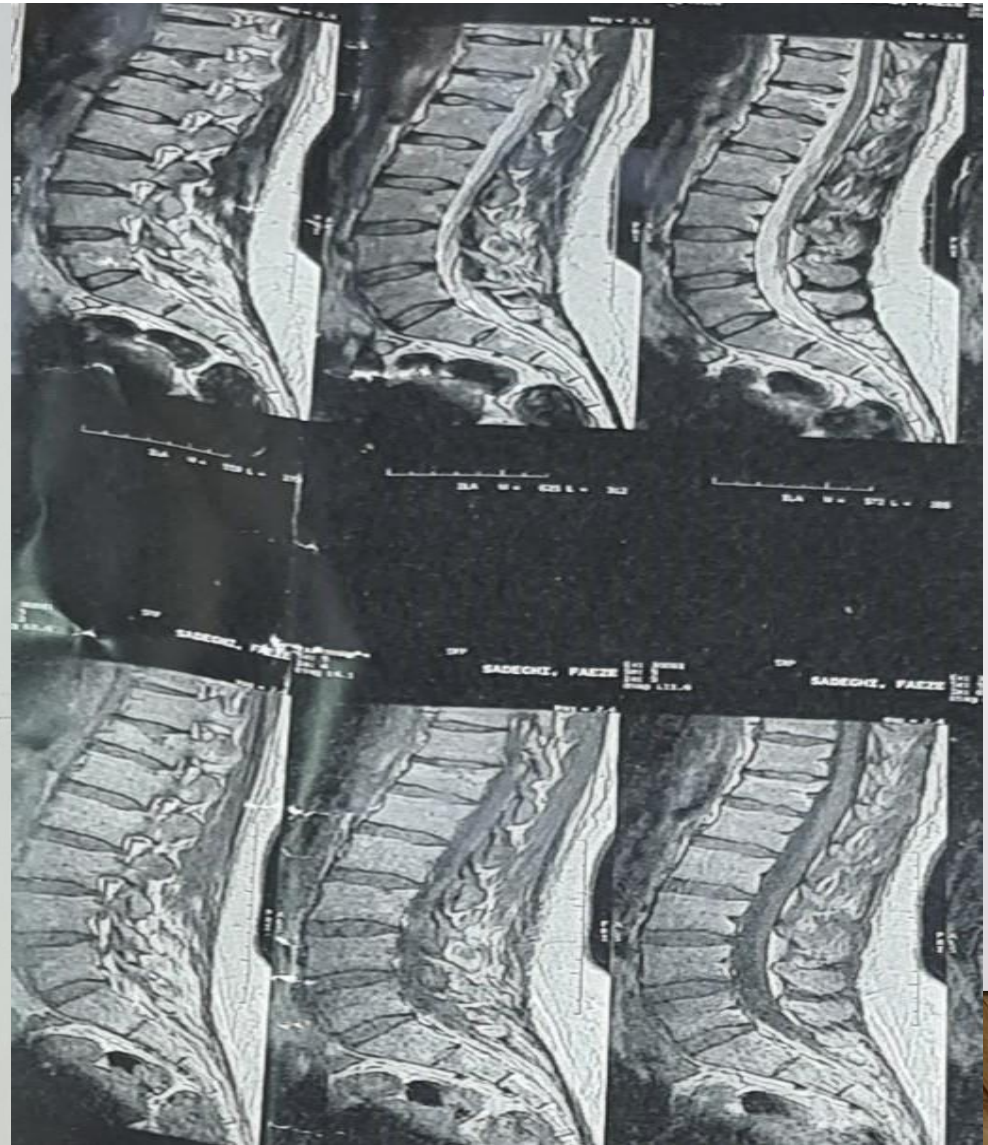
MRI of the lumbosacral spine without IV gadolinium:

Multiplanar, multislice and multisequence images without gadolinium injection revealed:

Wedge deformity of T12 is seen can be due to chronic fracture.
Multilevel Schmorl's nodes are seen.
Abnormal signal intensity is seen in inferior endplate of T11 maybe due to chronic damage.
Abnormal signal intensity is seen in superior endplate of L5 can be due to type I of MODIC change, however clinical correlation and follow up for R/O of fracture is recommended.
Normal disc height and signal intensity are noted at other levels.
Conus medullaris and cauda-equina rootlets are intact.
Neural foramina appear normal.
Atrophic changes is seen in paravertebral muscles.



PRESENT ILLNESS

- She advised to stop breast feeding(after 2.5 months) and take oral analgesics but patient's pains continued to be more intense,
- 3 weeks later, she referred to a neurosurgery specialist in Tehran and an thoracolumbar MRI & BMD was requested.

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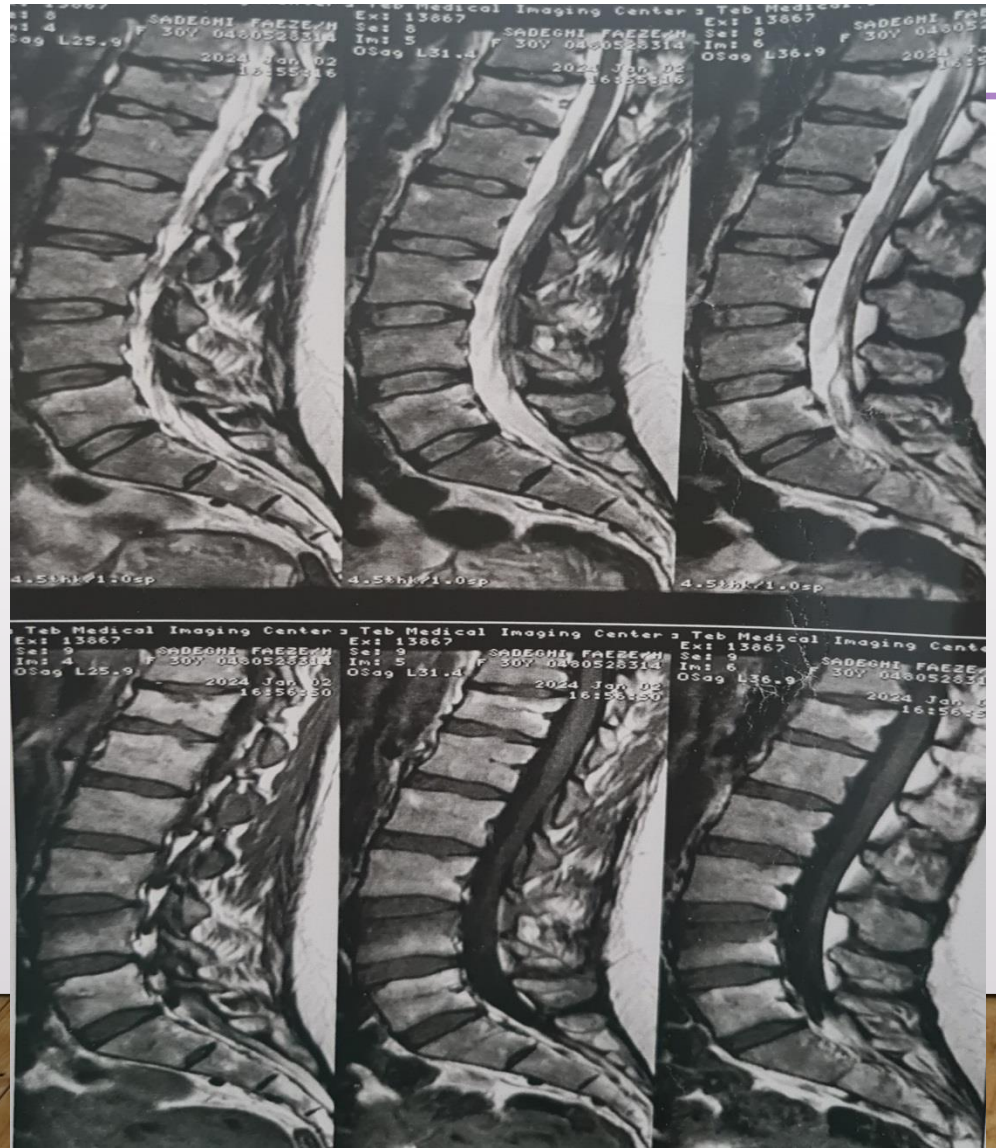
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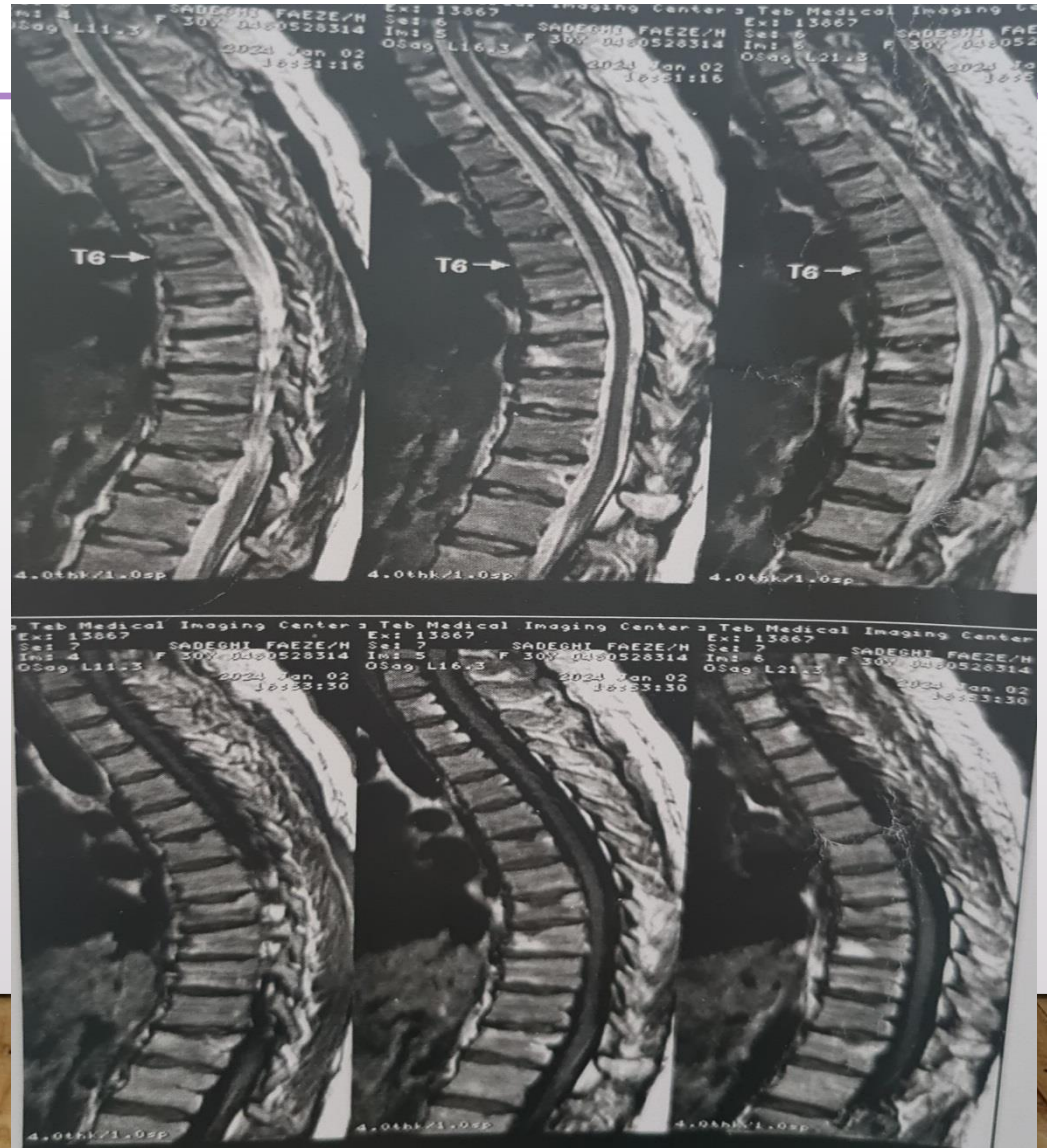
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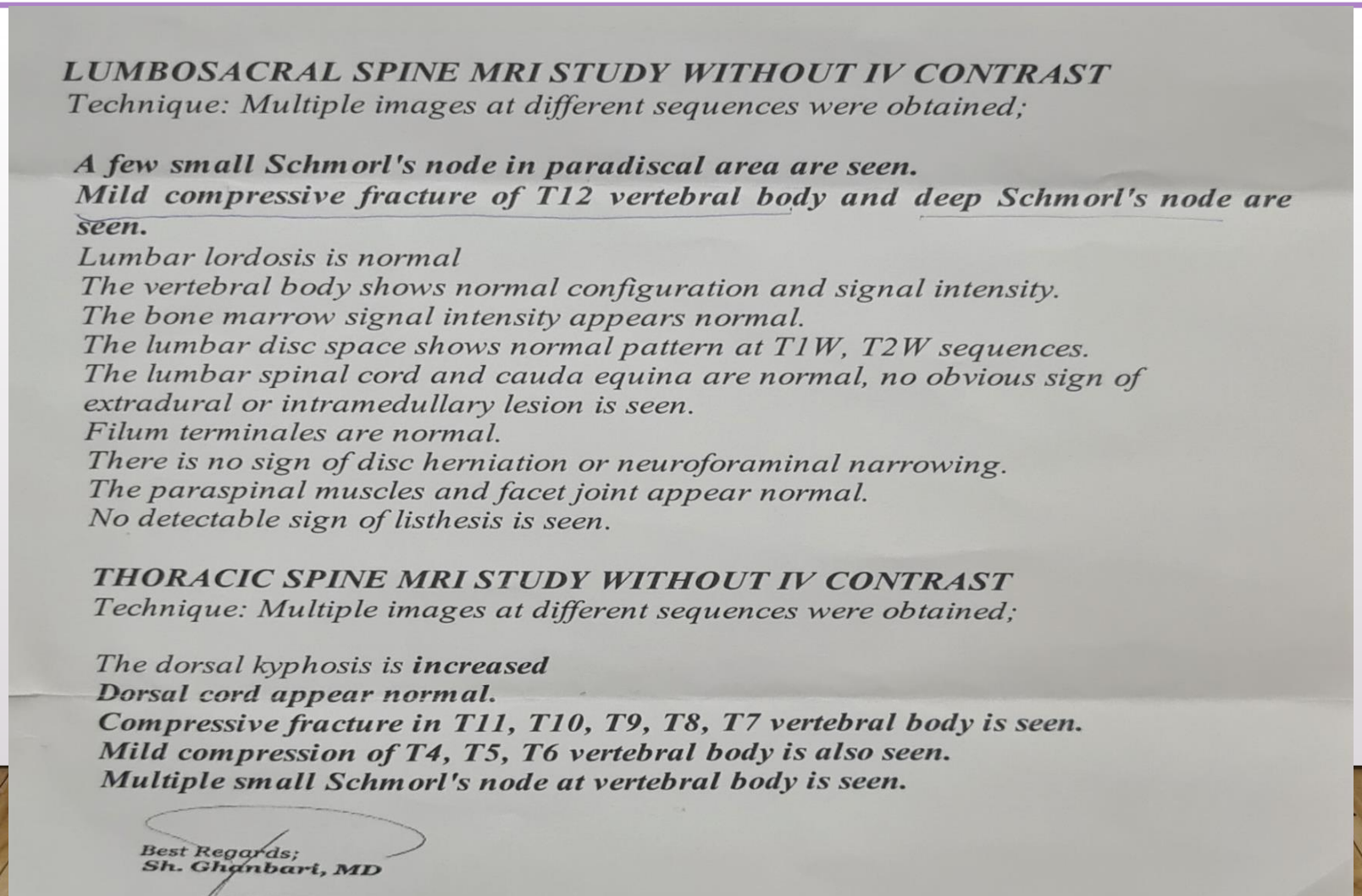


LUMBOSACRAL SPINE MRI STUDY WITHOUT IV CONTRAST
Technique: Multiple images at different sequences were obtained;

A few small Schmorl's node in paradiscal area are seen.
Mild compressive fracture of T12 vertebral body and deep Schmorl's node are seen.
Lumbar lordosis is normal
The vertebral body shows normal configuration and signal intensity.
The bone marrow signal intensity appears normal.
The lumbar disc space shows normal pattern at T1W, T2W sequences.
The lumbar spinal cord and cauda equina are normal, no obvious sign of extradural or intramedullary lesion is seen.
Filum terminales are normal.
There is no sign of disc herniation or neuroforaminal narrowing.
The paraspinal muscles and facet joint appear normal.
No detectable sign of listhesis is seen.

THORACIC SPINE MRI STUDY WITHOUT IV CONTRAST
Technique: Multiple images at different sequences were obtained;

The dorsal kyphosis is ***increased***
Dorsal cord appear normal.
Compressive fracture in T11, T10, T9, T8, T7 vertebral body is seen.
Mild compression of T4, T5, T6 vertebral body is also seen.
Multiple small Schmorl's node at vertebral body is seen.

Best Regards;
Sh. Ghanbari, MD

1402.10.12

DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMD (g/cm²)	T-score	PR (%)	Z-score	AM (%)
Neck	5.58	2.95	0.528	-2.9	62	-2.8	63
Troch	10.41	4.30	0.413	-2.9	59	-2.9	59
Inter	24.72	19.09	0.773	-2.1	70	-2.1	71
Total	40.70	26.34	0.647	-2.4	69	-2.4	69
Ward's	1.01	0.45	0.440	-2.5	60	-2.3	62

Total BMD CV 1.0%

WHO Classification: Osteoporosis

FRAX® WHO Fracture Risk Assessment Tool

10-year Fracture Risk[1]

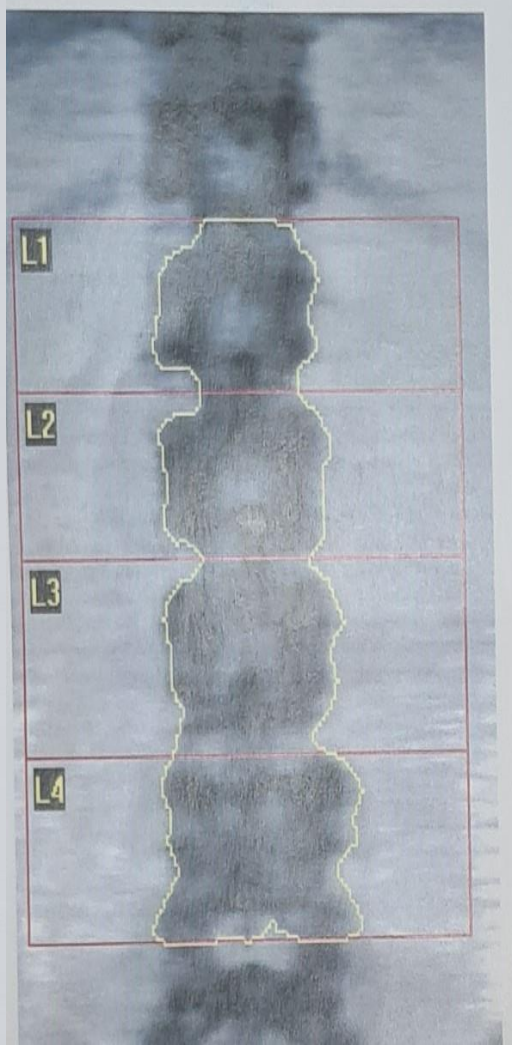
Major Osteoporotic Fracture 8.9%

Hip Fracture 4.6%

Reported Risk Factors:

Turkey, T-score(WHO)=-2.7, BMI=21.7

Input outside FRAX® limits. Adjusted to:Age=40



Scan Information:

Scan Date: 02 January 2024 ID: A01022418

Scan Type: fe Lumbar Spine

Analysis: 02 January 2024 17:40 Version 13.6.0.2 02/10/12
Lumbar Spine

Operator: HE

Model: Explorer (S/N 91672)

Comment:

DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMD (g/cm²)	T-score	PR (%)	Z-score	AM (%)
L1	11.83	7.51	0.635	-2.6	69	-2.6	69
L2	12.61	9.61	0.762	-2.4	74	-2.4	74
L3	15.49	11.94	0.771	-2.8	71	-2.8	71
L4	17.90	14.33	0.801	-2.9	72	-2.9	72
Total	57.83	43.39	0.750	-2.7	72	-2.7	72

PRESENT ILLNESS

- A medical belt was prescribed for the patient, and she was referred to an endocrinologist.
- The endocrinologist requested lab test for the patient.

LAB TESTS: 1402.11.02 , 1402.11.23

- Hb: 13.2 g/dl
- ESR: 5
- FBS: 84 mg/dl
- Hb A1C: 5.1%
- Cr: 0.6 mg/dl
- ALP: 61 u/l
- HIV: neg
- Ferritin: 42.9 ng/ml
- Ca: 9.5 and 9 mg/dl
- P: 3.7 mg/dl
- iPTH: 40.4 pg/ ml
- 25 (OH)D: 26 ng/ml
- TSH: 2.7 mIU/ml
- Anti TTG Ig A: 2.7
- Anti Endomysial Ab Ig A: 8.8
- FANA, Anti ds DNA, RF, Anti CCP: neg
- Urine 24h: Volume: 700 cc Ca: 65.3 mg/24h

PAST MEDICAL & SURGICAL HISTORY

- She had two normal pregnancy without any problem such as back pain or bed rest.
- Lab test in first trimester: 25(OH)D: 30 ng/ml, TSH: 1.2 mIU/ml, viral markers: neg
- She had two elective cesarean section.

DRUG & SOCIAL HISTORY

- She used only pregnancy supplements(bone fit & folic acid).
- Dairy intake seemed to be sufficient in pregnancy but after delivery she had low intake of dairy products and she used calcium supplement for a short time.
- Tab sertraline 50 mg and chlordiazepoxide 5mg for 3 weeks (panic attack)
- Tab vitamin B1 300 mg for 1 month
- Glucocorticoid, anticonvulsants, heparin: neg
- Smoking & alcohol: neg

FAMILY HISTORY

- Parents have a family relationship (cousins).
- Four sisters: all normal.
- Mother: 46 y/o with hypothyroidism (Hashimoto), no drug use but a Hospital admission at 1402.03.25 for hypercalcemia and AKI.
- Grand mother: 63 y/o with 5 childbirth, osteoporosis at 41 y/o that she treated, history of hypercalcemia and parathyroid surgery at 1394.
- Family Fracture history: neg

REVIEW OF SYSTEM

POSITIVE

- Severe back pain
- Left wrist pain

NEGATIVE

- Nausea, vomiting, bloating, diarrhea
- Lactose intolerance
- Weight loss & Height loss
- Oligomenorrhea, amenorrhea(first mens 50 days after delivery then regular periods)
- Anorexia nervosa
- Renal stone

PHYSICAL EXAMINATION

- Weight: 65 kg
- Hight: 172 cm
- BMI: 22 kg/ m2
- BP: 120/90 mmHg
- PR: 82/min

NEGATIVE

- Joint laxity
- Blue sclerae
- Scoliosis
- limb deformities
- Anemia
- Edema
- Neurological deficit

PROBLEM LIST

- A 30-year-old woman without specific past medical history that referred for progressive back pain at early lactation period and multi thoracic vertebral fractures in MRI and low bone mass in BMD with normal lab tests.

AGENDA

- Definition of early-onset osteoporosis
- Etiology of early-onset osteoporosis
- Physiology During Pregnancy and lactation
- Pregnancy and lactation associated osteoporosis
- Management of Patients with PLO
- Long Term Follow-Up

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SHORT REVIEW

Bone fragility and osteoporosis in children and young adults

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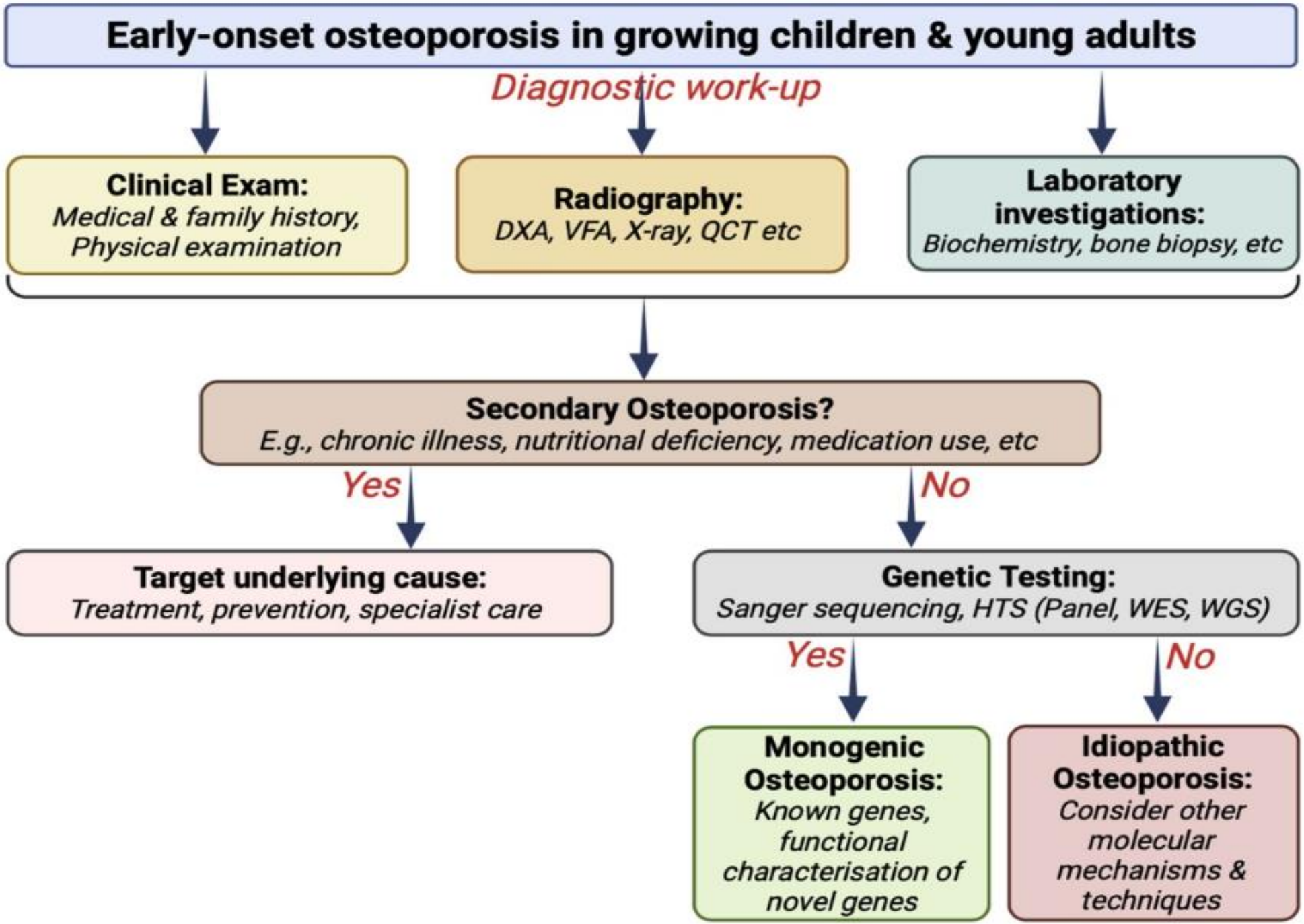
Received: 5 July 2023 / Accepted: 16 August 2023

Abstract

Osteoporosis is a metabolic bone disorder which increases fragility fracture risk. Elderly individuals, especially postmenopausal women, are particularly susceptible to osteoporosis. Although rare, osteoporosis in children and young adults is becoming increasingly evident, highlighting the need for timely diagnosis, management and follow-up. Early-onset osteoporosis is defined as the presence of a low BMD (Z-score of ≤ -2.0 in individuals aged < 20 years; T-score of ≤ -2.5 in those aged between 20 to 50 years) accompanied by a clinically significant fracture history, or the presence of low-energy vertebral compression fractures even in the absence of osteoporosis. Affected children and young adults should undergo a thorough diagnostic workup, including collection of clinical history, radiography, biochemical investigation and possibly bone biopsy. Once secondary factors and comorbidities are excluded, genetic testing should be considered to determine the possibility of an underlying monogenic cause. Defects in genes related to type I collagen biosynthesis are the commonest contribu-

DEFINITION OF EARLY-ONSET OSTEOPOROSIS

- ISCD recommends the use of BMD Z-scores in these populations (compared with age-matched norms).
- In premenopausal women and men aged < 50 years, a Z-score ≤ - 2.0 is interpreted as below the expected range for age and a Z-score>- 2.0 as within the expected range for age.
- In this age group, osteoporosis diagnosis should not be based only on low BMD, but also on a history of low-trauma fracture or a secondary cause of osteoporosis.
- In this age group, one or more vertebral compression fractures is indicative of osteoporosis, in the absence of local disease or high-energy trauma, even if the BMD Z-score is not subnormal.


Early-onset osteoporosis in growing children & young adults
Diagnostic work-up
Clinical Exam:
Medical & family history, Physical examination
Radiography:
DXA, VFA, X-ray, QCT etc
Laboratory investigations:
Biochemistry, bone biopsy, etc
Secondary Osteoporosis?
E.g., chronic illness, nutritional deficiency, medication use, etc
Yes
No
Target underlying cause:
Treatment, prevention, specialist care
Genetic Testing:
Sanger sequencing, HTS (Panel, WES, WGS)
Yes
No
Monogenic Osteoporosis:
Known genes, functional characterisation of novel genes
Idiopathic Osteoporosis:
Consider other molecular mechanisms & techniques

IDIOPATHIC OSTEOPOROSIS

- Males and females are equally affected
- A family history of osteoporosis is common
- The age at diagnosis is approximately 35 years
- Fractures are usually multiple occurring over 5–10 years and involve sites rich in cancellous bone, such as the vertebrae, and the hip is affected in approximately 10% of affected individuals.

Table 2 Secondary causes of low bone mass/fractures in children and young adults

Endocrine diseases	**Medications**
Cushing's syndrome (ACTH, non-ACTH dependent)	Anticonvulsants
Diabetes mellitus	Aromatase inhibitors
GH deficiency	Chemotherapy
Hypercalciuria	Depot medroxyprogesterone acetate
Hyperparathyroidism	Excess levothyroxine
Hyperprolactinaemia	Glucocorticoids
Hyperthyroidism	GnRH agonists
Hypogonadism (hypogonadotropic, hypergonadotropic)	Heparin
Hypophosphatasia	Immunosuppressants
Hypophosphataemia	Proton pump inhibitors
Vitamin D and/or calcium deficiency	SSRI
	Thiazolidinediones
Haematologic diseases	**Metabolic diseases**
Bone marrow transplantation	Gaucher's disease
Haemophilia	Glycogen storage disease
Hereditary haemochromatosis	Homocystinuria
Leukaemia	Mucopolysaccharidoses
Lymphoma	**Malnutrition/malabsorption**
Mastocytosis	Anorexia nervosa
Multiple myeloma	Celiac disease
Thalassemia major	Gastrointestinal surgery
Chronic inflammatory diseases	**Other**
Inflammatory bowel disease	Alcoholism
Liver diseases	Cystic fibrosis
Lung diseases	Duchene muscular dystrophy
Kidney diseases	Excessive exercise
Rheumatic diseases	HIV
Skin diseases	Pregnancy and lactation

GENETIC CAUSES OF OSTEOPOROSIS

- Genetic factors play an important role in osteoporosis and determine up to 80% of BMD.
- In monogenic forms, osteoporosis is caused by a single variant in a gene that has a major role in the skeleton.
- Osteogenesis imperfecta (OI) is the most common of these monogenic disorders with skeletal fragility.
- Only a small number of genetic entities presenting with early-onset osteoporosis without the classical features of OI or syndromic features have been recognized.
- Biallelic mutations in the WNT receptor, *LRP5*, lead to severe childhood-onset osteoporosis and blindness, while heterozygous loss-of-function variants lead to milder forms of osteoporosis, often presenting later in childhood or in adulthood.

Table 3 Genes linked to early-onset osteoporosis

Gene	OMIM	Inheritance	Mutation	Protein	Function
LRP5	259770 166710	AR, AD	LoF	Low-density lipoprotein-related receptor 5	WNT signalling
WNT1	615220	AR, AD	LoF	Wingless-type MMTV integration site family, member 1	WNT signalling
PLS3	300910	XL	LoF	Plastin 3	Formation of F-actin bundles
SGMS2	126650	AD	LoF	Sphingomyelin synthase 2	Mineralisation
ARHGAP25	610587	AD	LoF	Rho GTPase-activating protein 25	Bone cell function and bone metabolism

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REVIEW

Recent Insights into Pregnancy and Lactation-Associated Osteoporosis (PLO)

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1227

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Abstract: During pregnancy and lactation, female physiology adapts to fulfill the fetal and neonatal calcium and phosphorus requirements. The physiological changes that take place during these periods do not affect maternal skeleton resistance to fracture in most of the cases. However, there is a small percentage of women that do experience fragility fractures during these times of life. Pregnancy and lactation-associated osteoporosis (PLO) is an infrequent condition defined by the occurrence of non-traumatic fractures – most frequently vertebral – during the third trimester of gestation and/or the first months of postpartum. Its physiopathology has not yet been completely elucidated. Several authors have reported that risk factors for secondary osteoporosis might be present in up to 80% of the cases of PLO patients. According to recent studies, genetic factors might also play a relevant role in PLO. Given its rarity, the available literature on this condition is limited. Most of the published data consist on case reports and case series articles.

PHYSIOLOGY DURING PREGNANCY AND LACTATION

Period of life	Adaptation mechanisms	Effect	Bone loss?
Pregnancy	1-25 OH Vitamin D increase →	Doubled-up intestinal absorption of calcium	No
	PTHrp increase →	Mild bone resorption increase	
Lactation	Suckling>> HyperPRL>>(-) GnRH>> HypoE2 →	Increased bone resorption	Yes.
	PTHrp increase		
However, pregnancy and lactation do not increase the risk of fracture in the long term			

HyperPRL: Hyperprolactinemia.

HypoE2: Hypoestrogenism

Figure 1 HyperPRL: Hyperprolactinemia. HypoE2: Hypoestrogenism. During pregnancy, the fetal demand of calcium is met by an increase of the levels of calcitriol and PTHrp. As a consequence, intestinal absorption of calcium doubles and bone resorption increases. This leads to little or no change in BMD by the end of pregnancy. During lactation, the suckling of the breast generates an increase of PRL, thus inhibiting hypothalamic-pituitary-ovarian axis. The breast also releases PTHrp. Hypoestrogenism and the high circulating levels of PTHrp enable boost bone resorption leading to an important loss of BMD during lactation.

PHYSIOLOGY DURING PREGNANCY AND LACTATION

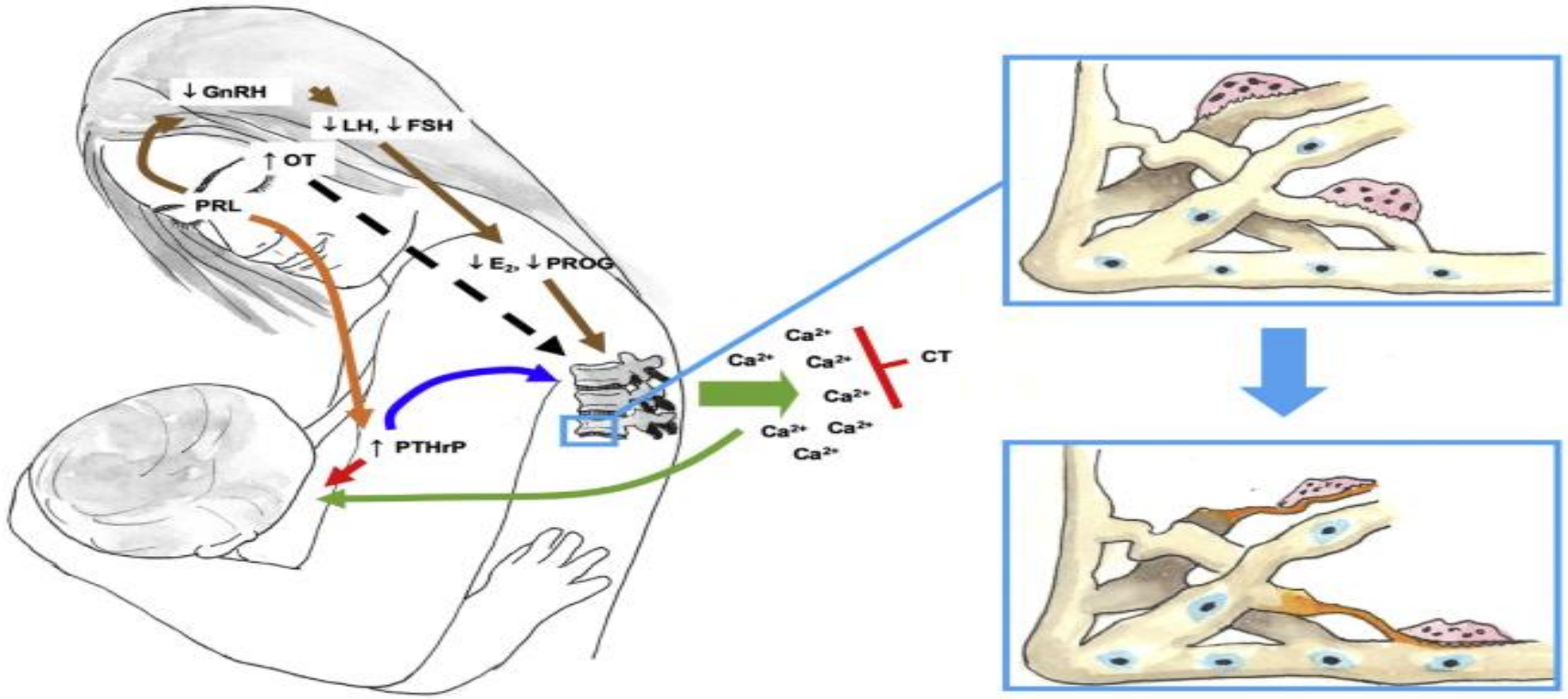

Fig. 1. Hormonal regulation of calcium mobilization during lactation. The upper right image shows osteoclastic bone resorption of maternal trabecular bone, resulting in degradation of trabecular microarchitecture seen in the lower right image. Original drawing by Christopher S. Kovacs, MD.

PHYSIOLOGY DURING PREGNANCY AND LACTATION

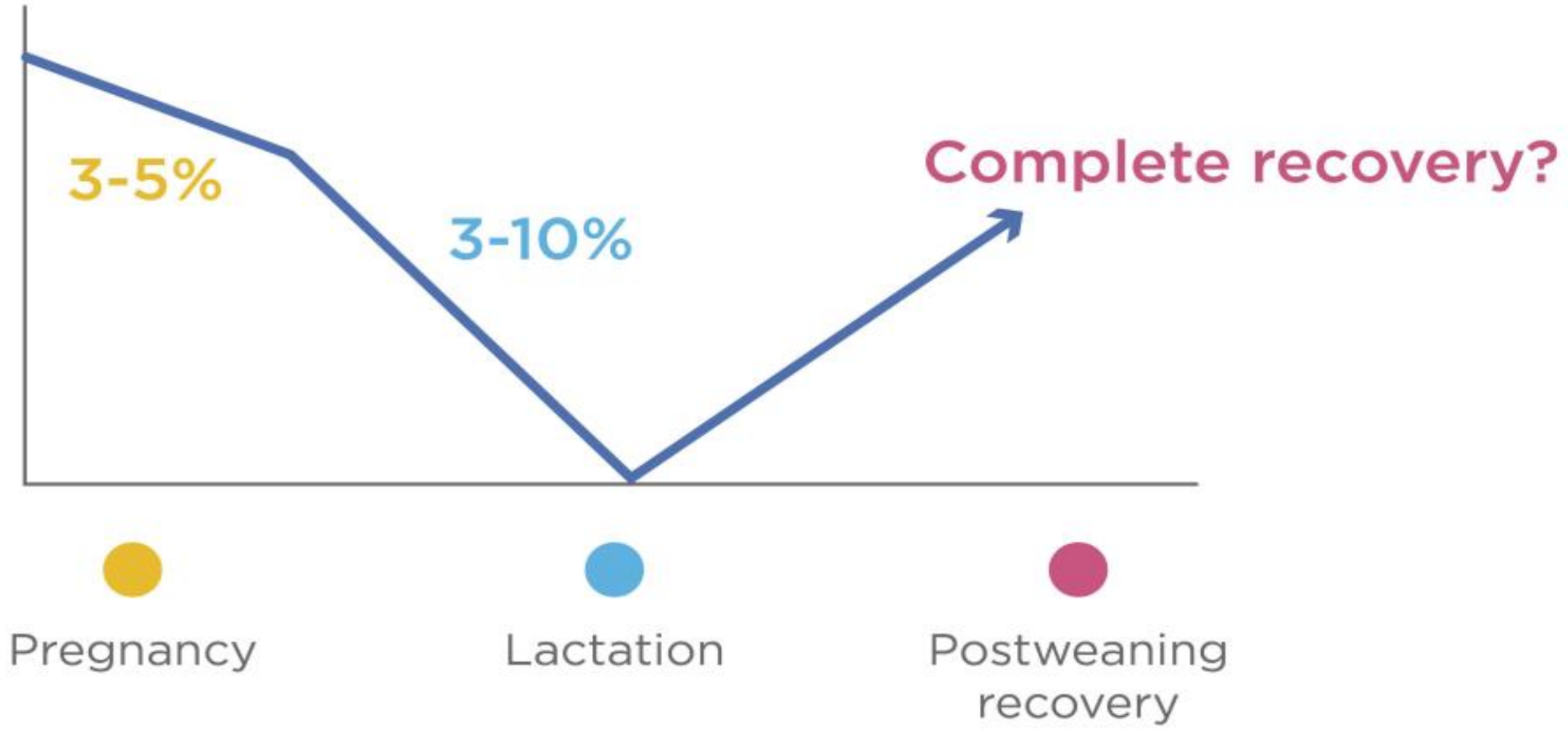

Figure 2 During pregnancy, a little decrease of BMD might occur during pregnancy. During lactation, bone resorption exacerbation leads to a significant decrease of BMD, especially during the first 2 to 6 months. After discontinuing lactation, female skeleton experiences an important increase of BMD. In most women, the loss of bone density is completely reversed between 6 to 12 months after weaning.

PREGNANCY AND LACTATION ASSOCIATED OSTEOPOROSIS(PLO)

- A rare condition in which women suffer fragility fractures, most commonly vertebral, during the third trimester of pregnancy or early postpartum (Less frequently, patients might suffer hip fractures).
- The incidence is calculated to be around 0.4 per 100000 women.
- This condition usually affects primiparous women in their fourth decade of life.
- Experiencing PAO (as a first-time event) during the second pregnancy is described in less than 10–30% of cases.

PREGNANCY AND LACTATION ASSOCIATED OSTEOPOROSIS(PLO)

- Severe back pain is the most frequent form of presentation and it is often interpreted as a typical pregnancy or postpartum symptom. Thus, this condition is usually misdiagnosed.
- The pathophysiology of this disorder is still not well known. According to most studies performed in women with PLO, risk factors are present in up to 80–85%.
- PAO remains one potential indication for a non-obstetric cause-related cesarean section.

Table 1 Risk Factors and/or Conditions for Pregnancy and Lactation Associated Osteoporosis

Non-Modifiable

Low peak bone mass?
Genetic factors (eg LRP5 mutations)
Impaired calcium absorption
Inadequate high release of parathyroid hormone-related peptide

Modifiable

Nutritional
Inadequate calcium intake
Vitamin D insufficiency
Lactose Intolerance

Endocrine
Primary hyperparathyroidism
Hyperthyroidism
Hypercortisolism
Conditions associated with low estrogen levels:
- Pituitary disorders involving sex steroid deficiency
  - Anorexia nervosa
  - Longstanding oligomenorrhea
  - Premature ovarian failure
  - Low Body mass index

Gastrointestinal
Celiac disease
Inflammatory bowel disease
Cystic fibrosis
Other malabsorptive disorders

Renal
Hypercalciuria
Chronic renal insufficiency
Renal tubular acidosis

Medications
Heparin
Oral glucocorticoids
Hypothalamic releasing hormone analogues
Proton pump inhibitors
Medroxyprogesterone acetate
Anticonvulsants
Certain anti-seizure medications (phenytoin, carbamazepine)
Cancer chemotherapy

Others
- Smoking
- Alcohol
- Bed rest
- Osteogenesis imperfecta
- Connective tissue disorders
- Ehlers-Danlos syndrome

Table 2 Laboratory Assessments in Women with PLO

General Laboratory	Bone Metabolism Laboratory	Secondary Osteoporosis Causes
Hematology panel	Serum calcium and phosphorus	Serum protein electrophoresis
Complete metabolic panel	24 h urine calcium, phosphorus and creatinine	CRP
Urine panel	PTH	Total IgA
	25-OH Vitamin D	Antitransglutaminase IgA
	Bone formation markers*(serum):	TSH
	P1NP	Other specific tests:
	BAP	Dexamethasone suppression test (hypercortisolism)
	Osteocalcin	FT4, TPO Ab.
	Bone resorption markers**:	FSH, Estradiol (if premature ovarian failure is suspected)
	CTX (serum)	PRL
	NTX (24 h urine)1	

Notes: *P1NP is the preferred formation bone marker, although it is expensive and not always available; **The level of CTX is considered the best resorption marker, due to its lower variability with diet changes, circadian rhythm and kidney function.

Abbreviations: PTH, Parathormone; P1NP, Amino-terminal propeptide of type 1 procollagen; BAP, Bone alkaline phosphatase; CTX, Beta-Crosslaps; NTX, Amino-terminal telopeptides; DPD, Deoxy-pyridinoline; CRP, C-reactive protein; Ig, Immunoglobulin; TSH, Thyroid stimulating hormone; FT4, Free thyroxine; Ab, Antibody; FSH, Follicle stimulating hormone; PRL, Prolactin.

MANAGEMENT OF PATIENTS WITH PLO

- Typically, PAO/LAO is self-limited, but its devastating effects such as hip fracture or serial VFs might have a dramatic impact.
- Once recognized, it is difficult to decide on a drug free option for patients from the perspective of specific medication against osteoporosis in addition to deciding the type and timing of orthopedic surgery.

NON-PHARMACOLOGICAL TREATMENT

- Calcium and vitamin D should be optimized.
- Calcium intake between 1000 and 1500 mg/day, whereas 25 OHD levels should be ≥30 ng/dl.
- Through a daily dairy products intake. (a cup of milk: 250–300 mg, fortified yogurt: 500 mg, one serving of cheese (50 g): 200–350 mg of calcium).
- If the patient cannot achieve the required intake of calcium through a daily diet, supplementation with calcium tablets is also available.
- It is important to explain to the patients that calcium should be taken in different servings of a maximum of 500 mg each throughout the day to maximize its absorption.

NON-PHARMACOLOGICAL TREATMENT

- Vitamin D can be obtained mostly by sun exposure.
- If the recently fractured PLO patient presents with lower than 30 ng/mL levels, vit D supplement at least 1000 to 2000 UI per day (depending on baseline levels).
- Significant spontaneous increase in BMD of about 6 to 12% at LS at 6–12 months after weaning. Similar significant improvement has been reported at the hip.
- Women with PLO should be advised to discontinue breastfeeding as early as possible (in order to resume the hypo-estrogenic status and potentially to reduce the levels of PTHrP).

NON-PHARMACOLOGICAL TREATMENT

- Other considerations include adequate analgesia for painful vertebral fractures and physical therapy.
- When fractures consolidate, after 3 to 6 months and pain has diminished, these patients should be encouraged to perform reasonable, but not excessive, weight-bearing and physical resistance activity to help maintain bone and muscle mass and mobility.

UPTODATE

Osteoporotic thoracolumbar vertebral compression fractures: Clinical manifestations and treatment

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INTRODUCTION

— Osteoporotic fractures (fragility fractures, low-trauma fractures) are those occurring from a fall from a standing height or less, without major trauma such as a motor vehicle accident. Vertebral compression fractures are the most common type of osteoporotic fracture [1]. They often occur at the midthoracic (T7-T8) spine and the thoracolumbar junction (T12-L1). Fractures may result in significant back pain, limited physical functioning and activities of daily living, and can lead to loss of independence, depression, and chronic pain. Osteoporotic fracture is an important risk factor for subsequent fracture.

MILD TO MODERATE PAIN

- Treated initially with nonopioid oral analgesics.
- In small randomized trials, calcitonin hastened the relief of pain from vertebral fractures, and it can be a useful adjunct to traditional analgesics in the acute setting, because it is not effective immediately. It is generally continued for a 2 to 4 week course.
- Nasal calcitonin, 200 units (one spray) once daily alternating nostrils.

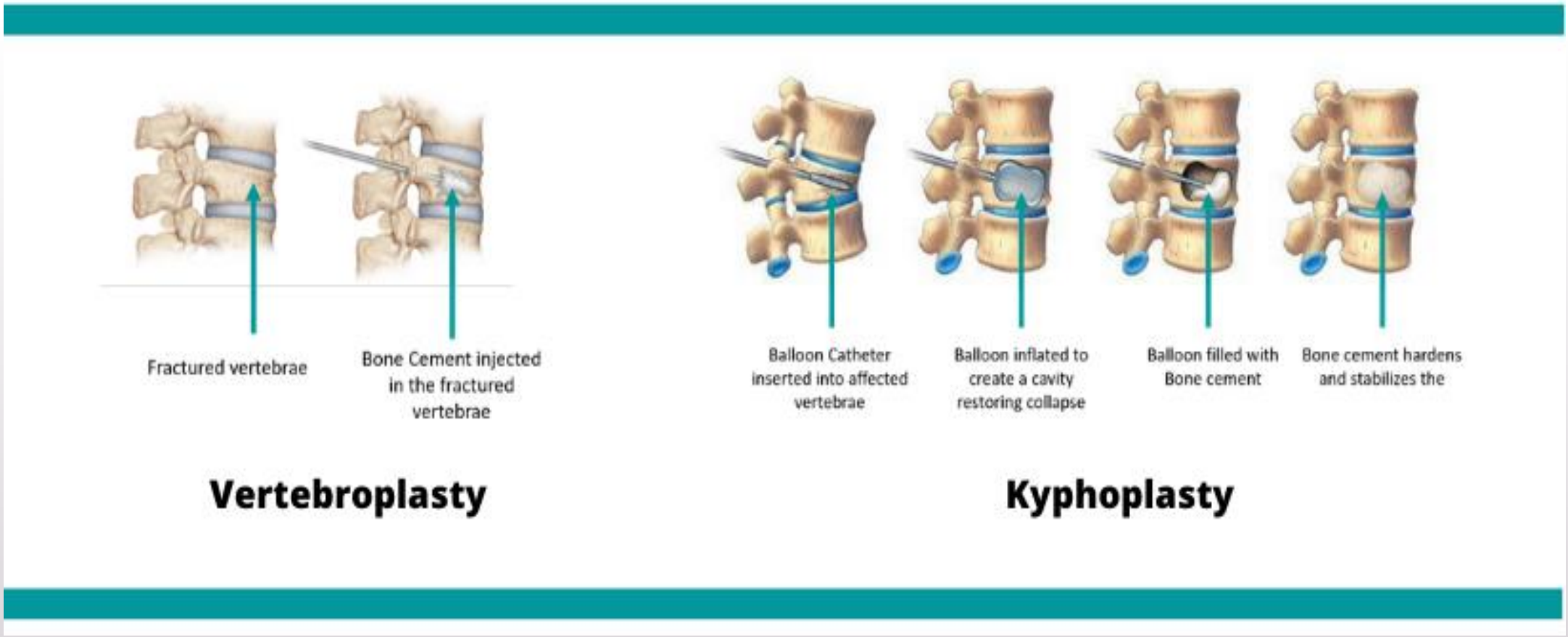
PERSISTENT PAIN

- Greater than 6 weeks of medical management
- Treatment: continued medical management or vertebral augmentation.
- Continued medical management for patients who have noticed some improvement in pain and who are able to tolerate, maintain, or taper opioids and begin a physical therapy program.
- In some patients with persistent pain, the degree of vertebral compression may progress with time to such an extent that vertebral augmentation may be difficult to perform successfully. In such cases, continued medical management is the only option.

CHRONIC PAIN

- 3 to 6 months post fracture
- Require further evaluation to determine if the fracture remains metabolically active (as evidenced by the presence of bone marrow edema) or if additional fractures or other pain generators may have developed.
- Treatment of nonhealing or slowly healing fracture: continued medical management or vertebral augmentation.
- Patients should be informed that there are few data evaluating vertebral augmentation in patients with chronic fractures and that pain may not improve after the procedure.

VERTEBRAL AUGMENTATION PROCEDURES (VERTEBROPLASTY AND KYPHOPLASTY)



SELECTION OF PATIENTS

- Mild to moderate pain that is responding to medical management, vertebral augmentation is **not** indicated, because placebo (sham) controlled trials show no benefit compared with controls.
- For patients with incapacitating pain who are unable to taper parenteral opioids and for those who are not improving with or are intolerant of oral opioids, some clinicians, suggest vertebral augmentation, while others prefer continuing medical management.

SELECTION OF PROCEDURE

- Vertebroplasty is performed when there is little to no compression of the vertebral body, but MRI shows bone marrow edema consistent with fracture.
- Kyphoplasty relies on the use of a balloon tamponade system that can have technical difficulties, but it may partially restore vertebral height.
- Systematic reviews and meta-analyses of randomized trials comparing the procedures have not shown significant differences in short- or long-term pain scores, short or long-term disability scores, or adjacent level fracture rates.

ADVERSE EFFECTS

- **New fractures:** In most, but not all, randomized trials, the incidence of new fractures was not significantly different in the vertebroplasty/kyphoplasty group when compared with controls. However, retrospective reviews of patients treated with vertebroplasty found a high rate of new vertebral fractures.
- Risk factors for new vertebral compression fracture after vertebroplasty: low BMD, intradiscal cement leakage, and vertebral height restoration, age > 80 years, vitamin D deficiency, and need for procedures at multiple levels.

BRACING

- Not typically use bracing for the management of pain.
- If a brace is used to relieve pain, it should be used in the acute and subacute phases of treatment for pain control, as atrophy of the core musculature may occur with prolonged use.

diagnostics

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Review

Bridging the Gap: Pregnancy—And Lactation—Associated Osteoporosis

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Abstract: Early diagnosis of pregnancy- and lactation-associated osteoporosis (PLO) is mandatory for a good outcome. Standard care is not a matter of conventional guidelines, rather it requires an individualized strategy while true overall incidence and pathogeny remain open issues. This is a narrative review based on full-length English articles, published between January 2021 and March 2023 and accessed via PubMed (no traumatic fractures or secondary osteoporosis are included). Our case-sample-based analysis included 836 females with PLO (the largest cohort based on published cases so far) through 12 studies and 24 single case reports. Except for one survey, these involved retrospective cohorts of small size (6–10 females/study) to medium size (23–47 women/study), and large cohorts with >50 subjects per study (a maximum of 379). Age of diagnosis: from 24 to 40 years for case reports (most subjects being over 30 and primigravida), while original studies indicated an average age between 31 and 34.18 years. Type of fractures underlined a most frequent vertebral phenotype (a mean of 2 to 5.8 vertebral fractures per patient) versus a most severe non-vertebral phenotype (hip and femoral neck fractures mostly requiring surgery). Potential contributors varied: smoking (1/3–1/2 of subjects), family history of osteoporosis (1/3), heparin and glucocorticoid use in pregnancy, low body mass index (majority of cases), hypovitaminosis D; and (with a low level of statistical significance) anti-psychotic medication, gestational diabetes, lupus, thrombophilia, anemia, in vitro fertilization (1/3 in one study), twin pregnancy, tocolysis with MgSO4, and postpartum thyroiditis. Most remarkably, up to 50% of PLO patients harbor mutations of *LRP5*, *WNT1*, and *COL1A1/A2* (more damaged form with potential benefits from osteoanabolic drugs); gene testing might become the new norm in PLO. The low index of clinical suspicion should be supported by performing magnetic resonance imaging (gold standard in pregnancy) with DXA (in lactation). Low

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First author Year of Publication Reference Number	Type of Study	Studied Population	Results	Outcome
Toussia-Cohen 2023 [38]	retrospective	n = 34 pregnant females with TOH (mean age: 34.18 y)	50% with PAO 50% with LAO	29%: family history of OP 47%: smokers 32%: IVF
Çataltape 2022 [39]	retrospective	n = 29,291 pregnant females	0.078% with SSF (n' = 23)	30%: 25OHD < 20 ng/mL
Hadji 2022 [40]	retrospective	n = 47 patients with PAO/LAO treated with TPT (20 µg/day, 24 mo)	mean VFs: 4 incidental VF under TPT: 7.8%	After 24 mo (p < 0.001): lumbar BMD +30.1% femoral neck BMD + 11.7% hip BMD + 12.2% after 12 mo since TPT (p = NS): lumbar BMD + 1.4% femoral neck BMD + 2.6% hip BMD + 4.1%
Toba 2022 [41]	retrospective	n = 837,347 females who had 2-year history of obstetric admission	rate of fractures within first 2 y after birth: 4.5/10,000 pregnancies (n' = 379)	7.5%: recommendation for stopping breastfeeding or anti-osteoporotic drugs Other contributors: ■ maternal age ≥ 4 y ■ smoking ■ glucocorticoid use ■ Charlson Comorbidity Index score ≥ 1

Aytar 2022 [42]	retrospective	n = 10 females with LAO (median age: 30 y)	LAO median diagnostic: 1 mo 7/10 with VFs	n = 1: vertebroplasty Potential contributors: ■ 1/10 twin pregnancy ■ 4/10 smoking
Condon 2022 [43]	survey	n = 69 females with PAO	4.4%: PAO diagnostic after 1 mo since pain started	42%: were able to provide the child care by themselves after 6 mo
Miles 2021 [44]	TriNetX-based study	n = 135 patients with osteporotic fractures within the 1st year postpartum	44%: lumbosacral VFs	Therapy (n = 70): each of 7% for DEN, TPT, ZOL, pamidronate, ibandronate, calcitonin, cinacalcet, etidronate, alendronate, risendronate
Lampropoulou-Adamidou [45]	multicenter, retrospective, 2-year study	n = 19 patients with PAO/LAO treated with TPT (20 µg/day, 24 mo) n' = 8 patients with VD + calcium	median VFs: 4 versus 2.5	After 12 mo: lumbar aBMD +20.9 versus +6.2% ($p < 0.001$) hip aBMD +10% versus 5.8% ($p = 0.43$) TBS +6.7% versus 0.9% ($p = 0.09$) After 24 mo: N1 = 7 versus N1′ = 6 +32.9% versus +12.2% ($p = 0.001$)
Lee 2021 [46]	retrospective	n = 33 patients with PAO/LAO treated with TPT (12 mo) followed by anti-resorptive drugs (N1 = 13, 18 mo) versus none (N2 = 20)	similar age (mean of 31 y) and BMD at baseline (N1 versus N2)	similar lumbar and hip BMD increase after 1, 2, and 3 y (N1 = N2)
Scioscia 2021 [47]	retrospective	n = 7 females with PAO	6/7 VFs 1/7 TOH	HRPQCT (versus healthy controls): trabecular density < 34% ($p < 0.01$) cortical thickness < 22% ($p = 0.01$)
Butscheidt 2021 [48]	multicenter	n = 42 females with PAO/LAO (genetic analysis)	50% with genetic variants (*LRP5*, *WNT1*, and *COL1A1/A2*)	Females with genetic variants versus non-genetic: higher number of VFs ($p = 0.02$) lower Z-score ($p = 0.002$) HRPQCT: lower trabecular and cortical density
Yıldız AE 2021 [49]	retrospective	n = 1260 females with MRI scans	0.5% had PAO/LAO VFs (n' = 6)	mean VFs = 5.6

PHARMACOLOGICAL TREATMENT

- Most experts still suggest that pharmacological treatment should be reserved for the most severe cases with multiple vertebral fractures, persistent disabling pain, or those patients who do not experience a satisfactory recovery in BMD after weaning and adequate calcium and vitamin D supplementation.

PHARMACOLOGICAL TREATMENT

- **Bisphosphonates** are used less because they accumulate in bone, but DEN, TPT, and calcitonin display lesser long-term effects so should be considered first.
- **Calcitonin** may be a viable alternative to the pharmacological treatments (but its not a first line) because it does not pass the placental barrier, and it inhibits bone resorption and relieves bone pain. However, its use is poorly documented, and only has been used nasally alongside vitamin D.

TERIPARATIDE

- Indications: improve BMD after a failed trial of bisphosphonates, fewer side effects compared to bisphosphonate, severe presentation or inadequate response to conservative treatment.
- Teriparatide treatment showed increased bone turnover in individuals with missense variants in *LRP5*, *LRP6* and *WNT1*, and splicing variants in *PLS3*.
- TPT was prescribed from 6 to 24 months (20 μg/day) and a second gestation should be at least 2–3 years after starting TPT.

TERIPARATIDE

- Side effects: dizziness and leg cramps, arthralgia, headache, and depression, osteosarcoma?!
- In a patient presenting with multiple thoracic compression fractures from PAO, after treatment with calcium, Vit D, and teriparatide at 20 μg/day, the patient's BMD increased by 8% at 12 months and 27% by 18 months in the lumbar spine, and her back pain completely resolved in several months .

TERIPARATIDE

- Lee et al published a retrospective study of a cohort of 64 women with PLO. 43 of them were treated with teriparatide for 12 months and followed up for 3 years. After teriparatide, 13 women received antiresorptive treatment (TPDT-ART), while 20 of them did not receive any anticatabolic drug (TPDT-no ART).
- They concluded that BMD gain by teriparatide administration in premenopausal women with PLO can be maintained without sequential antiresorptive treatment.
- This is in line with previous reports that suggested that the presence of estrogens might avoid the bone loss described in postmenopausal women after stopping teriparatide.

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Article type : 3 Original Article - Australia, Japan, SE Asia

Changes in bone mineral density and bone turnover markers during treatment with teriparatide in pregnancy- and lactation-associated osteoporosis

Running title: Bone density and bone turnover markers after TPTD in PLO

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DESIGN: RETROSPECTIVE COHORT STUDY

Patients: 32 patients with PLO who presented with multiple vertebral fractures to a tertiary institution between 2007 and 2015 were included.

Measurements: Changes in BMD at the lumbar spine (LSBMD) and proximal femur after 12 months of daily subcutaneous injections of 20 mg TPTD (n = 27) were assessed. Subjects who rejected the TPTD treatment were used as controls (n = 5). Serum calcium, phosphate, creatinine, 25(OH)D, iPTH, OCN, and serum CTX levels were assessed every 3 months during the follow-up period.

- **Results:** LSBMD increased in both subjects treated with TPTD and controls, with greater increases in the TPTD group (15.5 ± 6.6 % vs. 7.5 ± 7.1 %, p = 0.020) after adjustment for age and baseline LSBMD.
- During follow-up, serum levels of osteocalcin (OCN) and CTX increased significantly in the TPTD group. TPTD treatment and younger age, were independently associated with greater increases in LSBMD.

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REVIEW

Pregnancy-Associated Osteoporosis: A Literature Review

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Abstract

Pregnancy-associated osteoporosis (PAO) is a rare pathology affecting women in pregnancy or the postpartum period. During normal pregnancy and lactation, there are substantial physiological changes in the woman's skeletal structure as well as calcium homeostasis to meet demands of the developing fetus. While these adaptations and generally of no clinical consequence for the mother, and subsequently resolve postpartum, a small number of women will develop osteoporosis and suffer from non-traumatic fragility fractures. Due to the rarity of PAO, systematic study to date has been limited. Etiology is poorly understood, but endocrine effects, nutrient deficiency, genetic predisposition, biomechanical factors, and medication exposures are likely to play a role. Management of PAO is not well understood, due both to a poor evidence base and the rarity of the condition. However, traditional osteoporosis drugs such as bisphosphonates, denosumab, and teriparatide have all been reported in literature. Early diagnosis and treatment of these patients are especially important in the prevention of reoccurrence fractures and to improve the quality of life for these patients.

LONG TERM FOLLOW-UP & PREVENTION OF COMPLICATIONS OF PAO

- women who are diagnosed with PAO during the index pregnancy should be informed about the increased risk of fragility fractures with subsequent pregnancies.
- Kyvernitakis et al. conducted a prospective cohort study investigating fracture risk during subsequent pregnancies in 107 patients. Patients with one fracture at the time of the initial diagnosis had a 10% fracture rate during their next pregnancy, compared to patients with more than one fracture at the time of initial diagnosis, which showed a 27% fracture rate in their next pregnancy ($p = 0.047$).
- These results suggest that the number of fractures during the first pregnancy correlates with an increased risk of new fractures in subsequent pregnancies.

MANAGEMENT OF THIS CASE

- Nasal spray Calcitonin 200 microgram 1 puff daily
- Tab Naproxen 500 mg PO BD
- Tab Calcium & pearl Vit D Daily
- Pen Cinnopar 20 microgram (8 unit) SC daily for at least 18 months
- BMD after 12 months of treatment
- Physical therapy after pain control
- Spine specialist orthopedic surgery consult


Thanks for your attention