Atypical Femoral Fractures

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Disclosures

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Learning Objectives

- Definition and radiographic characteristics
- Epidemiology
- Clinical Risk Factors
- Surgical and Medical Management
- Canadian AFF Registry
DEFINITION AND RADIOGRAPHIC CHARACTERISTICS
Atypical femoral fractures (AFF)

- low-trauma stress fractures
- in subtrochanteric or shaft region of the femur
- specific radiographic findings
- can be associated with bisphosphonate therapy
Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Report of a Task Force of the American Society for Bone and Mineral Research

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Femur Fractures
64yoF Caucasian with bilateral incomplete AFFs

Typical Femoral Stress Fracture
Incomplete AFFs: Plain Radiographs

Lucent line + Focal periosteal reaction on lateral cortex
Beaking

Lucent line + Focal periosteal reaction on lateral cortex
Beaking
Complete AFFs: Plain radiographs

Transverse fracture line
Subtrochanteric

Transverse fracture line
Mid-diaphyseal

Focal Periosteal Reaction on Lateral cortex
Oblique extension
Medial spike
AFF: ASBMR Case Definition 2013

- Major features (4 out of 5 criteria):
  - Below lesser trochanter, above supracondylar flare
    1. Little or no trauma
    2. Transverse (or mostly transverse) or short oblique configuration
    3. Non-comminuted (or minimally comminuted)
    4. Complete fractures extend through both cortices and may have a medial spike; Incomplete fractures involve only the lateral cortex
    5. Localized periosteal or endosteal reaction of the lateral cortex

- Minor features (none required):
  - Generalized increase in cortical thickness
  - Delayed healing
  - Prodromal symptoms such as dull aching pain in groin or thigh
  - Bilateral fractures and symptoms
AFF: Key Clinical Feature

ASBMR Task Force review

- 75% have prodromal pain
  - These features are fundamentally different from common osteoporotic femur fractures and strongly suggest a distinct pathogenesis

Ontario AFF Cohort (n~300)

- ~80% have prodromal symptoms: pain, ache, weakness, loss of function

Shane et al., ASBMR Task Force Report, J Bone Miner Res 2010
Specific radiographic findings

Plain X-rays

Bone Scan

MRI

DXA

Densitometer-based femur scans
Pseudofractures in Patients With Low-Turnover Osteoporosis

ERIC S. ORWOLL, MD
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Portland

PSEUDOFRACTURES (Looser’s zones, Milkman’s fractures) were first described in Germany and Austria in the period immediately following World War I. Their cause was considered to be lack of adequate nutrition (hunger osteopathy) or esophageal reflux (two years) and one multivitamin per day that contained 400 IU of ergocalciferol (two months). She had received a two-month course of estrogen therapy that had been discontinued five years before.

On physical examination she was mildly obese and had mild dorsal kyphosis without vertebral tenderness or scoliosis. There was minimal tibial and clavicular tenderness and slight generalized weakness. An initial laboratory evaluation elicited the following values: serum creatinine, 1.0, calcium, 9.6, and phosphorus, 3.5 mg per dl; total protein, 7.4 grams per dl; alkaline phosphatase, 118 mU per ml (normal, 35 to 105). Serum glutamic oxaloacetic transaminase (AST) formerly ali-

The fractures, which appeared on roentgenograms as transverse radiolucent zones with variable callus formation, healed slowly or not at all despite Women with osteoporosis, who, in addition to having "typical" fractures associated with trauma, had multiple undisplaced, frequently asymptomatic fractures that developed in the absence of trauma or apparent stress. The latter resembled pseudofractures (Looser's, transformation zone) but bone turnover. No subperiosteal resorption was seen. Also noted were compression fractures of the bodies of the 7th, 9th and 12th thoracic vertebrae. Roentgenologic photodensitometry of the proximal radius indicated decreased bone mineral mass, combined cortical thickness and bone mini-

FIG. 2.—Left, Radiograph of proximal left femur of patient in case 2 showing femoral pseudofracture (arrow). Middle, Close-up of left femoral pseudofracture (arrow). Right, Right femoral radiograph showing zone of lucency at the site of a previous fracture.

FIG. 3.—Case 2. Development of spontaneous fractures in right 4th and 5th metatarsals. Left: 6 years after reported admission, metatarsals intact. Centre: 6 months later, faint transverse radiolucent line through proximal shaft of 4th metatarsal, with surrounding callus. Right: further 15 months later, radiolucency in 4th metatarsal more prominent and accompanied by transverse radioluclency and adjacent sclerosis in distal shaft of 5th metatarsal. Both “fractures” occurred without obvious stress and were painless.

FIG. 4.—Case 2. Spontaneous transverse fractures of right femur 2 cm inferior to lesser trochanter (T); callus present only in medial cortex.
Trends in Incidence of Subtrochanteric Fragility Fractures and Bisphosphonate Use Among the US Elderly, 1996–2007

Zhong Wang and Timothy Bhattacharyya

Intramural Research Program, National Institute of Arthritis, Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, USA
Trends in Incidence of Subtrochanteric Fragility Fractures and Bisphosphonate Use Among the US Elderly, 1996–2007

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“In the context of declining typical hip fractures among the US elderly, we observed small but significant increases in the incidence of subtrochanteric fragility fractures.”

“We estimated that for every 100 or so reduction in typical femoral neck or intertrochanteric fractures, there was an increase of one subtrochanteric fragility fracture.”
Incidence of Complete AFFs

Ontario CANADA Data

~1-2/1000 py after 6 - 7 years

Kaiser Permanente California Data

~1/1000 py after 8 - 9.9 years

Bisphosphonate Use and the Risk of Subtrochanteric or Femoral Shaft Fractures in Older Women

Laura Y. Park-Wyllie, PharmD, MS

Context Osteoporosis is associated with significant morbidity and mortality. Calciton

~1-2/1000 py after 6 - 7 years

Objective To determine whether prolonged bisphosphonate therapy is associated with an increased risk of subtrochanteric or femoral shaft fracture.

Design, Setting, and Patients A population-based, nested case-control study to explore the association between bisphosphonate use and fractures in a cohort of women aged 68 years or older from Ontario, Canada, who initiated therapy with an oral bisphosphonate between April 1, 2002, and March 31, 2008. Cases were those hospitalized with a subtrochanteric or femoral shaft fracture and were matched to up to 5 controls with no such fracture. Study participants were followed up until March 31, 2009.

Main Outcome Measures The primary analysis examined the association be-
New Cautions About Long-Term Use of Bone Drugs

BY TARA PARKER-POPE  MAY 9, 2012 6:32 PM  ↓ 136

In an unusual move that may prompt millions of women to rethink their use of popular bone-building drugs, the Food and Drug Administration published an analysis that suggested caution about long-term use of the drugs, but fell short of issuing specific recommendations.

The F.D.A. review, published in The New England Journal of Medicine online on Wednesday, was prompted by a growing debate over how long
Osteoporosis drugs may not be best choice
CLINICAL RISK FACTORS
Clinical Risk Factors

- Age
- Sex
- Race
- Genetics
- Medical Conditions
- Drugs
- Bone characteristics
Age and Sex

- Mostly women, very few men
- Younger women

Ontario AFF Cohort (n~320):
Mean age ~70 years
Range= 19 to 90 years

Dell et al. JBMR 27 (12):2544-2550, Dec 2012
Race and Genetics

- Asians (Ontario AFF cohort, Kaiser Permanente, Singapore and Asian groups)

- Hypophosphatasia

*Fig. 3. Anteroposterior and lateral view of diaphyseal femoral fractures without previous deformities of the femur, in the absence of prior bisphosphonate treatment (A–D) and after bisphosphonate treatment (E–H). A) Five-year-old girl with OI type IV due to a glutamic substitution in COL1A1, B–D) Five-year-old boy with OI type V due to a mutation in ITK/NX (E, F) Seven-year-old girl with OI type VI due to a homogyous hypomethylated mutation in CRTAP, after 2.3 years of pamidronate treatment, G) A) Six-year-old boy with OI type VII due to a hypomethylated mutation in SIBMPF1 after 3.2 years of pamidronate treatment.*

Sutton R et al. JBMR
Defect in osteoclast function
- Pycnodysostosis: CTSK gene
- Osteopetrosis: TCIRG1, OSTM1, PLEXHM1, SNZ10, TNFS11, TNFRSF11A, CAIL, CLCN7 genes

Defect in mevalonate pathway
- GGP51 gene

Defect in osteoblast function
- Osteoporosis pseudoglioma syndrome: LRP5 gene

Bone remodeling unit

Bone matrix

Defect in osteocyte function
- X-linked osteoporosis: PLS3 gene

Defect in collagen synthesis and structure
- Osteogenesis imperfecta: COL1A1, COL1A2, CRTAP, LEPRE1, PPIB, SERPINH1, FKBPI0, PLOD2, SP7 genes

Mineralization defect
- Hypophosphatasia: ALPL gene
- X-linked hypophosphatemia: PHEX gene
Medical Conditions

- Rheumatoid Arthritis
- Vitamin D deficiency
- Diabetes
- Breast Cancer
- Dementia
Drugs

- Long duration of BP therapy
- Multiple anti-resorptive medications
- Glucocorticoid use
- PPIs
Incidence of AFFs increase with duration of BP therapy

Fig. 4. Incidence of atypical femur fractures according to duration of bisphosphonate exposure (unadjusted and age-adjusted, showing incidence and 95% confidence intervals).
BP exposure is heterogenous

Ontario AFF Cohort (n~320):
Mean ~10.6 years
Range= 0 to 30 yrs

Fig. 2. Age at time of atypical femur fracture and duration of bisphosphonate exposure. $R = 0.01, p = 0.85$.  

Dell et al. JBMR 27 (12):2544-2550, Dec 2012
Other OP therapies

- Denosumab (n=2:0 in FREEDOM)
- Odanacatib (n= 5:0 in LOFT)
- Romosozumab (n=1:0 in FRAME; n=2:4 in ARCH open phase)
- None reported in Abaloparatide
Bone Characteristics

- BMD (osteopenia)
  - Shaft diameter
- HRpQCT
  - CTh
  - CPo
  - BV/TV
- TBS

Fig. 3. Bone density and duration of bisphosphonate exposure in cases with atypical fracture. Bone density was the lowest T-score from hip or spine. $R = 0.03, p = 0.7$.

Dell et al. JBMR 27 (12):2544-2550, Dec 2012
Varus hip angle, bow leg deformity
Pathogenetic Mechanisms

- Effect of suppression of bone remodeling on:
  - Bone’s material properties – collagen, AGEs, increased tissue mineral density etc.
  - Healing of stress fractures

- Relationship of hip and lower limb geometry

- Genetic susceptibility – collagen abnormality, low bone turnover at baseline, etc…
SURGICAL AND MEDICAL MANAGEMENT
Surgical Management

Complete Fractures
- Fixation with IMR
- Reduce the gap

Incomplete Fractures
- Unclear when to prophylactically fix
- Most will not require fixation
Case

64yo Caucasian postmenopausal woman with bilateral incomplete AFFs
My recommendations → X-rays

Focal Cortical Reaction on plain X-ray

Yes

CT scan to determine depth of lucent line through the cortex and extent around circumference

No

1) Reassess cause of discomfort
2) ? Stop and reassess in 6 months
My recommendations: DXA-Femur

Focal Cortical Reaction on DXA-Femur

- **Yes**: CT scan to determine depth of lucent line through the cortex and extent around circumference
- **Equivocal**: Plain Radiographs
- **No**: 1) Reassess cause of discomfort 2) ? Stop and reassess in 6 months

Bone scan (if you can’t see lucent line on X-rays)
Medical Management

ASBMR Task Force Recommendations

STOP

anti-resorptive therapy
(bisphosphonates and denosumab)

Then prophylactic nailing or teriparatide therapy or both
Medical Management

Decrease weight-bearing

Muscle strengthening exercises
Case Series of 30 pts with iAFFs

- After an average of **14.8** months of TPD therapy:
  - healing or healed: 41%
  - stable: 41%
  - prophylactic surgical intervention: 18%

However, 4 developed new lucent lines in the same femur
Mrs. W – healing
TAFF Trial

Teriparatide for healing of incomplete Atypical Femur Fractures

- RCT – teriparatide vs placebo
- Recruiting 60 postmenopausal women
- Outcomes – radiographic and functional outcomes

CALL (416)340-4843 for the TAFF trial
GOING FORWARD…
How do we communicate the real risk to patients?

1. Low:
   - Complete AFFs – ~1/1000 patient years after 6-10 years
   - Incomplete AFFs -- ? ~1/100

2. Drug treatment according to fracture risk – benefit/risk ratio

3. Reassess drug therapies after 3-5 years, consider drug holiday for stable moderate (and ? high) risk patients
How do we communicate the real risk to patients?

If AFF:

- stop antiresorptive therapy
- decrease weight bearing activities
- consider bone formation therapies
It's a Fan!

It's a Wall!

It's a Spear!

It's a Rope!

It's a Snake!

It's a Tree!
AFF Registries

- Ontario AFF Cohort
- Quebec AFF Cohort
- TRAFFIC – in Australia and Singapore

In Canada,
- Canadian AFF Registry
CIHR grants

- Pharmacogenomics
- Prediction rule

We will be recruiting controls for this study

Ontario AFF Cohort – (416)340-4843
SUMMARY
Summary

- Definition and radiographic characteristics
- Epidemiology
- Clinical Risk Factors
- Surgical and Medical Management
- Canadian AFF registry
One Take Home Message

Patients with AFFs are **HETEROGENEOUS**
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Questions and Discussion