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NATURAL HISTORY OF FEMORAL STRESS LESIONS IN LONG-TERM BISPHOSPHONATE THERAPY

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Background

- More than 10 years after the introduction of bisphosphonates, clinical effects of osteoclastic oversuppression presenting as spontaneous nonspinal fractures¹ as well as low energy femoral cortical stress fractures with very distinctive patterns have been reported in patients on prolonged bisphosphonate therapy.²⁻⁶
- **Cortical stress reactions in the form of lateral cortical thickening documented when radiographs were performed during the prodromal period preceding these fractures.³**
- **More than half (53%) of patients presenting with the atypical fractures showed these contralateral stress reactions.⁶**

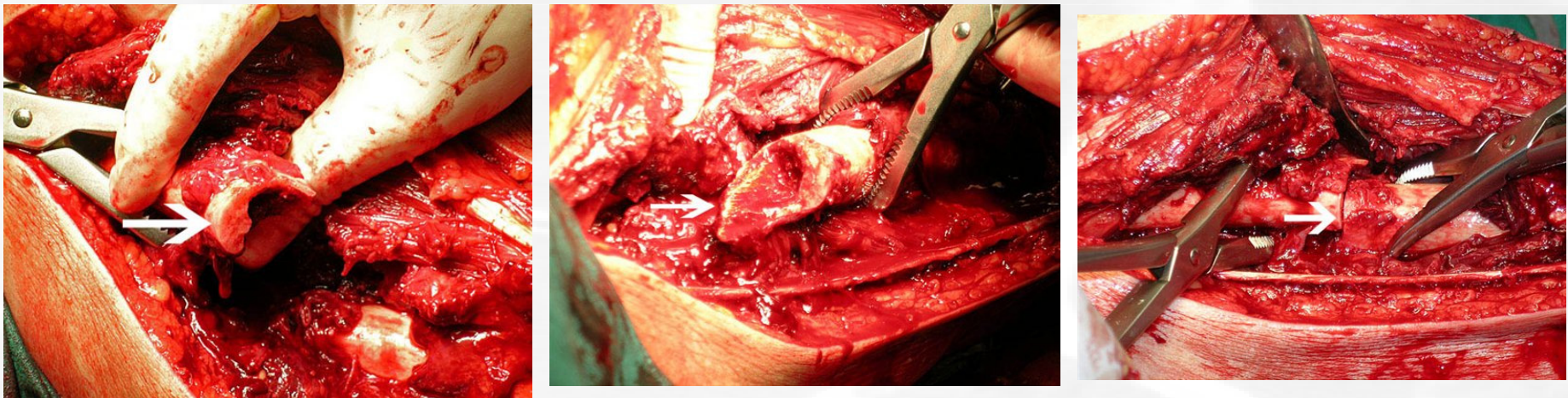


Atypical transverse metaphyseal-diaphyseal fracture of the right femur with contralateral cortical stress lesion in patient on 4 years alendronate therapy

Aim

This article studies the natural history of femoral stress lesions associated with long term bisphosphonate therapy with emphasis on :

- ***Clinical features that predispose to complete stress fractures***
- ***Symptomatic and radiological outcome of unfractured lesions at follow-up***



Intra-operative pictures showing distinct lateral cortical thickening (*arrowed*) ,medial cortical spike (*arrowed*) with a transverse configuration

Methodology :

Hospital database :

1,463 geriatric hip fractures occurring from 1 May 2004 to 31 July 2008

Inclusion criteria

- Pure cortical involvement
- Low energy/spontaneous fractures
- Lateral cortical thickening
- Transverse pattern with medial spike

Exclusion criteria

- Extensions of intertrochanteric fractures
- High energy, polytrauma
- Bony metastases from cancer
- Metabolic bony conditions

32 (97.0%) of 33 patients satisfying these criteriae identified from this database were on prior bisphosphonate therapy

Of these, 16 patients with radiographic documentation of femoral stress reactions in the form of lateral cortical thickening either in pre-fracture radiographs or in the contralateral femur formed the study cohort.

Outcome assessment

Clinical features predisposing to complete fracture

Femurs that fractured (**4 femurs, Group F**) were compared with intact femurs (**12 femurs, Group C**) in terms of :

- Presence of symptoms (thigh discomfort, pain, or “weakness”)
- Radiological evidence of the “dreaded black line”⁷

Follow-up of intact lesions

- Symptomatology at last follow-up
- Radiological outcome at last follow-up
- Occurrence of new lesions on the same femur
- Subsequent pharmacological intervention

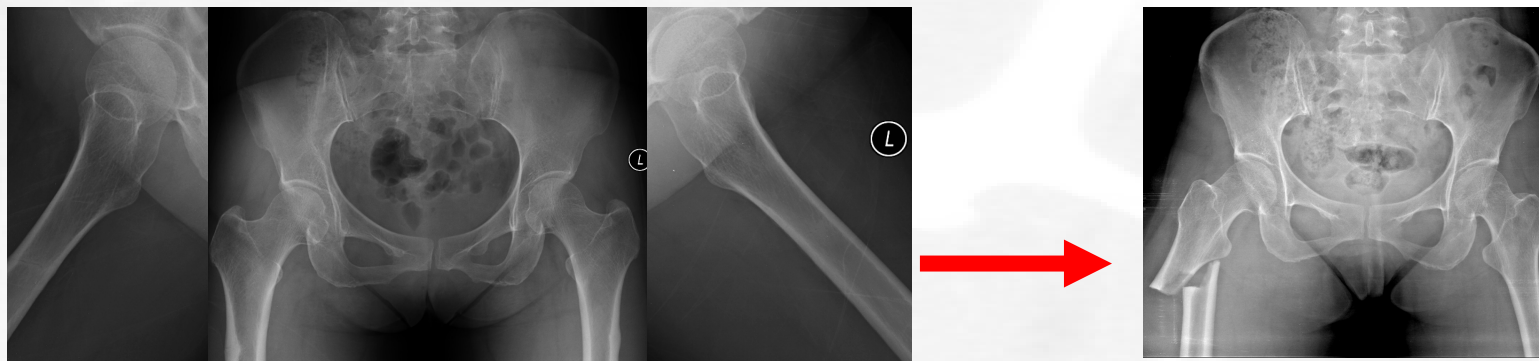
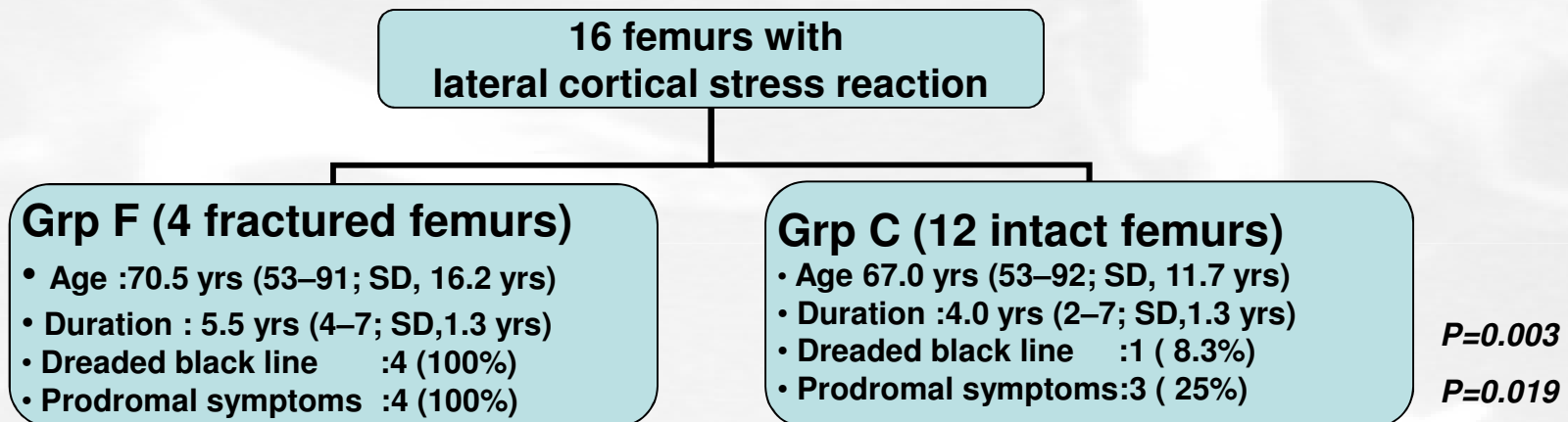
*“Dreaded black line”
across lateral cortical
thickening*



Results :

Factors predisposing to complete fractures

- *Median age was 68.0 years (range, 53.0–92.0 years; SD, 11.9 years)*
- *Median duration of bisphosphonate therapy was 4.5 years (range, 2–7 years; SD, 1.2 years)*
- *Thirteen patients had lesions occurring in the subtrochanteric (metaphyseal–diaphyseal junction), three patients had them in the femoral shaft*



Right femur lateral cortical thickening with “dreaded black line” fracturing in 18 days, left femur cortical thickening, in the absence of the black line remained intact on follow-up.

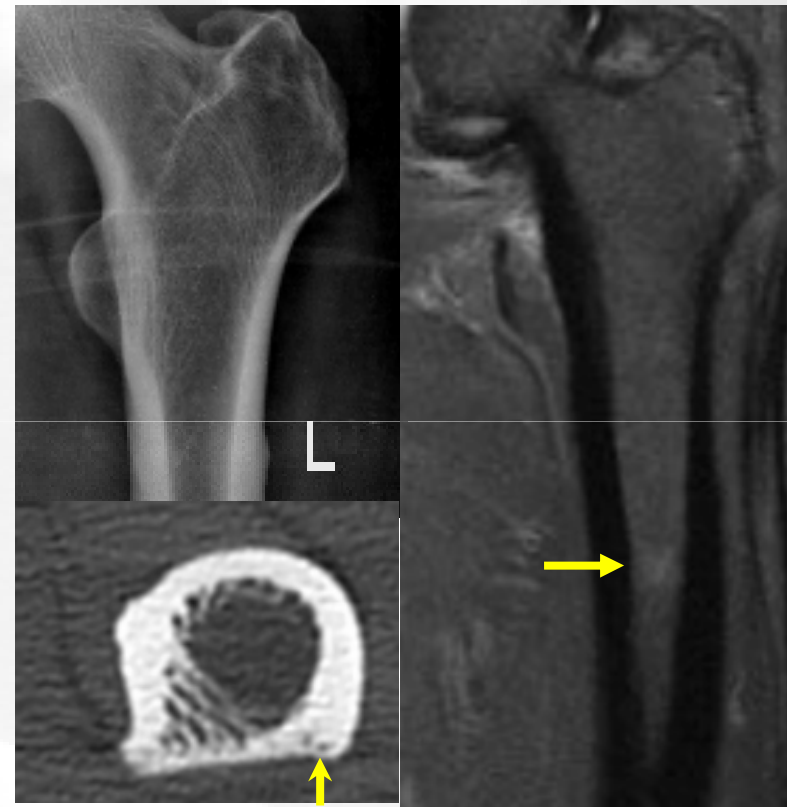
Follow-up of intact femurs

Patient	Age at Diag (yrs)	Dur of BP (yrs)	Follow Up (mths)	Subseg therapy	Symptoms at last follow-up	Stress line on initial contralat X-ray	Stress line on last available X-ray	New lesion
1	65	4	30	Risedronate	Nil	Nil	Nil	Nil
2	67	3	29	Nil	Reduced	Nil	Nil	Nil
3	55	5	30	Strontium ranelate	Same	Nil	Nil	Nil
4	69	5	35	Strontium ranelate	Nil	Present	Nil	Nil
5	53	7	19	Nil	Reduced	Nil	Nil	Nil
6	79	4	15	Teri-paratide	Nil	Nil	Nil	Nil
7	64	5	24	Nil	Nil	Nil	Nil	Nil
8	64	3.5	9	Strontium ranelate	Nil	Nil	Nil	Nil
9	74	2.5	8	Nil	Nil	Nil	Nil	Nil
10	92	4	23	Nil	Nil	Nil	Nil	Nil
11	65	3.5	5	Teri-paratide	Nil	Nil	Nil	Nil

- One patient lost to follow-up due to severe dementia
- No significant difference in the ratio of the lateral cortical thickening to the width of the femur between the initial plain anteroposterior radiograph (median ratio, 34.3%; range, 26.9%–42.5%) and the last available radiograph (median ratio, 32.5%; range, 27.6%–41.0%) ($P = 0.310$).

Discussion

- Significantly increased risk of complete fracture in the presence of the “dreaded black line” and thigh discomfort in cortical stress reactions after prolonged bisphosphonate therapy.
- Distinct region of cortical thickening traversed by “dreaded black line” :
Callus reaction in response to cortical microdamage, as evidenced by resorptive cavities, with bone marrow insinuation and thinning of the overlying cortex on MRI ⁶ with region of chronic non-union ⁸ represented radiologically by the black line.
- Discontinuation of alendronate seems to result in partial or full resolution of symptoms and radiologic “stabilization” of these lesions.
- Possible reversibility of disturbance in bone remodelling associated with prolonged anti-resorptive therapy



Resorptive cavities, with bone marrow insinuation and thinning of the overlying cortex on MRI

Conclusion

- Cortical stress reactions associated with prolonged anti-resorptive therapy, in the presence of pain and the “dreaded black line”, have an increased risk for complete stress fractures.
- Prophylactic surgical stabilization is indicated when these features are present.

References

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