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Case Series

Atypical femur fractures: A case series study from a tertiary care hospital in urban India

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Abstract

Anti-osteoporosis medications have led to a significant improvement in the quality of life of the elderly. Amongst them, bisphosphonate therapy has reported the most impressive outcomes in terms of reduction in the incidence of fractures. With increasing use of the drugs an association was reported from Asian countries with low energy femur fractures. The cause for a higher incidence of such low energy atypical femur fractures in Asian population could be due to genetic variances in bone remodelling and bisphosphonate metabolism, a higher incidence of osteomalacia (Vitamin D deficiency), or a tendency for increased femoral bowing resulting in accumulation of localized cortical stresses. From 2020 to 2023, we studied 19 cases of atypical femur fractures that presented to our trauma unit. Most of the patients had unilateral pathology. A diligent search for the pathology on the contralateral side was positive in only 3 of the 19 patients. Five patients did not report the use of bisphosphonates. Spontaneous onset of some unease or discomfort in the thigh in the elderly females must not be ignored. Intramedullary femoral nail seems to be the most effective treatment strategy. Prophylactic nailing must be recommended to avoid progression to complete fracture.

Keywords: Atypical femur fractures, Bisphosphonates, Prophylactic femur nailing.

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1. Introduction

The introduction of anti-osteoporosis medications has led to a remarkable improvement in the quality of life of the elderly. Amongst them, bisphosphonate therapy has reported the most impressive reduction in the incidence of fracture occurrence.[1] However, long-term use of this drug may lead to alteration in the bone metabolism, structure, and biomechanics.[2] The incidence of this typical fracture pattern in the general population remains relatively low.[3,4] The earliest commentaries of atypical femoral fractures were reported from Asia in individuals who were on long-term bisphosphonate use in Singapore followed by large case-series from Japan and Korea.[5-7] The cause for a higher incidence of atypical femur fractures in Asian population could be due to.

1. Genetic variances in bone turn-over and bisphosphonate drug metabolism,
2. A higher incidence of osteomalacia, i.e., Vitamin D deficiency, or
3. A tendency for increased femoral bowing resulting in focal accumulation of cortical stresses.[8]

The American Society of Bone and Mineral Research (ASMBR) released their first consensus report in 2010 which was then revised in 2014.

ASMBR task force revised case definition for Atypical Femur Fractures 2014:[9]

1.1. Major criteria

1. The fracture follows minimal trauma or no trauma, as in fall from a standing height.
2. The fracture line arises in the lateral cortex; usually transverse in its orientation, although it may become oblique as it progresses medially across the femur.

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3. Complete fractures progress through both the cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex.
4. The fracture is simple or with minimal fragmentation.
5. Periosteal or endosteal thickening of the lateral cortex is confined to the fracture site location (beaking or flaring) as shown in **Figure 1**.

1.2. Minor criteria:

1. Generalized increase in lateral and medial cortical thickness of the femoral diaphysis.
2. Prodromal symptoms such as dull aching pain over the groin or thigh.
3. Bilateral incomplete or complete femoral diaphyseal fractures.
4. Delayed fracture healing.
5. To satisfy the case definition of atypical femur fractures, the fracture line must be located along the lateral femoral diaphysis from distal to the lesser trochanter to just proximal to the supracondylar flare.

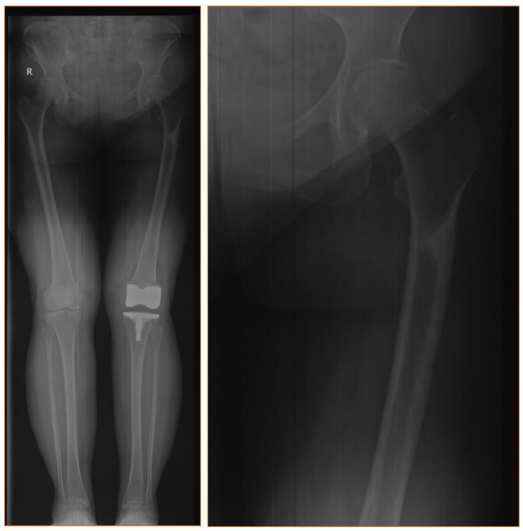

Figure 1: (a): Showing cortical thickening over lateral cortex of left femur in the subtrochanteric region - an early sign of AFF (**b**) close up view of the thickened lateral cortex

2. Predisposing Factors for Atypical Femoral Fractures

2.1. Pharmacotherapy

1. Bisphosphonates: The mechanisms responsible for the benefit of these drugs include, direct cellular cytotoxicity, inhibiting the attachment of osteoclasts, interference in osteoclast maturation and direct intra-cellular impact.[14] As a result of decreased osteoclast function, bone remodeling is reduced increasing the relative density of bone. However, in exchange the ability of bone to repair microtrauma from activities of daily living is impaired. Long-term use of bisphosphonate medication predisposes to progressive accumulation of bone microdamage over time. This suppression of bone turnover changes bone matrix (organic) and mineral (inorganic) properties by increasing mineralization, which is visible as increased cortical thickness in radiographs. The resulting boosted bone content makes the skeleton strong but brittle, increasing the susceptibility to fracture with trivial trauma.[10]
2. Proton pump inhibitors (PPI): Long-term consumption of proton pump inhibitors is very common. These drugs are easily available over the counter and a careful history will uncover this pattern. Decreasing stomach acid interferes in absorption of calcium and other elements. This alters bone resorption properties and a causal association has been reported with an increased risk of general fractures. Studies now also show a correlation between long term PPI use and atypical femoral fracture risk.[11]
3. Other causes: Systemic diseases such as non-Hodgkins's lymphoma cause structural changes in bone leading to atypical femoral fractures. Other bone diseases such as hypophosphatasia, pycnodysostosis, osteopetrosis, Vitamin D deficiency and rheumatoid arthritis are seen to directly affect the bone structure in a manner like bisphosphonates.

3. Screening and Diagnosis

A transverse line in the femur diaphysis on plain radiographs is pathognomonic for atypical femoral fractures.[13] In patients receiving bisphosphonate therapy clinical features typical of atypical femoral fractures must arouse a high degree of suspicion. Radiographs of the upper two-thirds of both femurs must be obtained and carefully analysed. Examination for thickening of the lateral cortices and the presence of fracture lines is highly recommended. The sensitivity and specificity of these two signs is high. To pick up subclinical and asymptomatic atypical femoral fractures, computed tomography and magnetic resonance imaging may provide valuable diagnostic information regarding the water and mineral content of the bone. Bone scintigraphy has also been used in addition. However, its role in the clinical scenario is very limited due to paucity of facilities performing this test.

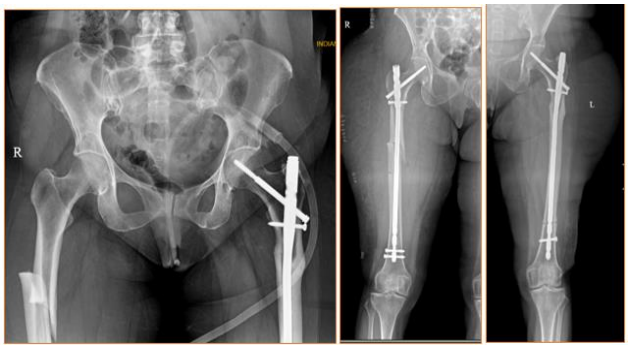

Figure 2: Atypical Femur fracture stabilized by Intramedullary Femoral Nailing on the left side with union. The lady had the dark line on the other side but did not consent for prophylactic nailing. The femur broke on getting up from a chair a few months later

4. Methodology

From 2020 to 2023, 22 cases of atypical femur fractures that were presented to our trauma unit were selected and analysed. To classify the fractures, the criteria outlined by American Society of Bone and Mineral Research criteria were used. Fractures of neck of femur, inter-trochanteric fractures with subtrochanteric extension, pathological fractures and peri-prosthetic fractures were excluded.

5. Results

All the patients with atypical femur fractures were females. The overwhelming number of patients (15/19 - 79%) presented with unilateral fractures. Screening of the opposite femur using x-ray, MRI, and bone scan revealed an abnormality in 3 more patients. Four patients (21%) had the pathognomonic signs on the opposite side. One patient who had an abnormal pedestal on the opposite side understood the condition but did not consent for prophylactic surgery. Five patients did not report use of bisphosphonates. They may have been administered injectable bisphosphonates but could not confirm it. The duration and type of bisphosphonate use was very heterogenous and ranged from a few oral doses to more than 4 years of regular use.

Table 1: Distribution of study participants according to their fracture location and duration of follow up

S. No.	Age	Sex	UL/BL	Fracture Location	Use of drugs	Duration of drug use	EUROQOL 5D Score	Duration of follow up
1	73	F	Unilateral	Midshaft	Yes	3 years	5	1 year
2	84	F	Unilateral	Subtrochanter	No	No	5	1 year
3	75	F	Unilateral	Subtrochanter	Yes	5 years	-	LTF
4	73	F	Unilateral	Midshaft	No	No	6	2 years
5	84	F	Bilateral	Midshaft	Yes	4 years	8	2 years
6	72	F	Unilateral	Midshaft	Yes	3 years	5	2 years
7	70	F	Bilateral	Subtrochanter	Yes	4 years	-	LTF
8	83	F	Unilateral	Subtrochanter	Yes	3 years	Expired	3 years
9	86	F	Unilateral	Midshaft	Yes	6 years	-	LTF
10	67	F	Unilateral	Midshaft	Yes	11 years	-	LTF
11	83	F	Unilateral	Subtrochanter	Yes	8 years	-	LTF
12	87	F	Unilateral	Subtrochanter	Yes	6 years	-	LTF
13	78	F	Unilateral	Subtrochanter	Yes	8 years	15	4 years
14	60	F	Bilateral	Subtrochanter	Yes	5 years	-	LTF
15	79	F	Unilateral	Midshaft	Yes	5 years	12	5 years
16	78	F	Unilateral	Midshaft	Yes	5 years	-	LTF
17	60	F	Bilateral	Subtrochanter	Yes	10 years	7	3 months
18	69	F	Unilateral	Midshaft	No	No	6	4 months
19	61	F	Unilateral	Subtrochanter	Yes	4 years	-	LTF

Figure 3: Atypical femur fracture left side stabilised with nailing. The patient reported difficulty in walking due to pain in the opposite thigh and the radiograph showed the dark line in the lateral cortex. This was stabilized with prophylactic plating

6. Discussion

All the patients were women. More than 75% of the patients had unilateral fracture. A diligent search for the pathology on the contralateral side was positive in only 7 of the 19 patients. The search involved an X-ray of the entire opposite femur in the post-operative period. If the radiograph was normal, MRI of the opposite femur or bone scan was obtained. The changes in bone biology and architecture following drug use affect the entire skeleton. Why then does the pathology manifest unilaterally? A possible mechanical cause may be the confounding variable. All the patients had a similar mechanical alignment in the opposite lower limb suggesting a hidden cause yet to be discovered.

Spontaneous onset of some unease or discomfort in the thigh in the elderly females must not be ignored. According to the ASBMR study, impending fractures have a significantly high chance of progressing to a complete fracture. The risk is estimated at almost 30% within 6 months of detection.[13] Five patients had back pain with referral down the thigh. A more detailed enquiry into the history and awareness of this condition may have avoided unnecessary spinal decompression surgery in the unfortunate patients. The femur eventually fractured uncovering the real cause of thigh pain. Screening radiographs of the femur must be taken to identify or rule out the presence of cortical thickening or the dark transverse line in the lateral cortex. A visible transverse defectmore than 50% of the lateral cortex indicates a high probability of progression to a complete fracture. Prophylactic intramedullary nailing is the most effective treatment strategy in avoiding the progression to complete fracture as shown in **Figure 2** and **Figure 3**.

The ASBMR recommends that patients with asymptomatic incomplete fractures with periosteal thickening should be educated about the condition and use devices to limit weight bearing and avoid vigorous impact activity. Though sound in theory its practical translation remains limited. Reduced activity should be continued until there is no oedema detected on MRI or no increased activity detected on bone scan. One lady with abnormal pedestal presented a few months later with AFF on the opposite side while trying to get up from a chair (**Figure 2**). She was aware of the risk but had not consented for prophylactic fixation. A possible explanation could be that the Vitamin D deficiency had been corrected. The femur broke at the highest point in the pedestal. This suggests that the bone was destined to break there. During the surgery, it was challenging to negotiate the ball tip guide wire across the fracture. This suggests that the weak repair processes had filled the endosteal canal with insufficient callus.

Several studies have shown delayed healing in atypical femoral fractures. Lee et al reported on 46 atypical femur fractures. Only two thirds of the fractures had healed within six months. Eventually 95.7% fractures healed without further intervention.[6] Another study by Egol et al reported that 98% of the fractures healed within 12 months of surgery and almost two-thirds returned to their self-reported baseline function.[14] The same study also revealed that malreduction was associated with delayed healing. A study by Koh et al concluded that 733 patients with 834 fractures showed an overall healing rate of 85% with a revision rate of 12.6%.[15] The authors summarized that non operative treatment methods must not be used in incomplete fracture treatment. Persistent pain unresponsive to medical managenent must be addressed by prophylactic intramedullary femur nailing.

Kim et al tested 46 variables for healing time more than six months or non-union. They found that high body mass index and subtrochanteric location of the fracture were significantly associated with delayed healing time. The study also reported that delayed union or non-union was significantly associated with deficiencies in the quality of reduction. Residual gaps at the fracture site at the lateral or anterior cortex indicate inadequate fracture reduction. Gap at the lateral cortex indicates a varus reduction. Failure to restore the native femur neck-shaft angle has been reported to result in significant longer healing time with higher complication rates.[12]

Bone turnover is suppressed by bisphosphonates. Teriparatide, a recombinant form of parathyroid hormone enhances bone healing and is a good option for supplement treatment in the post-operative period to enhance fracture healing in patients with bisphosphonate associated atypical femoral fractures. There is only limited clinical evidence available on this subject but its role in treatment of atypical femur fractures is promising.

7. Conclusion

1. Calcium and Vitamin D levels are easily measurable and available. Physicians must counsel the patients to take regular supplements and stay active. Weight

bearing exercises are the best prophylaxis for maintaining good bone health.

2. Physicians must be aware of this uncommon condition and prescribe bisphosphonates with more caution. The duration of treatment must be individualized and a drug holiday must be given to help bone recover its remodeling abilities.
3. It may be possible that osteomalacia increases the sensitivity of bone remodeling to interference with bisphosphonates. Vitamin D must be aggressively prescribed in the elderly patients to prevent this easily remedial condition.

8. Source of Funding

None.

9. Conflict of Interest

None.

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