



## Atypical Femoral Fractures: Possible association with long-term Bisphosphonate usage

### Orthopaedics

**Dr. Rakesh Kumar Gautam** Associate professor, Department of Orthopaedics, Maharishi Markandeshwar Institute of Medical Sciences & Research, Mullana, Ambala.

**Dr. Manjeet singh** Professor & HOD, Department of Orthopaedics, Maharishi Markandeshwar Institute of Medical Sciences & Research, Mullana, Ambala.

**Dr. Jaiveer Singh Hunjan** Senior Resident, Department of Orthopaedics, Maharishi Markandeshwar Institute of Medical Sciences & Research, Mullana, Ambala.

**Dr. Shireen Singh** Post graduate student, Department of Dermatology, Maharishi Markandeshwar Institute of Medical Sciences & Research, Mullana, Ambala.

**Dr. Alambeer singhVirk** Post graduate student, Department of Orthopaedics, Maharishi Markandeshwar Institute of Medical Sciences & Research, Mullana, Ambala.

### ABSTRACT

**Introduction:** Atypical femoral fractures are a special type of femoral fracture in respect to the fracture pattern, anatomical location, low energy trauma. Over recent years, reports have suggested a direct relationship between long-term use of bisphosphonates and the development of such fractures but mechanism is still unclear, the recent increase in reporting of such fractures in patients under long-term usage of bisphosphonates justifies the need for research into the association between the two.

**Case series:** We intend to report three such cases that presented to our institution. All patients presented with the characteristics of atypical femoral fractures which included low energy trauma, anatomical location, transverse or short oblique configuration with a medial spike, no comminution and lateral cortical thickening. Patients underwent surgical fixation and were followed-up till union of the fracture.

**Conclusion:** Identifying this specific fracture and treating it with caution is necessary as they tend to take more time to heal in comparison with high energy trauma femoral fracture. Educating physicians and surgeons regarding this type of fracture is of prime importance both in prevention as well as treatment of this type of fracture, which contributes to significant reduction of morbidity and mortality to the patient. Careful prescription of bisphosphonates for patients with definite indications and proper monitoring during follow-up would be another justifiable preventive measure.

### KEYWORDS:

Atypical femoral fracture, bisphosphonates, stress fracture

### INTRODUCTION

Atypical femoral fractures are being identified as a special type of femoral fracture with regards to the anatomical location extending from subtrochanteric to supracondylar region of femur, fracture pattern showing transverse or short oblique configuration with medial spike, low energy trauma, female preponderance and possible association with long-term usage of bisphosphonates<sup>1-4</sup>. Bisphosphonates have a well established therapeutic role in the prevention of osteoporosis-related fractures. They have been shown to reduce the risk of insufficiency fractures of the hip and spine in post-menopausal, osteoporotic females.<sup>1-4</sup>

It becomes essential to continue therapy in certain conditions but there have been incidences where the patient continues therapy beyond the necessary duration of therapy<sup>1</sup>. Over recent years, reports have suggested a direct relationship between long-term use of bisphosphonates and the development of subtrochanteric and femoral diaphyseal fractures with an 'atypical' site and configuration.

The exact mechanism underlying this apparent increase in fracture risk is still unclear. The clinical challenge posed by this type of fracture is identifying and treating it accordingly as this has a major bearing on post-injury functionality status and on quality of life<sup>1</sup>.

We intend to report three such cases that presented to our institution. Informed consent was obtained from the patients to use their clinical data for academic purposes alone. All three patients presented were females with the characteristics of atypical femoral fracture which included low energy trauma, characteristic anatomical location, transverse or short oblique configuration with a medial spike, no comminution and lateral cortical thickening

A 52-year-old female without any pre-existing co-morbid conditions reported to our institution during September 2015 with alleged history of fall from standing position and sustained fracture of shaft right femur (figure 1). The patient revealed history of taking bisphosphonates for three years on prescription by a primary care physician for Osteopenia. The patient underwent fixation with intermedullary interlocking femoral nail (figure 2) and was under follow-up. The fracture showed delayed union, therefore the patient was kept under toe touch weight bearing. The patient also admitted to have had thigh pain since one week prior to the fracture. We stopped bisphosphonate medication. Fracture healed at about six months (figure 3). At one year follow-up patient is doing full weight bearing without any difficulty



Fig 1

Pre op xray



Fig 2

post op xray



Fig 3

xray at 6 month follow up

A 40-year-old female, a known case of hypertension and dyslipidemia, presented with proximal third femur fracture right side with alleged history of fall from standing position. The radiograph (Figure 4) showed features matching the description of atypical femoral fractures and on detailed elucidation of history the patient revealed that she was on bisphosphonate medication for last four years on prescription by a general practitioner. The patient too had been having vague thigh pain since two weeks prior to the injury. We advised stopping the

medication and patient underwent fixation with ante-grade femoral nail for femur fracture (proximal femoral nail antirotation 2) (figure 5). Patient is presently under follow-up and radiograph taken 12 weeks following surgery showing evidence of fracture union on operated side. (figure 6)



Fig 4  
Pre op xray



Fig 5  
post op xray



Fig 6  
xray at follow up

The patient was a 90-year-old woman of weight 75 kg, who presented a painful condition of mechanical pattern in her right thigh, she had been able to walk within her community. She suffered involution of her gait pattern as the painful condition intensified and became capable of walking only at home, with the help of a walking frame. She did not have any history of falls or any local traumatic factor. She was known to present systemic arterial hypertension, non-insulin-dependent diabetes mellitus, cardiopathy and osteoporosis, which were all being treated with drugs.

She was brought to the orthopedics and traumatology outpatient clinic of our service, in order to have her complaint investigated. She had a history of a left-side proximal femoral fracture 6 years previously, for which she was operated and since then, she had been using calcium replacement and had kept on using bisphosphonates over the same period. She did not present any abnormality in the clinical examination, except for discomfort in her right lower limb, at thigh level when walking (figure 7). Serial radiographs demonstrated normality and good evolution of the left-side fracture that had previously been treated, but with arching of the femoral cortical bone and sclerosis of the lateral wall in its middle third. In the light of these findings, magnetic resonance imaging of the thigh was requested. This showed the presence of incomplete fracturing of the posterolateral/lateral cortical bone with thickening of the adjacent cortical bone and bone edema, in association with slight unilamellar periosteal thickening.

Given these factors and the symptomatic condition, a surgical approach was indicated. There was discussion regarding the best fixation method: intramedullary fixation using a cephalomedullary nail or fixation using a plate. In this specific case, an initial attempt was made to use an intramedullary nail, but because of diaphyseal arching and the risk of worsening the existing fracture, it was decided to place a locked plate as a bridge.

Today, the patient presents 4 months of postoperative evolution (figure 8), with involution of the symptomatic condition and improvement of the gait pattern, and without any complaints. She already presents radiological indications of fracture consolidation. Because of the history of a previous proximal femoral fracture and the atypical fracture induced by bisphosphonates (high risk of new fractures), it was decided to maintain the supplementation of calcium and vitamin D, withdraw the use of bisphosphonates and start the patient on denosumab.



Fig 7  
Pre op xray

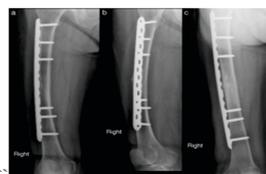


Fig 8  
xray at follow up

## DISCUSSION

Bisphosphonates being a very important class of drugs in management of osteoporosis have been prescribed very commonly by primary care physicians and surgeons. There have been many publications reporting

fractures in patients on long-term bisphosphonate medications.<sup>2-4</sup> Majority of these fractures have been reported in female patients.<sup>2</sup> The percentage of population who took bisphosphonate medication and developing fracture while on treatment is low.<sup>3</sup> There have been postulates indicating genetic polymorphism among general population that may contribute to increased risk of development of these fractures in certain individuals in comparison to general population.<sup>2</sup> The American Society of Bone and mineral research has devised a diagnostic criteria with major and minor features to classify a fracture as atypical femoral fracture.<sup>1</sup> The important features being low energy trauma, location of fracture which should be distal to lesser trochanter and proximal to supracondylar region, transverse or short oblique configuration with a medial spike without comminution, presence of prodromal thigh pain. The fracture may present bilateral in some cases or may show features of lateral cortical stress reaction.<sup>1,5</sup> All the above features have been noted in our cases. It should be noted that stress fractures which occur in young and fit athletes usually starts from the medial cortex in contrast to atypical femoral fractures where the fracture line starts from the lateral cortex and progresses medially.<sup>1</sup> The possible mechanisms by which bisphosphonates could contribute to development of fractures include altering collagen integrity, homogeneity of bone mineral density distribution, decreased bone remodeling which is manifested as micro-architectural deterioration, crack initiation, crack progression, delayed healing of cracks.<sup>1,2</sup> Though bisphosphonates do not interfere with callus formation they have been postulated to interfere with fracture healing during the phase of remodeling from immature callus to mature bone.<sup>1</sup> This causes retention of callus which is seen as lateral cortical thickening in radiograph. They have also postulated that bisphosphonates could cause indirect inhibition of angiogenesis which is usually coupled with osteoclastic remodeling.<sup>1</sup> But majority of the above postulates are based on animal studies and there is no conclusive evidence yet to establish a causal association between bisphosphonates and atypical femoral fractures. In vitro studies to demonstrate that bisphosphonates do inhibit osteogenesis have also been published.<sup>6</sup>

There have been reports of fractures occurring in other bones in patients on long-term bisphosphonate medications but majority seem to be case reports.<sup>7,8</sup> There have been debates about the ideal duration of therapy for bisphosphonates but evidence from literature supports that there is no proven efficacy beyond five years of continuous therapy.<sup>1</sup> Literature review shows the duration of treatment in cases reported with atypical femoral fractures ranged from 2–8 years.<sup>2</sup> With regards to diagnosis, majority of the fractures are identified based on the typical radiograph findings. In case of patients who present with incomplete fractures or doubtful findings on routine radiographs, it is suggested to do CT scan or MRI scan to confirm the lateral cortical stress reactions.<sup>1,2</sup> Some publications also include bone scan studies to detect stress reactions.<sup>1,2</sup> Histomorphometric analysis with biopsy samples obtained from iliac crest or fracture site have been considered to be added valuable evidence for research purposes.<sup>1</sup>

Recommendations regarding management of these fractures depend on the patient presentation, with all manifested fracture to be ideally fixed with intramedullary devices, since they did not interfere with fracture hematoma and are biomechanically in advantage when compared to extramedullary devices.<sup>1,9</sup> All three of our cases were fixed with intramedullary device. For patients who present with thigh pain and lateral cortical stress reaction, current literature suggest prophylactic fixation which significantly reduces morbidity to the patient.<sup>10</sup> For patients not willing for surgery, after explaining the risk of fracture the physician may advise partial weight bearing until radiological appearance of union.<sup>1</sup> Literature evidence also supports use of teriparatide to hasten healing in this type of fracture, but we have not used it in any of our cases. Supplementation of vitamin D and calcium is justified for patients in whom investigations confirm deficiency.<sup>1</sup>

## CONCLUSION

Identifying this specific fracture and treating it with caution is necessary as they tend to take more time to heal in comparison with high energy trauma femoral fracture. Educating physicians and surgeons regarding this type of fracture is of prime importance both in prevention and treatment of this type of fracture, which contributes to significant reduction of morbidity and mortality to the patient. More research is needed to arrive at a risk benefit ratio which might justify administration of bisphosphonates in a patient and to decide on the appropriate duration of individualized therapy.

**REFERENCES**

1. Shane E, Burr D, Ebeling PR, et al. Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2010 Nov;25(11):2267–94.
2. Kwek EB, Goh SK, Koh JS, Png MA, Howe TS. An emerging pattern of subtrochanteric stress fractures: a long-term complication of alendronate therapy? *Injury* 2008 Feb;39(2):224–31.
3. Schilcher J, Michaëlsson K. Bisphosphonate use and atypical fractures of the femoral shaft. *N Engl J Med* 2011 May 5;364(18):1728–37.
4. Shkolnikova J, Flynn J, Choong P. Burden of bisphosphonate-associated femoral fractures. *ANZ J Surg* 2013 Mar;83(3):175–81.
5. Capeci CM, Tejwani NC. Bilateral low-energy simultaneous or sequential femoral fractures in patients on long-term alendronate therapy. *J Bone Joint Surg Am* 2009 Nov;91(11):2556–61.
6. Patntirapong S, Singhatanadgit W, Arphavasin S. Alendronate-induced atypical bone fracture: evidence that the drug inhibits osteogenesis. *J Clin Pharm Ther* 2014 Aug;39(4):349–53.
7. Bjørgul K, Reigstad A. Atypical fracture of the ulna associated with alendronate use. *Acta Orthop* 2011 Dec;82(6):761–3.
8. Pradhan P, Saxena V, Yadav A, Mehrotra V. Atypical metatarsal fracture in a patient on long term bisphosphonate therapy. *Indian J Orthop* 2012 Sep;46(5):589–92.
9. Egol KA, Park JH, Rosenberg ZS, Peck V, Tejwani NC. Healing delayed but generally reliable after bisphosphonate-associated complete femur fractures treated with IM nails. *ClinOrthopRelat Res* 2014 Sep;472(9):2728–34.
10. Banffy MB, Vrahas MS, Ready JE, Abraham JA. Nonoperative versus prophylactic treatment of bisphosphonate-associated femoral stress fractures. *ClinOrthopRelat Res* 2011 Jul;469(7):2028–34.