Open Journal of
Clinical & Medical
Case Reports

Volume 1 (2015)
Issue 8

ISSN 2379-1039

Bilateral Subtrochanteric Femur Fractures in a Patient with Polymyalgia Rheumatica and Ibandronate Use

Shawn P. Mountain, DO[*1]; Elisha A. Chance, BSAS[1]; James E. Boniface, MD[2]

[*]Shawn P. Mountain, DO

Dept. of Orthopedic Surgery, St. Elizabeth Youngstown Hospital, 1044 Belmont Avenue, Youngstown, OH 44501, USA
Tel: 330-910-0250; Fax: 330-480-2242; Email: shawn.mountain@gmail.com

Abstract

We report on a 62-year-old woman with polymyalgia rheumatica who sustained simultaneous, bilateral, low-energy femoral fractures (AO/OTA classification 32-A3) while on methotrexate, prednisone, PPI, and ibandronate sodium therapy. Due to the rarity of atypical fractures, specific diagnosis and procedural codes for atypical fractures should be created and based on the major and minor criteria delineated by the ASBMR to facilitate large sample analyses from national databases.

Keywords

Atypical fracture; Bilateral femur fractures; Bisphosphonate related fracture; Femur

Abbreviations

PPIs: Proton Pump Inhibitors; HIPAA: Health Insurance Portability and Accountability Act; AO/OTA: Association for Osteosynthesis-Orthopaedic Trauma Association; mg/dL: milligram per deciliter; DEXA: Dual-energy X-ray absorptiometry; ASBMR: American Society for Bone and Mineral Research.

Introduction

There is no dispute that bisphosphonates have prevented innumerable osteoporotic fractures in the population. Case reports, retrospective analyses, and systematic literature reviews evaluating the relationship between bisphosphonates and atypical femoral fractures have been reported and show mixed evidence suggesting that long-term bisphosphonate use increases atypical fracture risk [1-18]. The absolute risk of an atypical fracture while on bisphosphonate therapy is extremely low at 5 cases per 10,000 patient years[16], making atypical fractures the exception and not the rule. Notably, atypical fractures have been reported in patients who do not take bisphosphonates [1,2,16]. Additionally, concomitant use of proton pump inhibitors (PPIs) and glucocorticoids, and multiple comorbid conditions have been identified as compounding risk factors for atypical fractures in patients on bisphosphonate therapy [2,5,8,11,12,17-19].

Bisphosphonates are a class of drugs that have been used to prevent or treat osteoporosis caused by many different factors such as long-term corticosteroid use and in elderly females with estrogen

depletion. These drugs work by decreasing osteoclastic resorption of bone thereby inhibiting bone turnover [20]. More specifically, ibandronate sodium is a nitrogen-containing bisphosphonate that acts through the inhibition of the mevalonate pathway; this in turn disrupts regulatory protein signaling in the osteoclast leading to apoptosis [20]. Many previous examples of bisphosphonates had a poor compliance due to required daily regimens for effectiveness. Next generation bisphosphonates had better adherence because of weekly dosing, however this was still not perfect. Ibandronate was developed to improve usage by offering monthly dosing.

This article presents a case of a 62-year-old woman who sustained bilateral simultaneous subtrochanteric fractures while on methotrexate, prednisone, PPI, and ibandronatesodium therapy. She was informed that data concerning the case would be submitted for publication in accordance with HIPAA regulation, and she provided her written informed consent.

Case Report

A 62-year-old Caucasian female presented to a level I trauma center after a low-energy fall at home. The patient reported that while attempting to dress herself, she felt her left leg give way, lost balance, and started to fall. In attempting to break her fall, she felt her other leg give out. She had immediate pain bilaterally and was unable to bear weight. Upon further questioning, she reported a history of experiencing several weeks of bilateral thigh pain, but she did not have this investigated by a physician. Hip radiographs revealed complete, displaced, angulated fractures (AO/OTA classification 32-A3) throughout the proximal femurs just inferior to the lesser trochanters, bilaterally (Figures 1 and 2). The fractures were both transverse in nature with bilateral cortical thickening and medial spikes present.

Her medical history included a body mass index of 33.2 kg/m^2, hypertension, hyperlipidemia, polymyalgia rheumatica, arthritis, hypothyroidism, and a left 5^{th} metatarsal stress fracture 2 years prior. Her extensive surgical history included but was not limited to a complete thyroidectomy, left breast lumpectomy, complete hysterectomy, and hemangiopericytoma removal with skin grafting. Her home medications were levothyroxine, bisoprolol fumarate, clonidine, nabumetone, ibandronate sodium, pantoprazole, simvastatin, prednisone, methotrexate, and tramadol. Her additional supplements were folic acid, vitamins C and E, and calcium with vitamin D_3. Notably, she had been taking prednisone 10 mg daily for over 6 years and oral ibandronate sodium therapy 150 mg monthly for less than 1 year for glucocorticoid-induced osteoporosis.

At admission, her calcium level was 8.5 mg/dL (range 8.6-10.5 mg/dL), creatinine 1.1 mg/dL (range 0.5-1.1 mg/dL), and vitamin D 25-hydroxy was 46 mg/dL (range 30-80 mg/dL). She did not have a parathyroid hormone lab assessment performed. Four months prior to the femur fractures, dual energy x-ray absorptiometry (DEXA) bone scan T-score in her hip was -0.3 and 2.8 in her lumbar spine, indicating normal bone density. She did not have a (DEXA) scan performed at admission.

She was taken to the operating room where her fractures were fixed bilaterally with T2™ Recon nails (Stryker, Kalamazoo, Michigan, USA), both 9 mm x 340 mm x 125º, and 80-mm proximal lag screws and 75-mm proximal lag screws with distal locking screws (Stryker, Kalamazoo, Michigan, USA). Specimens for bone histomorphometry were not obtained. She went on to physical and occupational therapy at 6 days post-fixation. She resumed her home medications including prednisone and

methotrexate at 6 days post-operatively and resumed ibandronate sodium at 34 days post-op. At 2 months follow-up, the fracture showed healing. At 6 months follow-up, both fractures healed, and the patient was ambulating with the use of one cane only, and radiographs were obtained a final time at 15 months follow-up (Figures 3-4).

Discussion

The task force of the American Society for Bone and Mineral Research (ASBMR) classified common features of atypical femur fractures as either major or minor [17]. Major features include fractures located anywhere from just distal to the lesser trochanter to just proximal to the supracondylar flair, those occurring after minimal or no trauma, transverse or short oblique, noncomminuted, complete fractures extending through both cortices with or without a medial spike, and incomplete fractures involving only the lateral cortex [17]. Minor features include prodromal thigh pain, local periosteal reaction of the lateral cortex, increase in cortical thickness of the diaphysis, delayed healing, comorbid conditions (e.g.,vitamin D deficiency, rheumatoid arthritis, and hypophosphatasia), and use of other pharmaceuticals (e.g., bisphosphonates, glucocorticoids, and PPIs) [17]. Our case included all of the major features, and all of the minor features except delayed healing.

The direct causation between bisphosphonate usage and atypical femoral fractures has been studied and no direct link has been clearly demonstrated. Black et al. evaluated the effects of bisphosphonates on femoral shaft fractures from three large randomized controlled trials of bisphosphonates with more than 14,000 patients and 10 years of follow-up [2]. They identified 12 atypical femoral fractures in 10 women with 3 of the 12 patients receiving placebo [2]. The authors concluded that the risk of atypical fracture with bisphosphonate use alone is very low, specifically, an annual rate of 2.3 subtrochanteric fractures per 10,000 patient years [2]. However, they recognized that there may be a subgroup of especially high-risk patients—those taking corticosteroids, PPIs, or antiretroviral medications [2].

Simultaneous bilateral atypical femur fractures while on bisphosphonate therapy is rare, and to our knowledge, none have been reported on ibandronate sodium. However, there have been a few reports of simultaneous bilateral atypical subtrochanteric femur fractures in patients taking other bisphosphonates (i.e., alendronate sodium, risedronate sodium, and pamidronate disodium) [3,5]. Capeci et al. in 2009 reported on low-energy diaphyseal femur fractures [3]. In the sample, 7 patients sustained bilateral femur fractures while on alendronate sodium therapy, and 1 sustained simultaneous bilateral femur fractures [3]. They concluded that if a low-energy fracture occurs unilaterally in patients on bisphosphonates, the contralateral femur should be fixed prophylactically [3]. A review of all bisphosphonate-related fracture case reports by Giusti et al. in 2010 revealed that 19/120patients had simultaneous bilateral femur fractures, and 53/120 patients had subsequent contralateral femur fractures [5]. The authors went on to report that 23% of the patients had 3 or more comorbid conditions, and 10.3% of the patients reported rheumatoid arthritis. More than 25% of the cases were on long-term glucocorticoid treatment. PPIs were the most common co-medication prescribed 39% of the time [3].

The causes of atypical fractures in patients on bisphosphonate therapy, while unknown, have been discussed by several investigators [21-23], andthe following different theories have emerged: (1) microdamage accumulation and impaired stress healing,(2) reduced heterogeneity of organic matrix

and mineral properties, and (3) increased advanced glycation end-products [21-23]. Moreover, it has been observed that patientson long-term steroids are at higher risk for fracture, regardless of bisphosphonate use [5,11,17-19,24-25].

This case report was a perfect storm for the development of an atypical femur fracture. First, the patient's thyroidectomy and hysterectomy placed her at a higher risk for fracture. Second, the patient was on long-term corticosteroids and methotrexate for her polymyalgia rheumatica. Third, she had more than three comorbidities, a known history of a stress fracture, and she was taking a PPI. Due to these risks , she was prescribed ibandronate sodium for induced osteoporosis. Despite a normal DEXA bone scan months prior, the patient had prodromal thigh pain and sustained simultaneous bilateral femoral fractures.

Ideally, more randomized controlled trials studying the development of atypical femoral fractures in patients taking multiple medications, especially corticosteroids and PPIs, in combination with bisphosphonates are warranted. Given the rarity of atypical fractures, randomized, controlled trials may not be feasible or ethical. Therefore, specific diagnosis and procedural codes for atypical fractures should be created and based on the major and minor criteria delineated by the ASBMR to facilitate large sample analyses from national databases.

Figures

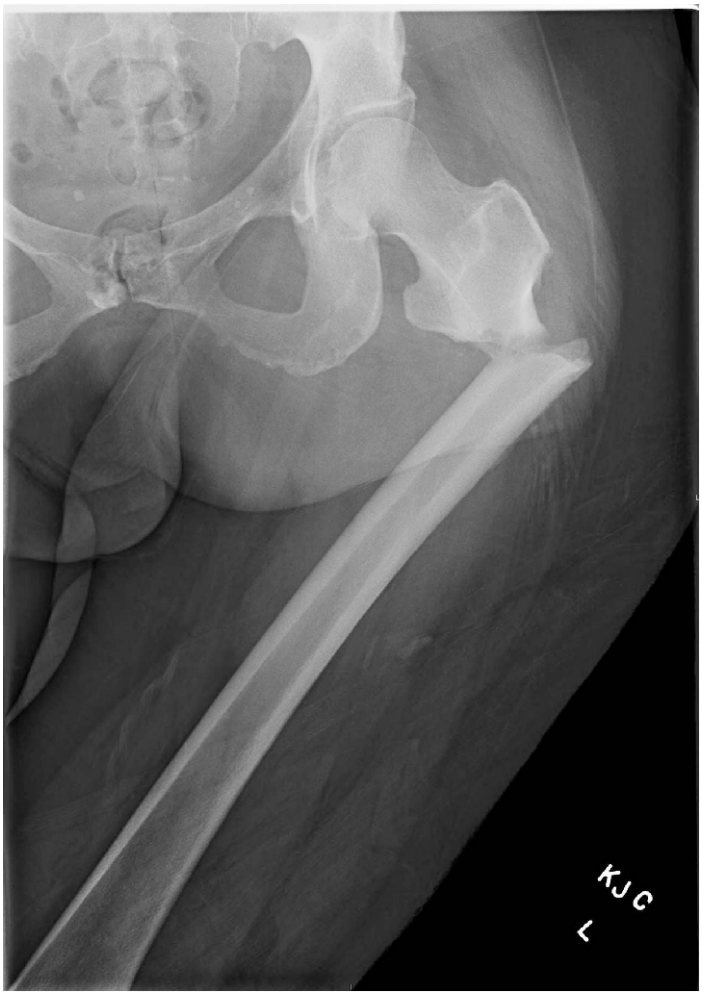

Figure 1: Hip radiograph of the left femur showing a complete, displaced, angulated fracture that is transverse in nature.

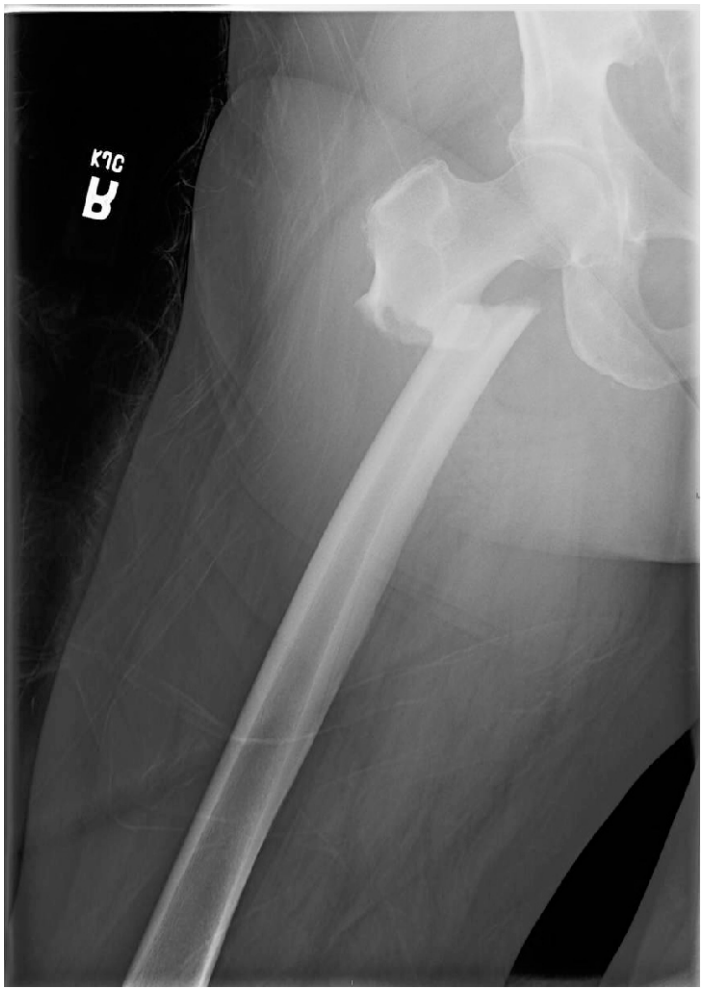

Figure 2: Hip radiograph of the right femur showing a complete, displaced, angulated fracture that is transverse in nature.

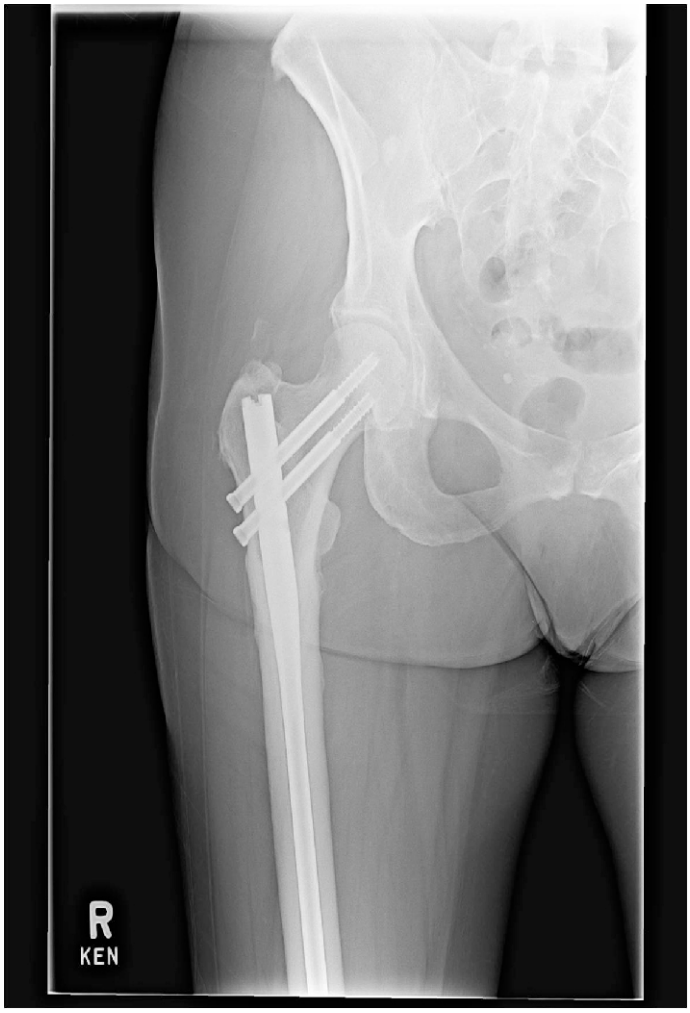

Figure 3: Anteroposterior view of the right hip showing a healed fracture.

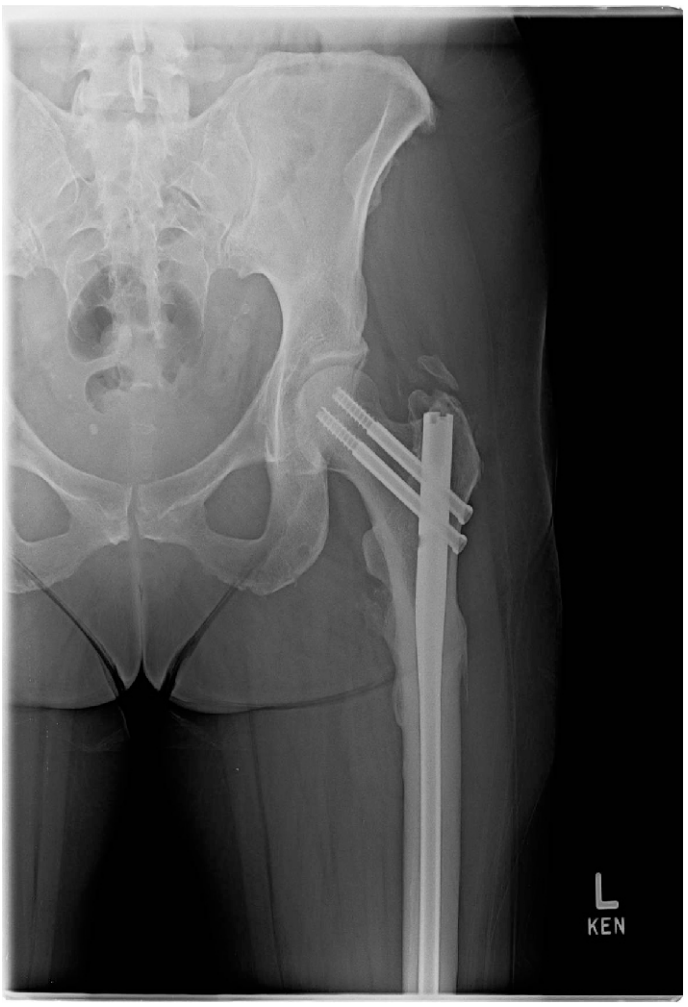

Figure 4: Anteroposterior view of the left hip showing a healed fracture.

References

1. Agarwal S, Agarwal S, Gupta P, Agarwal PK, Agarwal G, Bansal A.. Risk of atypical femoral fracture with long-term use of alendronate (bisphosphonates): a systemic review of the literature. ActaOrthop Belg. 2010;76:567-571.

2. Black DM, Kelly MP, Genant HK, Palermo L, Eastell R, Bucci-Rechtweg C, et al. Fracture intervention trial steering committee; HORIZON pivotal fracture trial steering committee. Bisphosphonates and fractures of the subtrochanteric or diaphyseal femur. N Engl J Med. 2010;362:1761-1771.

3. 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;91:2556-2561.

4. Girgis CM, Seibel MJ. Atypical femur fractures: a review of the evidence and its implication to clinical practice. TherAdvMusculoskel Dis. 2011;3:301-304.

5. Giusti A, Hamdy NAT, Papapoulos SE. Atypical fractures of the femur and bisphosphonate therapy: a systematic review of case/case series studies. Bone. 2010;47:169-180.

6. Goddard MS, Reid KR, Johnston JC, Khanuja HS. Atraumatic bilateral femur fracture in long-term bisphosphonate use.Orthopedics. 2009;32. [Hyperlinked with orthosupersite.com/view.asp?rID=41933].

7. Gunawardena I, Baxter M, Rasekh Y. Bisphosphonate related subtrochanteric femoral fractures. Am J GeriatrPharmacother. 2011;9:194-198.

8. Ing-Lorenzini K, Desmeules J, Plachta O, Suva D, Dayer P, Peter R.Low-energy femoral fractures associated with the long-term use of bisphosphonates. Drug Saf. 2009;32:775-785.

9. Isaacs JD, Shidiak L, Harris IA, Szomor ZL. Femoral insufficiency fractures associated with prolonged bisphosphonate therapy. ClinOrthopRelat Res. 2010;468:3384-3392.

10. Kim SY, Schneeweiss S, Katz JN, Levin R, Solomon DH. Oral bisphosphonates and risk of subtrochanteric or diaphyseal femur fractures in a population-based cohort. J Bone Miner Res. 2011;26:993-1001.

11. Odvina CV, Zerwekh JE, Rao DS, Maalouf N, Gottschalk FA, Pak CY. Severely suppressed bone turnover: a potential complication of alendronate therapy. J ClinEndocrinolMetab. 2005;90:1294-1301.

12. Odvina CV, Levy S, Rao S, Zerwekh JE, Rao DS. Unusual mid-shaft fractures during long-term bisphosphonate therapy. ClinEndocrinol (Oxf). 2010;72:161-168.

13. Patel VC, Lazzarini AM. Bilateral simultaneous femoral diaphyseal fractures in a patient with long-term ibandronate use. Orthopedics. 2010;33:775.

14. Puah KL, Tan MH. Bisphosphonate-associated atypical fracture of the femur: spontaneous healing with drug holiday and re-appearance after resumed drug therapy with bilateral simultaneous displaced fractures a case report. ActaOrthopaedica. 2011;82:380-382.

15. Rizzoli R, Åkesson K, Bouxsein M, Kanis JA, Napoli N, Papapoulos S.Subtrochanteric fractures after long-term treatment with bisphosphonates: a European society on clinical and economic aspects of osteoporosis and osteoarthritis, and international osteoporosis foundation working group report. Osteoporos Int. 2011;22:373-390.

16. Schilcher J, Michaëlsson K, Aspenberg P. Bisphosphonate use and atypical fractures of the femoral shaft. N Engl J Med. 2011;364:1728-1737.

17. Shane E, Burr D, Ebeling PR, Abrahamson B, Adler RA, Brown TD, 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;25:2267-2294.

18. Somford MP, Draijer FW, Thomassen BJ, Chavassieux PM, Boivin G, Papapoulos SE. Bilateral fractures of the femur diaphysis in a patient with rheumatoid arthritis on long-term treatment with alendronate: clues to the mechanism of increased bone fragility. J Bone Miner Res. 2009;24:1736-1740.

19. Hetsroni I, Markusevitz M, Nyska M. Bilateral femoral neck fractures in long-term steroid use for systemic lupus erythematosus and chronic lung disease. Orthopedics. 2008;31:180.

20. Epstein S, Zaidi M. Biological properties and mechanism of action of ibandronate: application to the treatment of osteoporosis. Bone. 2005;37:433-440.

21. Unnanuntana A, Saleh A, Mensah K, Kleimeyer JP, Lane JM. Atypical femoral fractures: what do we know about them?: AAOS exhibit selection. J Bone Joint Surg Am. 2013;95:e8 1-13.

22. Tang SY, Allen MR, Phipps R,Burr DB, Vashishth D. Changes in non-enzymatic glycation and its association with altered mechanical properties following 1-year treatment with risedronate or alendronate. Osteoporos Int. 2009;20:887-94.

23. Saito M, Mori S, Mashiba T, Komatsubara S, Marumo K. Collagen maturity, glycation induced-pentosidine, and mineralization are increased following 3-year treatment with incadronate in dogs. Osteoporos Int. 2008;19:1343-1354.

24. Arai K, Hoshino M, Murai T, Fujisawa J, Kondo N, Netsu T, et al. Proximal femoral fracture in patients with rheumatoid arthritis. Mod Rheumatol. 2007;17:317-321.

25. Sinigaglia L, Nervetti A, Mela Q, Bianchi G, Del Puente A, Di Munno O, et al. A multicenter cross sectional study on bone mineral density on rheumatoid arthritis. Italian study group on bone mass in rheumatoid arthritis. J Rheumatol. 2000;27:2582-2589.

Manuscript Information: Received: August 17, 2015; Accepted: October 12, 2015; Published: October 26, 2015

Authors Information: Shawn P. Mountain, DO[*1]; Elisha A. Chance, BSAS[1]; James E. Boniface, MD[2]
[1]Department of Orthopedic Surgery, St. Elizabeth Health Center, 1044 Belmont Avenue, Youngstown, OH 44501
[2]Department of Orthopedic Surgery, Sharon Regional Health System, 880 West Liberty Street, Hubbard OH, 44425

Citation: Mountain SP, Chance EA, Boniface JE. Bilateral subtrochanteric femur fractures in a patient with polymyalgia rheumatica and ibandronate use. Open J Clin Med Case Rep. 2015; 1045

Journal: Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.

Visit the journal website at **www.jclinmedcasereports.com**

For reprints & other information, contact editorial office at **info@jclinmedcasereports.com**