

1 **Propagation of Bisphosphonate related femoral stress fractures despite femoral nailing - A**
2 **cautionary tale from two cases.**

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- 38 **Propagation of Bisphosphonate related femoral stress fractures despite femoral nailing - A cautionary**
39 **tale from two cases.**

40 **Abstract:**

41 We report two cases of atypical femoral fracture displacement despite treatment with intramedullary
42 nailing. Both patients had received more than three years of bisphosphonates. One patient had
43 prophylactic fixation of an atypical femur fracture due to intractable pain. The other had undergone
44 nailing previously for a traumatic shaft fracture. The patient then received bisphosphonate later and
45 sustained an atypical fracture with the nail in place. Both femoral nails were slotted, cannulated
46 stainless steel piriformis entry designs. These two cases are amongst the first reported failures of
47 intramedullary fixation in preventing displacement of a bisphosphonate stress fracture. We advice
48 caution when using slotted nails in prophylaxis of atypical femur fractures because of its significantly
49 reduced torsional stiffness compared to modern non-open sectioned nails.

50 **Keywords:**

51 Femur fractures, Bisphosphonates, Atypical Fractures, Intramedullary nailing, Case Report, Geriatric
52 Fractures

53 **Introduction:**

54 Atypical femoral fractures have been suggested to be associated with patients receiving
55 bisphosphonates for more than 3-5 years(1-7). The etiology of atypical femur fracture is thought to be
56 reduced bone turnover, leading to accumulation of unrepaired micro-fractures and eventual significant
57 weakening of the bone.(8) The sub-trochanteric and diaphyseal areas of the femur is subjected to high
58 tensile load hence most susceptible to fracture after minimal or no trauma.

59 Patients may present at an early stage before fracture completion and displacement. These patients
60 typically have cortical stress reactions in the femoral sub-trochanteric or diaphyseal regions, presenting
61 as lateral cortical beaking and cortical thickening. Some may also have prodromal pain and a 'dreaded
62 black line' representing an undisplaced stress fracture.(5, 6, 9-12) Pain and the dreaded black line may
63 indicate an increased risk of secondary displacement. Clinical studies have reported favorable results by
64 prophylactically treating these patients with intramedullary nailing, successfully preventing secondary
65 displacement and alleviating pain.(13-18) We present two cases where an atypical fracture displaced
66 despite previous intramedullary fixation with a slotted stainless steel nail.

67 **Case one (Figure 1):**

68 A 71 year old lady with a history of surgical menopause was prescribed alendronate for osteoporosis.
69 Despite being on treatment, she sustained a displaced femoral neck fracture four years later. She was
70 treated with a hemiarthroplasty. She continued to take the drug for a total duration of 5 years. The
71 patient was maintained on calcium and vitamin D supplements. She was able to ambulate outdoors with
72 a stick.

73 At the age of 77, around 14 months after stopping alendronate, she experienced right sided thigh pain
74 which worsened and became debilitating after two months. There was no significant pain over the
75 contralateral limb with previous hemiarthroplasty. X-ray revealed cortical 'beaking' and thickening over
76 the mid diaphysis of her right femur. There was corresponding local tenderness. The diagnosis was an
77 atypical femur fracture. She underwent prophylactic antegrade intramedullary nail fixation to prevent
78 secondary fracture displacement and to alleviate intractable pain.

79 Reaming was performed up to 12mm with use of a distal intramedullary suction vent. A 10mm piriformis
80 entry stainless steel slotted nail (Universal Femoral Nail, Synthes, Oberdorf, Switzerland) was inserted
81 with one static locking bolt distal and one proximal locking bolt in the dynamic position.

82 The patient recovered uneventfully after operation. She was allowed immediate full weight bearing
83 walking. She remained to be on calcium carbonate and multivitamin supplements. Strontium ranelate
84 was started 2 months after surgery. The patient had decreased pain but it was not completely alleviated
85 by the surgery.

86 The patient then sustained a minor fall injury on level ground 1 year and 3 months after intramedullary
87 nailing. X-ray showed a displaced comminuted fracture of the femur propagating from the original site
88 of the stress fracture despite the nail.

89 The patient was re-operated with nail exchange to a reamed trochanteric entry non-slotted cannulated
90 titanium femoral nail (A2FN, Synthes, Oberdorf, Switzerland). Open reduction was performed. Reaming
91 was performed to 13.5mm and a 12mm nail was used. Two reconstruction locking bolts were used
92 proximally and two static locking bolts were used distally. She was rehabilitated with progressive weight
93 bearing walking exercise. The fracture united after 4 months and the patient was able to return to her
94 pre-fracture functional status.

95 **Case Two (Figure 2):**

96 A 78 years old lady presented to the trauma unit 3 years ago when she missed a step while walking
97 downstairs. She sustained an oblique fracture at the distal shaft of her right femur. She had good
98 general health prior to this injury. The fracture was managed by intramedullary nailing. An 11mm
99 piriformis entry slotted stainless steel nail was used (Universal Femoral Nail, Synthes, Oberdorf,
100 Switzerland). Reaming was performed up to 13mm. Two proximal and two distal interlocking screws
101 were placed at the static positions. The fracture united uneventfully and the patient was put on
102 alendronate. The patient was eventually able to walk unaided with a pain free lower limb.

103 Two and a half years after the initial fracture, the patient began noticing increasing pain over the
104 operated hip. The patient continued to ambulate with a walking frame for four months.

105 The patient then had a low energy fall and was readmitted into hospital. Radiographs on admission
106 showed a displaced subtrochanteric stress fracture with bending of the intramedullary nail. X-ray
107 indicated a stress fracture with beaking and breakage of the lateral cortex occurring at the proximal
108 screw hole.

109 The patient underwent surgical fixation of the fracture. The implant was exchange to a long
110 cephalomedullary nail (PFNA, Synthes, Oberdorf, Switzerland). The retrieved IM nail showed fatigue
111 failure at its proximal locking screw hole.

112 Bisphosphonate therapy was stopped and the patient was rehabilitated with progressive weight bearing
113 walking exercise. The fracture eventually united on X-ray four months following surgery with alleviation
114 of pain.

115 **Discussion**

116 Aypical femur fractures may be difficult to diagnose at an early, undisplaced stage. They may be
117 appreciated by screening the contralateral femur in patients presenting with displaced fractures. The
118 typical features are, lateral cortical beaking, diaphyseal cortical thickening or a 'dreaded black line' with
119 prodromal pain in patients who has been on a few years of bisphosphonates. Judicious use of MRI and
120 bone scintigraphy can assist diagnosis when X-rays alone are non-confirmatory.

121 The recommend treatment is prophylactic surgical stabilization of these stress fractures. The indications
122 for surgery are to prevent secondary fracture displacement and to alleviate prodromal pain. The
123 reported rate of secondary displacement in un-operated cases is thought to be high. Banffy(14) reported
124 fracture displacement occurring in 5 out 6 patients who were not prophylactically stabilized. Ha(18) saw

125 secondary displacements in 5 out of 14 femurs and another 5 had to be operated due to intractable pain.
126 Koh(9) reported that patients with cortical stress reactions and subsequent fracture displacement were
127 more likely to have had pain and a 'dreaded black' line on X-ray. Prophylactic stabilization were reported
128 to be associated with shorter hospital stay (14, 16) when compared to treatment after fracture
129 displacement.(19) When there is persistent radiological features and prodromal pain after a drug
130 holiday of one to two months, prophylactic intramedullary nailing should be strongly advised.

131 Prophylactic treatment has shown to be generally effective. Ward(16) described 14 successful
132 prophylactic fixations with reconstruction nails. Banffy(14) treated 6 with cephalomedullary devices.
133 Capeci(15) reported 4 successful antegrade IM nailing as prophylaxis. Das De(13) reported success using
134 both IM nails in 2 cases and DCS plates in 2 other cases where the canal was too narrow. Wang(17)
135 reported 3 successful prophylactic fixations with non-reconstruction nails. Ha(18) reported 5 patients
136 treated with plate or IM nails with similar success. Oh(23) reported 20 similar successes with
137 intramedullary nails. From all the reported cases, there were no failures noted.

138 In our two cases both patients suffered from atypical fracture displacement despite presence of an
139 intramedullary nail. In the first case the fracture displaced despite antegrade nailing while the second
140 cases fracture developed with the nail in situ. In the literature, there were no other reports of failures of
141 prophylaxis in undisplaced fractures. Many authors have used newer generation solid nails with fixation
142 into the femoral head.

143 As illustrated by these two cases, we call for caution if not total avoidance of slotted nails with
144 bisphosphonate fractures. The torsional stiffness of slotted intramedullary nails is only 2% of the intact
145 femur compared to 13% for a solid nail(20). We believe it is important to select a more rigid implant that
146 can bear stress throughout an extended period of time for a biologically compromised femur to heal.
147 Our centers have therefore resorted to routine use of cephalomedullary nails.

148 A bone scintigraphy can be used to confirm delayed union when patient complains of persistent pain
149 despite prophylaxis. Anabolic agents for osteoporosis such as teriparatide and strontium renelate
150 increases bone formation and osteoblastic activity. The latter is currently licensed for use in Europe and
151 various other countries but not the United States (21, 22). Both had early results that may enhance
152 success after surgery in atypical femur fractures.

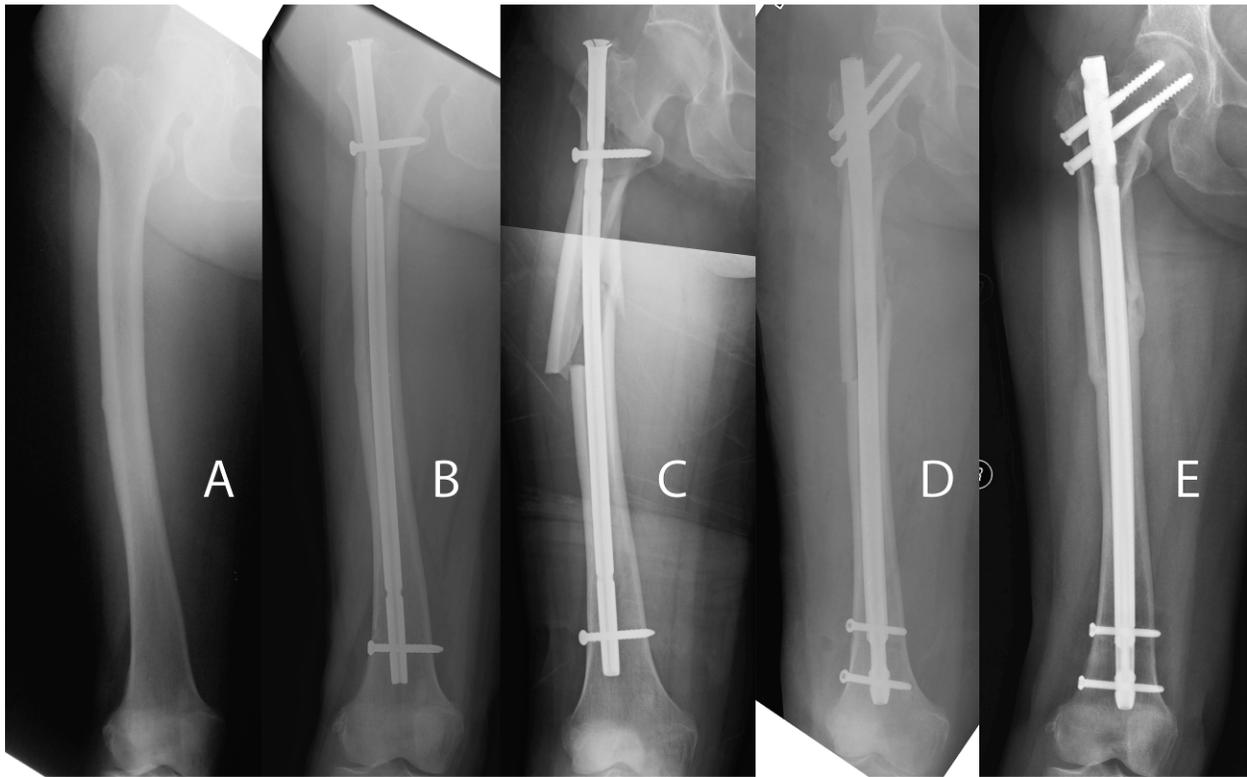
153 Extra effort has to be put in when tackling atypical bisphosphonate related fractures due to the high
154 reported rate of complications (12). Despite reinforcing on preventive measures such as strict adherence

155 to indications, close monitoring for complications, and cessation of the drug after 3 to 5 years,(1, 22, 24)
156 it is likely that orthopaedic surgeons will still increasingly face such fractures. The surgeon should make a
157 prompt diagnosis, establish a clear understanding with the patient, provide a stable mechanical
158 prophylaxis or fixation, respect the biology of the fracture and maintain vigilance at follow-up to assure
159 healing.

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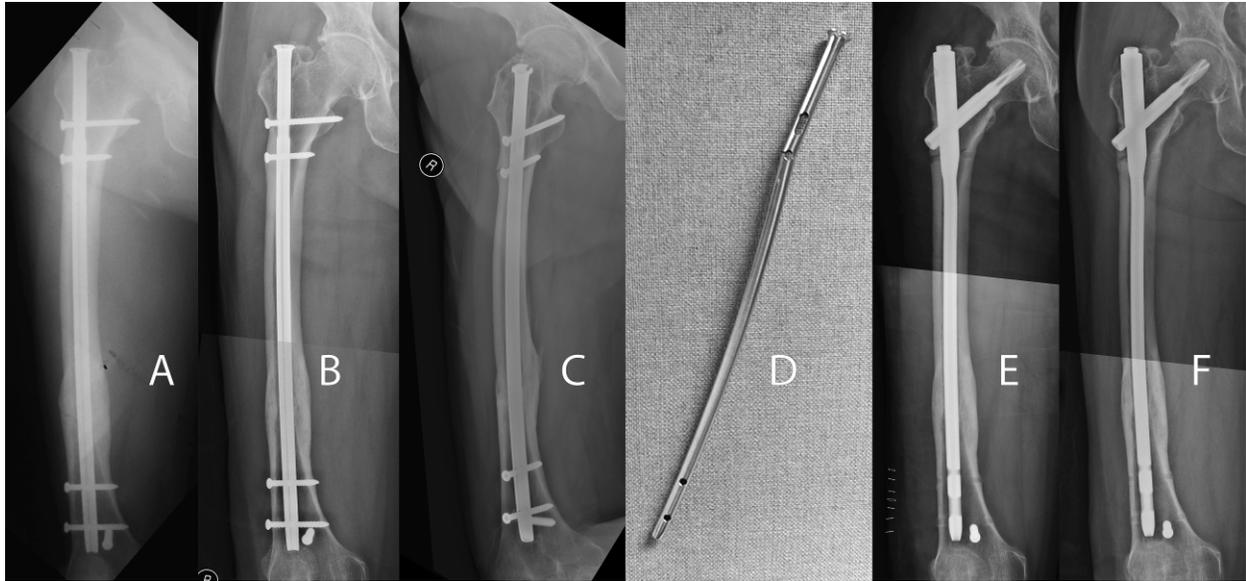


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216 **Figure 1:**

217 Case one. (A) A 77 years old lady who previously received 5 years of Alendronate presented with thigh
218 pain with X-ray showing features of an atypical cortical stress reaction at the mid diaphysis. (B)
219 Prophylactic fixation with a slotted stainless steel IM nail. (C) The atypical fracture failed to heal and a
220 secondary displacement occurred after a fall injury after thirteen months. (D) Revision with a
221 cephalomedullary nail. (E) Healing after seven months.

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Figure 2:

225 Case two. (A) A 78 years old lady with previous distal diaphyseal femur fracture treated with IM nailing,
226 with fracture healed nine months afterwards. (B) Patient complained of prodromal hip plane with no
227 definite X-ray changes on the anteroposterior view. (C) Oblique view showing a subtrochanteric atypical
228 fracture at the locking screw position. (D) Retrieval of a broken slotted IM nail. (E) Re-fixation with a
229 cephalomedullary nail. (F) The fracture has healed with patient pain free four months following revision
230 surgery.