Bilateral Bisphosphonate Related Femoral Shaft Fractures; Is this a Surgical Emergency?

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Abstract

Introduction: An 80 year old lady fell from standing sustaining bilateral fractures of the femora one year after stopping Alendronate treatment.

Case Presentation: History, radiographic and histological features were indicative of bisphosphonate related fractures. Fixation overnight was considered, as there was concern over potential for ongoing blood loss, combined with the fact that one fracture was open. On the other hand, the patient had a type 1 respiratory failure and it was felt that reamed intramedullary femoral nailings could potentially precipitate a respiratory crisis.

Conclusion: After a 12 hour period of optimization, early definitive fixation with bilateral reamed intramedullary nails was achieved with no hypovolaemia or worsening pulmonary failure. A long period of rehabilitation was required but the patient is now mobile and the fractures healed. The timing of surgery in this unusual injury pattern is examined here along with a brief review of the literature. Early surgery, after a brief period of resuscitation, is preferable to emergency surgery for this unusual bilateral fracture pattern.

Keywords: Femoral fracture; Bisphosphonates; Timing; Surgery

Introduction

Bilateral femoral fractures related to bisphosphonates are rare. Evidence on how and when to fix them is lacking [1]. This case illustrates a successful treatment strategy of early definitive fixation after a short period of resuscitation. A brief review of bisphosphonate fractures in included. As the literature is sparse in relation to bilateral bisphosphonate fractures, in particular how and when to operate upon them, we have examined the evidence on higher energy bilateral femoral fractures to ascertain some guidance.

Case presentation

An 80 year old lady sustained bilateral femoral fractures following a trip on flat ground (Figure 1a and 1b). There were no preceding symptoms and no thigh pain prior to falling. No other injuries were sustained.

On presentation, oxygen saturations on air were 92%, recovering to 100% on 15L oxygen. Bibasal fine crepitations could be heard at the lung bases. The patient was in fast atrial fibrillation but blood pressure was maintained at 154/80 mmHg.

Both thighs were swollen and deformed; the right having a puncture wound of 1 cm diameter on the lateral aspect. Thomas splints were applied and antibiotic prophylaxis administered in accordance with the British Orthopaedic Association Standards for Trauma guideline on the management of open fractures of the lower limb. Neurovascular examination of the limbs was normal [2].

As the patient was warfarinised for atrial fibrillation and transient ischaemic attacks, vitamin K and Berripplex were administered.

She had previously had a vertebral wedge fracture, metacarpal and metatarsal fractures.
Having had 6 years of alendronate therapy, a DXA scan 1 year prior to the injury showed normal bone density and the treatment was stopped. She was a non-smoker and prior to falling, was independently mobile.

**Investigations**

The patient was hypoxic on room air so a radiograph of the chest was taken but was normal.

An arterial blood gas taken on 15l/minute inspired oxygen showed a type 1 respiratory failure with relative hypoxia and a mild metabolic acidosis. Hydrogen ion concentration was 49nmol/l, pO2 of 21.6kPa, pCO2 of 5.5kPa, a base excess of -5mmol, bicarbonate of 20.6 mmol/l and a lactate of 1.2 mmol/l.

Admission haemoglobin level was 138 g/L, platelets were 350 x10⁹/l and International Normalised Ratio was 1.9. Bilateral femoral shaft fractures were seen on radiographs of the femurs. Both had a similar configuration with a transverse break in the lateral cortex roughly 10cm below the lesser trochanter. Both had a sclerotic edge with a flared appearance suggestive of stress fracture with callus reaction. The fracture lines extended proximally in an oblique fashion forming a medial spike (Figure 1a and 1b) [3].

**Differential Diagnosis**

Bilateral femoral fractures are usually associated with high energy trauma. The mechanism in this case, one of low force, suggested an underlying pathology. Malignancy (primary, secondary or haematological) and bisphosphonate related fractures are top of the differential.

Protein electrophoresis earlier in the year was normal making myeloma unlikely and radiographs did not show any features such as lytic or bone forming lesions suggestive of malignancy.

The history of alendronate use and the transverse, trumpeted, sclerotic appearances of the fracture in the lateral cortex and the medial spike all point towards the diagnosis of an alendronate related fracture.

**Treatment**

Two long bone fractures have the potential for life threatening blood loss so an initial decision was made to operate that evening. One fracture was open via an inside out puncture wound. While not an indication for out of hours surgery in itself, when combined with the potential bleeding it was felt that earlier intervention may be beneficial.

It was planned to treat the open fractures with a reamed cephalomedullary nail and, if the patient remained stable, to continue and nail the contralateral side. There was concern that the patients respiratory condition was poor and that pulmonary complications from nailing could precipitate a respiratory crisis.

Bilateral nails at one operative sitting would save a second anaesthetic, avoid provoking a subsequent inflammatory response, minimise immobilisation and recumbency, prevent problems with pressure areas from the Thomas splint and ongoing blood loss due to the unsecured contralateral fracture. Early postoperative mobilisation would also be
possible and was felt to be particularly important due to the patient’s already compromised respiratory function. Due to another emergency case of higher priority, surgery was postponed to the following day.

**Outcome, prognosis and follow up**

Overnight, the patient remained stable with only maintenance intravenous fluid. The next day, haemoglobin had fallen to 101g/l, a drop of 37g/l. Both femora were fixed with reamed cephalomedullary nails day 1 post injury without incident (Figure 2a and 2b). The open fracture was classified as a Gustilo and Anderson Type II injury and no issue with infection arose [4].

Post-operative haemoglobin was 91 g/l with a haematocrit of 0.285 l/l. Two units of packed red cells were transfused. As both femurs were involved, no restriction on weight bearing was made. Mobilisation began on the first postoperative day. Initially this involved transfers to a chair and subsequently weight bearing was supported with a pulpit walker to transfer weight through the arms. This progressed to a zimmer frame prior to discharge after 55 days as an inpatient. Radiographs at 7 weeks show callus formation at the fracture site (Figure 3a and 3b).
The bisphosphonates, a class of drugs inhibiting osteoclasts, are commonly prescribed for the treatment of osteoporosis and prevention of fragility fractures. A relatively rare, complication is that of low energy fractures in the subtrochanteric and diaphyseal region of the femur [1,5-7].

A retrospective study of all proximal femoral fractures presenting to three UK centres over two years identified 3515 patients with subtrochanteric or proximal diaphyseal fractures. 27 bisphosphonate fractures were found, 1 patient (0.028%) had bilateral simultaneous femoral fractures. The mean duration of bisphosphonate therapy prior to fracture was 4.6 years although the earliest occurred at just 6 months [1].

Risk of alendronate related femoral fractures is most evident in females and increases dramatically with duration of therapy. Schilcher et al reviewed the Swedish national database and found the absolute risk of fracture was 3 times higher in women. After 4-5 years of use, risk of atypical fracture was 100 times higher compared to those that were not taking the drug. On stopping, risk decreased rapidly by 70% each drug free year. The patient in our case had stopped alendronate one year prior to injury, an example of the latent potential for harm [8].

In terms of identifying these fractures; radiographic criteria for bisphosphonate related fractures of the femur were set out by the Task Force of the American Society for Bone and Mineral Research and further defined in a study by Schiller et al 2014. They found features with a high specificity for bisphosphonate use; fracture angle in the lateral cortex of between 75 and 105 degrees to the shaft; a medial spike and callus at the lateral fracture site [8,9].

The fractures in our patient both had a medial spike, callus formation at the lateral cortex and the angles measured were 77 degrees on the right and 81 degrees on the left. Pathology samples, taken intraoperatively, from the fracture site were reported as ‘No evidence of any neoplasm was found a mixture of lamellar and reactive woven bone was seen, consistent with a healing fracture’. This all indicate a stress type fracture likely related to bisphosphonate therapy.

More commonly encountered, high energy, bilateral femoral fractures are often regarded as a life threatening injury due to blood loss and pulmonary complications. This may result in a rapid move to fix one or both fractures. Mortality rates appear to be improving, possibly due to improving standards of care and decreased burden of injury. Little is documented on the topic of mortality with bilateral bisphosphonate femoral fractures [10].

Copeland., et al. compared mortality in patients with unilateral and bilateral femoral fractures. When matched for Injury severity scores (ISS), a second femoral fracture significantly increased mortality by a factor of 2.5. Perhaps the same may apply to bisphosphonate fractures [11]. No studies are available on the matter.

In this case, operation on the evening of presentation was planned. Circumstances dictated that this was not possible. Despite initial concerns that excessive blood loss may occur, a drop in haemoglobin of 37g/l was the result. While not insignificant, urine output and parameters were maintained preoperatively and only two units of blood were required after operation. Life threatening bleeding did not occur but in a patient that was already anaemic this may be a valid concern.

Pulmonary dysfunction has been observed to be significantly worse in high energy bilateral femoral fractures compared to unilateral injuries. It is not clear if this is due to the fractures themselves or whether the multiple associated injuries amount to an excessive inflammatory load predisposing to ARDS and pulmonary failure. No other cause was identified for the respiratory failure, which resolved in the days following operation [12].

Prior to injury, the patient did not have any respiratory symptoms and the respiratory failure resolved in the days following operation. We assume that this is a case of pulmonary dysfunction caused by bilateral femoral fractures from a low energy mechanism. Fixation of both fractures in one operative sitting and reaming both femora did not further impact upon respiratory function.

Timing of operation

We were unable to find any studies on optimal timing of fixation of bilateral bisphosphonate fractures. Given the lack of soft tissue injury and the absence of polytrauma, this begs the question; do these injuries need to undergo operation urgently?
No evidence on this topic was found in the literature. Extrapolating from studies on high energy femoral fractures offers some guidance.

In a review of 7,540 femoral fractures, Cantu et al found no difference in mortality between those operated upon in less than 12 hours from presentation, 12-24 hours and 24-48 hours. In the most severely injured they noted an advantage to having surgery between 12 and 24 hours after presentation. Of particular importance, a delay of greater than 48 hours was found to have a negative impact on mortality, particularly in the over 65s [13].

Nahm., et al. in a systematic review of femoral fractures published in 2012, found that early fixation was shown to decrease mortality in 3 studies, showed no difference in 10 and in one study showed an increase in mortality if fixation was done in the first 8 hours. In the two studies they found comparing early definitive fixation and damage control surgery with external fixation, mortality was reduced for those in the early definitive surgery groups [14].

Our experience in this case would suggest that as with high energy femoral fractures and fragility fracture of the hip, a period for resuscitation before early definitive care is a safe strategy.

**Postoperative recovery and rehabilitation**

After fracture fixation, the patient in this case had a stay of 55 days, far longer than those reported for high energy trauma.

Comparing 54 patients with bilateral femoral fractures to a cohort of 461 unilateral femoral fractures, O’Toole., et al. observed that hospital stays were longer for those with injuries to both legs. They had a higher injury severity score and were in hospital on average for 14 days compared to 9 days for patients with unilateral fractures. Giannoudis., et al. reported a mean stay of 36 days, in a retrospective review of 14 patients with bilateral femoral fractures with an average age of 38 [12]. The average age of patients with bilateral fractures in O’Tooles study was 29. Bisphosphonate fractures occur in an aged population with multiple comorbidities and limited physiological reserve. A lengthy period of rehabilitation should be expected.

**Conclusion**

In summary, treatment strategies should mirror those for fragility fractures of the hip and high energy femoral fractures; delaying until daylight hours and allowing time for adequate resuscitation. Early definitive fixation, rather than damage control surgery allows early mobilisation and the long recovery period to get underway.

**Learning points**

- A period of resuscitation prior to operation was not detrimental to the outcome; these cases can be dealt with in normal working hours.
- Pulmonary complications may occur even from low energy femoral fractures.
- Definitive fixation of both fractures at a single operation did not cause any complications and allows progression to rehabilitation.
- The use of reamed intramedullary nails did not cause any respiratory deterioration and is a suitable treatment in this patient group.
- Bisphosphonate use beyond five years should be approached with caution.

**Authors’ Contributions**

A. Macey wrote wrote the manuscript, all authors were involved in manuscript editing and care of the patient. T. Hems was the consultant in charge of the patients care.

**Patient Consent**

The patient has given written, informed, consent for publication of her case details and radiographs.

**References**


