Atypical femoral fractures: a complication of prolonged bisphosphonate therapy?

Michael P Falkenberg

To the Editor: Girgis and Seibel[1] are to be congratulated as endocrinologists for raising the important issue of bisphosphonate therapy and femoral fractures. This is a relatively new phenomenon that even a couple of years ago, although already documented, did not seem to be on many endocrinologists' radar.

However, I question the authors' statement that such fractures are rare. In my small outpost of the orthopaedic world (Northeast Health Wangaratta), three cases have been seen in 12 months. All patients characteristically had a spontaneous nontraumatic fracture, a short oblique or transverse fracture in the subtrochanteric area, and had been on alendronate for more than 5 years. If a journeyman orthopaedic sur-

geon is seeing a cluster of cases, I suggest that these fractures are not rare.

On the other hand, a review of our audit figures in Wangaratta in north-eastern Victoria (where we have a stable rural population of about 17 000) provides an interesting statistic. Over 15 years (1993–2008), Northeast Health Wangaratta admissions for fractured neck of femur fell steadily from 74 to 35 a year. This trend continues. We should not throw out the baby with the bathwater — osteoporosis treatment is likely partly responsible. Also, a deeper level of community aged care support and much better comorbidity management may have helped to reduce falls.

The real question is whether all patients who have been on alendronate (or any bisphosphonate) for 5 years need to have a mandatory holiday from the drug. In line with Wolff's law (bone will adapt to loads under which it is placed), the precursor femoral stress lesions will heal by remodelling, as long as bisphosphonate therapy is suspended. I suggest that the suspension should be for 2 years, which is the time required for full fracture remodelling. I agree with Girgis and Seibel that these drugs have been effective in reducing fracture incidence; however, their long-term use needs further study.

Michael P Falkenberg, Orthopaedic Surgeon
Northeast Health Wangaratta, Wangaratta, VIC.
ortho.rooms@bigpond.com

1 Girgis CM, Seibel MJ. Atypical femur fractures: a complication of prolonged bisphosphonate therapy [editorial]? *Med J Aust* 2010; 193: 196-198. ❑

Christian M Girgis and Markus J Seibel

In reply: We thank Falkenberg for his comments in reference to our article in the Journal.[1] Two recent large-scale population-based studies have suggested that subtrochanteric femur fractures are rare both in the general population and among bisphosphonate users.[2,3] While personal experience may often suggest otherwise, a cluster of atypical fractures cannot be used as an indicator of true incidence in the absence of data on the frequency of bisphosphonate use in a particular population.

It is certainly safe to say that atypical fractures occur much less frequently than osteoporotic hip fractures. In a 5-year retrospective analysis of femur fractures at our centre, osteoporotic hip fractures outnumbered atypical fractures by a factor of greater than 60.[4] Given the body of high-quality evidence on the antifracture efficacy of bisphosphonates, we agree that discarding an effective class of drugs because of a presumed association with an uncommon fracture pattern would be like throwing out the baby with the bathwater.

Should we routinely advise patients to take a drug holiday after, say, 5 years of bisphosphonate therapy? There is no good evidence for that either. Although bisphosphonates bind to bone for extended periods, severely suppressed bone turnover or signs of mechanical failure (microcracks) are rarely, if at all, seen in patients chronically treated with bisphosphonates. Similarly, the few bone biopsy studies in patients with atypical fractures do not uniformly support the hypothesis of severely suppressed bone turnover as a cause of these fractures.[5,6] Instead of being based on the theoretical assumption of an uncertain risk, the decision for a drug holiday should be made on a case-by-case basis, guided by factors such as the patient's on-drug fracture history, the presence of other relevant risk factors for osteoporosis, and changes in bone density and bone turnover.

Many questions remain unanswered regarding atypical femoral fractures and their biomechanical evolution. Until further research is conducted, the fear of the unknown, namely the impact of bisphosphonates on bone remodelling and microfracture accumulation, should not replace strong evidence in support of their antifracture efficacy.

Competing interests: Markus Seibel is a member of advisory boards for Merck Sharp and Dohme, Novartis, Amgen and Sanofi-Aventis. He has also received funding from these companies for institutional research.

Christian M Girgis, Clinical Associate Lecturer
Markus J Seibel, Professor of Endocrinology
University of Sydney, Sydney, NSW.
cgirgis@usyd.edu.au

1 Girgis CM, Seibel MJ. Atypical femur fractures: a complication of prolonged bisphosphonate therapy [editorial]? *Med J Aust* 2010; 193: 196-198.
2 Nieves JW, Bilezikian JP, Lane JM, et al. Fragility fractures of the hip and femur: incidence and patient characteristics. *Osteoporos Int* 2010; 21: 399-408.
3 Abrahamsen B, Eiken P, Eastell R. Subtrochanteric and diaphyseal femur fractures in patients treated with alendronate: a register-based national cohort study. *J Bone Miner Res* 2009; 24: 1095-1102.
4 Girgis CM, Sher D, Seibel MJ. Atypical femoral fractures and bisphosphonate use. *N Engl J Med* 2010; 362: 1848-1849.
5 Somford MP, Draijer F, Thomassen BJ, et al. Bilateral fractures of the femoral diaphysis in a patient with rheumatoid arthritis on long term treatment with alendronate. *J Bone Miner Res* 2009; 24: 1736-1740.
6 Visekruna M, Wilson D, McKiernan FE. Severely suppressed bone turnover and atypical skeletal fragility. *J Clin Endocrinol Metab* 2008; 93: 2948-2952. ❑