NDT Plus (2009) 2: 49–51
doi: 10.1093/ndtplus/sfn169
Advance Access publication 12 November 2008

NDT PLUS
Nephrology Dialysis Transplantation

Case Report

Bone histomorphometry after treatment with teriparatide (PTH 1-34) in a patient with adynamic bone disease subsequent to parathyroidectomy

Gabriele Lehmann[1], Undine Ott[1], Jörg Maiwald[2] and Gunter Wolf[1]

[1]Department of Internal Medicine III, Friedrich Schiller University of Jena and [2]Dialysis Center and Nephrological Surgery, Gera, Germany

Abstract

A 33-year-old male patient suffered from adynamic bone disease because of parathyroidectomy due to tertiary hyperparathyroidism. Histomorphometric analysis of bone biopsies taken before and 8 months after treatment with teriparatide (human parathyroid hormone 1-34 of recombinant DNA origin) for 18 months is demonstrated. A considerable increase in mineralized bone volume and also stimulated bone remodelling were detected after treatment with teriparatide. Although teriparatide is currently only licenced for treatment of severe osteoporosis, this case shows the potential therapeutic effect of this new drug to improve bone structure in a patient with adynamic bone disease.

Keywords: adynamic bone disease; end-stage renal disease; histomorphometry; teriparatide therapy

Background

Adynamic bone disease represents one form of the histopathologic bone lesions that can develop during the course of chronic renal insufficiency. Most severe forms are seen due to hypoparathyroidism subsequent to total parathyrectomy. Important clinical consequences of adynamic bone disease are the increased risk for skeletal fractures [1] as well as facilitation and progression of arterial calcification [2]. Therapeutical options are limited. We report here on a novel therapy with teriparatide, a recombinant human PTH 1-34 normally used for the treatment of severe osteoporosis.

Case report

A 33-year-old man suffering from hypoplastic kidney of unknown origin had been treated with haemodialysis since 1992. On 11 May 2004 severe tertiary hyperparathyroidism (PTH level 3000 ng/l, normal: 15–65 ng/l) required total parathyroidectomy. The procedure included an autotransplantation of parathyroid tissue into the upper leg, but the autotransplant failed to secrete PTH (PTH levels between 1.4 and 10.4 ng/l determined with chemiluminometric technology, Centaur, Bayer, Newbury, UK). Hypocalcaemia developed despite daily supplementation with calcium (calcium acetate 3 × 700 mg), calcitriol (0.5 μg) and dihydrotachysterol (3 × 0.5 mg). The patient developed hypocalcaemic tremor, agitation and muscle cramps. A therapy with teriparatide (20 μg administered daily, subcutaneously) was started from December 2005 until July 2007. The complaints totally diminished after a therapy with teriparatide, and did not relapse. Values of serum calcium, serum phosphate and PTH over the course of the disease are shown in Figure 1. Additional treatment consisted of phosphate-binding agents sevelamer (3 × 800 mg) and calcium acetate (2 × 1.8 g). Cholecalciferol (800 U) was given orally once a day and calcitriol (0.5 μg) was given orally twice weekly.

To further gain insight into the exact bone disease, a biopsy was performed 15 months after parathyroidectomy and before the initiation of teriparatide therapy in 2005.

Based on results obtained in normal controls, histomorphometric diagnosis was defined according to the amount of fibrosis, and static and dynamic parameters as previously described [3].

The first bone biopsy taken in December 2005. It represents typical characters of an adynamic bone disease including massive reduction in bone volume (bone volume/tissue volume 11.6%, normal: >20%), extremely reduced number and sites of osteoclastic resorption, missing osteoblasts (osteoclast- and osteoblast-covered surface/bone surface 0, normal 2.5 resp. 4.5%) and lack of peritrabecular or marrow fibrosis (Figure 2A).

The second bone biopsy performed 8 months after cessation of a teriparatide treatment period over 18 months shows a considerable increase in mineralized bone volume (bone volume/tissue volume 30.2%) and also an increase in bone remodelling. Flat and plumper lining cells (osteoblast progenitors) as well as mature osteoblasts are arranged in

Correspondence and offprint requests to: Gabriele Lehmann, Department of Internal Medicine III, Friedrich Schiller University of Jena, Erlanger Allee 101, 07747 Jena, Germany. Tel: +49-3641-9324327; Fax: +49-3641-9324362; E-mail: gabriele.lehmann@med.uni-jena.de

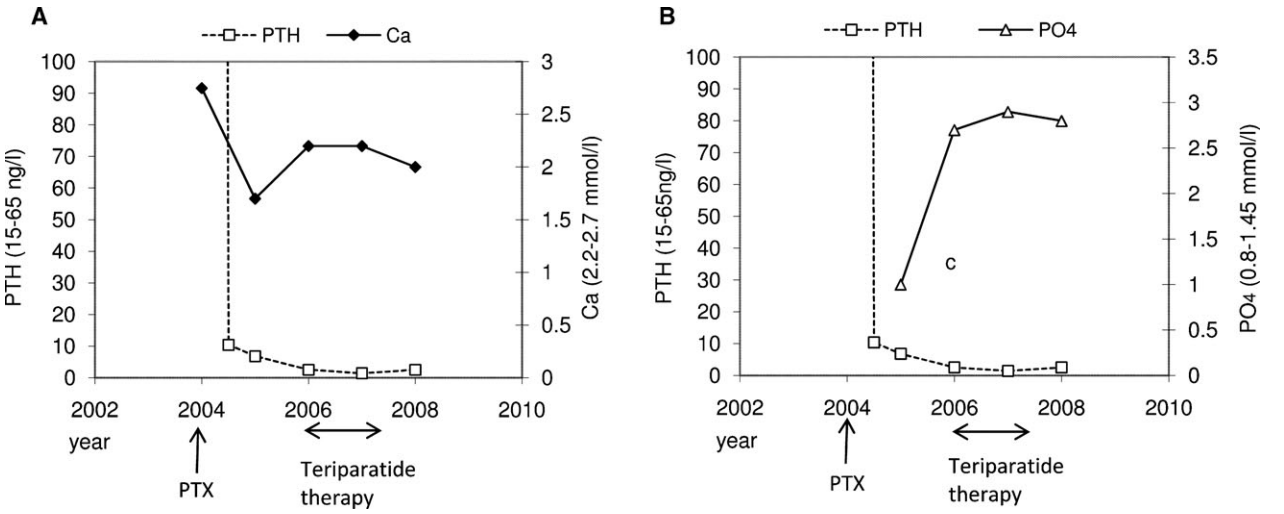

Fig. 1. (**A**) Serum calcium and PTH concentrations and (**B**) phoshate and PTH concentrations; arrows show time of parathyroidectomy and duration of teriparatide therapy.

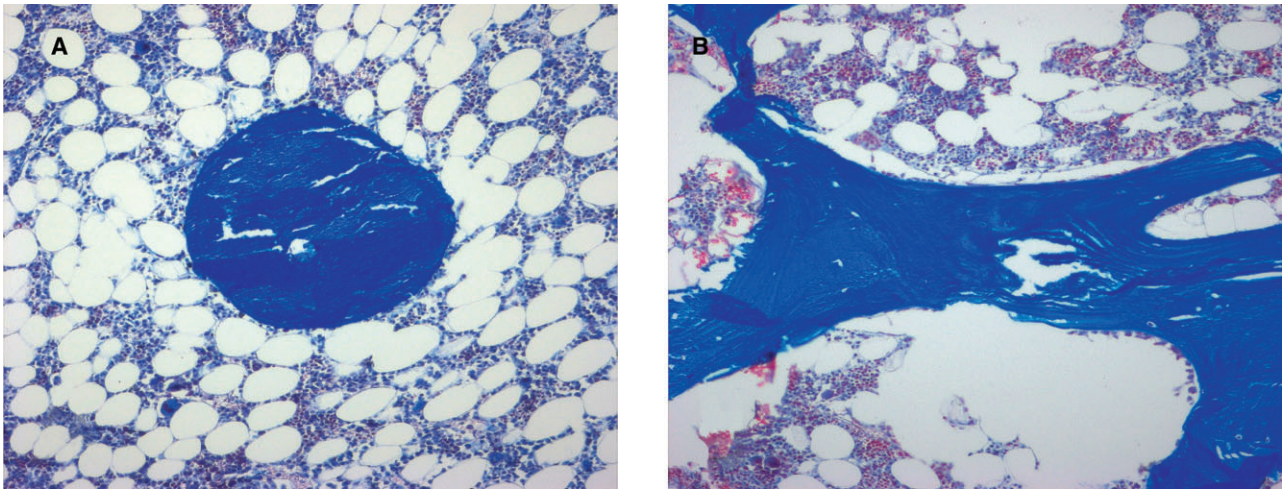

Fig. 2. (**A**) Bone biopsy before teriparatide therapy. Masson–Goldner stain (magnification ×100). Decreased bone volume with missing osseous remodelling and cellular paucity found being typical of adynamic bone disease. (**B**) Bone biopsy after teriparatide therapy. Masson–Goldner stain (magnification ×100). A high bone volume is detected. The trabecular surface is covered with osteoblasts and lining cells (lower right), osteoclast apart from the trabecular surface.

single and double layer along the trabecular surface. The osteoblast-covered surface/bone surface reached 2.6%. In a couple of trabeculae, they cover the boundary on both sides (Figure 2B) and they are even present in former resorption lacunae. There is no detectable osteoid. Osteoclasts are rare and apart from the trabecular surface (osteoclast-covered surface/bone surface 0.4%). The arrangement of cement lines in trabecular bone is distinct and lamellar.

Discussion

Balanced bone remodelling with osteoclast-induced bone resorption and osteblast-mediated bone formation is necessary to maintain skeletal integrity. Continuous high levels of PTH increase bone resorption while intermittent administration stimulates bone formation. Teriparatide (human PTH 1-34 of recombinant DNA origin) is an anabolic agent given once daily [4]. In patients with osteoporosis, the substance causes an improvement in bone microarchitecture and strength and may reduce fracture incidence [4–6]. Normal or decreased PTH levels are a basic condition for the administration of teriparatide in osteoporosis. In patients with renal osteodystrophy, serum intact PTH levels are often normal or even elevated in those with adynamic bone disease. Adynamic bone disease as a result of parathyroidectomy represents a special form [7] due to iatrogen-induced PTH deficiency. In this setting a replacement therapy seems a reasonable approach. Recently, teriparatide therapy was shown to be effective in a patient with severe hypoparathyroidism that was caused by gain-of-function mutation of the calcium-sensing receptor [8]. The therapy was well tolerated. There was no evidence of arthralgia, headache or nephrolithiasis. As proved in a *post hoc* analysis in

patients with mild and moderate renal insufficiency as a subgroup of the approval study of PTH (1-34), no differences occurred in kind, severity and frequency of adverse events when comparing patients with normal and impaired renal function [9].

In our case, teriparatide administration induced the expected effect on bone remodelling. In contrast to the initial cellular paucity, the second biopsy exhibits osteoblasts as well as osteoclasts on endosteal surfaces and, as a result of their impact, an increased bone volume. Studies in animals with high-dose teriparatide treatment have shown an increase in the development of osteosarcomas. It has been therefore argued that therapy with teriparatide should be limited to 2 years [10].

Conflict of interest statement. None declared.

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Received for publication: 21.9.08
Accepted in revised form: 15.10.08