The dialysis patient with persisting elevation of bone alkaline phosphatase after parathyroidectomy

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Case report

Mister Be … born in 1915, had chronic renal failure secondary to autosomal polycystic kidney disease (APCKD) discovered in 1980. Haemodialysis was started in 1989 and blood pressure normalized without antihypertensive drugs. Colon diverticulosis manifested by abdominal pain, was diagnosed in 1990 and operated on for colon perforation in 1994. Cardiac supraventricular arrhythmia observed in 1988, was treated by amiodarone.

Secondary hyperparathyroidism progressed to the severe stage despite oral vitamin D3 and phosphate binders treatment. In 1992 i.v. pulse alfacalcidol resulted in a good control of serum levels of intact parathyroid hormone (iPTH). Alfacalcidol was withdrawn when iPTH normalized and re-introduced a few months later because hyperparathyroidism recurred and serum levels of iPTH increased. Bone alkaline phosphatase closely followed the variations of iPTH during the different phases of the secondary hyperparathyroidism (Figure 1).

In 1995, calcium and phosphate levels rose and hyperparathyroidism became refractory to pulse alfacalcidol therapy (Figure 2). Because of the increase in calcium × phosphate product, despite having lowered dCa to 1.25 mM, parathyroidectomy was decided.

Key words: autosomal poly cystic kidney disease; bone phosphatase alkaline; hyperparathyroidism; Paget’s disease

Fig. 1. Bone alkaline phosphatase and PTH serum levels evolution over time. Severe hyperparathyroidism was satisfactorily corrected with pulse i.v. alfacalcidol. Subsequently, hyperparathyroidism recurred and was resistant to this treatment schedule and parathyroidectomy was performed.

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Fig. 2. Total Ca and phosphate serum levels evolution. Ca and phosphate serum levels were maintained within the aimed range during 1992 and 1993 and rose thereafter. They returned to normal after parathyroidectomy.

the serum level of total alkaline phosphatase, while the bone fraction remained over 2-fold the upper limit of normal, oriented us to a second bone disease in addition to the corrected hyperparathyroidism. Total body gammagrapy showed marked fixation of the tracer in the right side of the pelvis very suggestive of Paget’s disease (Figure 3). X-ray of this region confirmed the diagnosis (Figure 4).

Comment

The interest of the present case is 4-fold. It shows the natural history of hyperparathyroidism in a patient treated with the modern approach of lowering dCa and i.v. pulse doses of vitamin D3, properly responding first and becoming resistant thereafter. It reminds us of the problems associated to surgical parathyroidectomy (immediate severe hypocalcaemia, iatrogenic hypercalcaemia and recurrent nerve paresis). It shows the perfect correlation between iPTH and bALP serum levels over a 5 year period including different hyperparathyroidism stages (determined from frozen samples from 1992 to 1996). Finally, it presents the problem of a complex bone disease, since after secondary hyperparathyroidism had been resolved by parathyroidectomy, all the parameters normalized—except bone alkaline phosphatase.

Ureña et al. [1,2] have demonstrated a good correlation between total and bone alkaline phosphatase and intact PTH serum levels in dialysis patients. Our data during the pre-parathyroidectomy period fully confirm these reports. However, the persistence of high serum levels of bALP suggested a persistent high turnover bone remodelling disease in the patient presented here, while iPTH was lower than normal (after parathyroidectomy). In our patient bALP was persistently higher than 20 ng/ml, the reported threshold to think of a high turnover bone remodelling disease [1,2].

Fig. 3. Total bone gammagrapy showing a marked asymmetric hyperfixation of the tracer in the pelvic region (arrows).

Fig. 4. Pelvic X-ray evolution. Note the disappearance of bone striations and generalized increase in density, typical of Paget’s disease.
The differential diagnosis of an increased serum level of alkaline phosphatase used to include liver and cholestatic syndromes, bone metastasis and malignancies (multiple myeloma, breast, prostatic, gastric, colorectal, gallbladder, liver, adult T-cell leukaemia lymphoma), osteomalacia—rickets, hyperostosis corticalis generalisata, and Paget’s disease [3]. The introduction of the new assays specifically measuring the bone fraction of alkaline phosphatases, allows differentiation between bone disease and elevation of alkaline phosphatases unrelated to bone disease. Bone disease involving high turnover bone remodelling include: hyperparathyroidism, bone metastases of malignancies (particularly prostatic and breast) and Paget’s disease. The age of the patient (81-year-old) and the mild clinical evolution suggested Paget’s disease. As shown in Figures 3 and 4, total bone gammagraphy and X-ray confirmed our clinical diagnosis.

Teaching point

If the patient has renal bone disease—do not stop looking for additional bone disease if the data do not fit into the pattern of renal bone disease.

References