Case Report

A transplanted child with severe hypercalcaemic hyperparathyroidism despite only modest bone lesions

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Introduction

We report an unusual case of a child with advanced hyperparathyroidism (HPT), which became clinically manifest only after renal transplantation. Enlarged parathyroid glands could not be demonstrated by imaging methods (ultrasound, scintigraphy, MRI). Severe symptomatic hypercalcemia unresponsive to calcium-lowering medication prompted surgical intervention. Removal of three hyperplastic glands and one apparent adenoma resulted in resolution of hypercalcemia.

Case report

Patient SN was started on peritoneal dialysis at the age of 3 years because of dysplastic kidneys. Renal transplantation performed at age 6 years was unsuccessful. He was treated with maintenance haemodialysis after the failed transplantation.

At the age of 8 years severe hyperparathyroidism developed. No hypercalcemic episodes were seen at this time. Oral pulse therapy with 1,25(OH)2D3 was started. Intact parathyroid hormone (iPTH) levels which were elevated up to 20-fold above normal decreased to a level of fourfold above normal. Time course of iPTH and prescribed 1,25(OH)2D3 doses respectively, are shown in Figure 1. The maximum dose of 1,25(OH)2D3 was 3 µg three times weekly taken under observation at the time of dialysis sessions. Hypercalcemic episodes of short duration were seen with this dose, but maximum calcium levels rarely exceeded 3.0 mmol/l and responded promptly to cessation of 1,25(OH)2D3. Calcium acetate was used as a phosphate binder. The concentration of serum aluminium was not elevated (8 µg/l; normal <10 µg/l), as was PTH-related protein (0.9 pmol/l; normal <5 pmol/l).

X-ray of the right hand showed sclerosed distal epiphyses of the ulna and radius, a discrete radiolucent band in the metaphyses of the ulna and radius and rarefaction of the spongiosa. We report an unusual case of a child with advanced hyperparathyroidism (HPT), which became clinically manifest only after renal transplantation. Enlarged parathyroid glands could not be demonstrated by imaging methods (ultrasound, scintigraphy, MRI). Severe symptomatic hypercalcemia unresponsive to calcium-lowering medication prompted surgical intervention. Removal of three hyperplastic glands and one apparent adenoma resulted in resolution of hypercalcemia.

Discussion

It is quite unusual that following successful renal transplantation severe symptomatic hypercalcemia develops beyond the immediate postoperative period. Even more surprising is the fact that in this severely hypercalcemic child with excessive elevation of intact
Fig. 1. Time course of parathyroid hormone (iPTH) and 1,25(OH)2D3 therapy. PTX denotes parathyroidectomy.

PTH concentration, only modest fibro-osteoclastic changes were demonstrable in the skeleton.

The nodular and pseudoadenomatous growth of the parathyroids in our case is a well known complication of long-standing hyperparathyroidism. It is known that such growth is often monoclonal and accompanied by reduced expression of vitamin D receptors [1,2]. It has been argued that correction of hyperphosphataemia after renal transplantation sensitizes the bone to the hypercalcaemic action of PTH. It is nevertheless astonishing that this (suspected) release of calcium from the skeleton occurred despite only borderline histological evidence of fibro-osteoclasia. We emphasize that the patient did not have extraskeletal calcium phosphate deposits which might have dissolved following reversal of renal failure.

With the recent recognition of low bone turnover disease (so-called ‘adynamic’ renal bone disease) as a disease entity it became apparent that the bone response to PTH may be abnormally low in renal failure [3]. This may or may not be linked to diminished expression of the PTH receptor in several tissues of the uraemic organism [4,5], including bone. It remains enigmatic, however, why this should still have been the case after successful renal transplantation. We cannot completely exclude the possibility that immunosuppressive treatment, particularly steroids, interfered with the action of PTH on bone.

The case further illustrates the known problems of interpretation of circulating iPTH levels and the conclusions derived therefrom with respect to the events occurring in the bone. Cut-off points for iPTH levels have been proposed to distinguish patients with low and high bone formation rate [6]. Using these criteria iPTH values of our patient were in a range compatible with high-turnover bone disease (200 pg/ml, positive predictive value 82%, negative predictive value 91%, sensitivity 88% according to [6]). Our case illustrates the limits of this approach.

We conclude from this unusual case that PTH related hypercalcaemia and PTH-mediated bone disease do not strictly go in parallel, even after renal transplantation. A formal interpretation would be that bone is partially resistant to PTH, but the detailed mechanisms involved to cause divergent effects of PTH on calcium mobilization and bone turnover are currently unknown.

On a practical level we feel that a lesson should be learnt from this case, i.e. that parathyroidectomy should be considered early if iPTH levels do not appropriately decrease after high-dose 1,25(OH)2D3 treatment. It is also obvious that absence of marked bone involvement should not deter from this strategy.

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References


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