Reminder of important clinical lesson

Hyperparathyroidism in a renal transplant patient: an unusual cause of resistance to therapy

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Summary

A long-term renal transplant patient who was regularly followed up in the transplant clinic with stable renal allograft function was found to have elevated parathyroid hormone (PTH) levels on a bioactive PTH assay. The elevated PTH levels were resistant to suppression on increasing doses of 1-alfacalcidol. Detailed history taking and clinical examination revealed the reason for apparent resistance to therapy.

CASE PRESENTATION

Mrs MB, a 64-year-old Black woman presented with proteinuria and renal impairment in 1980, renal biopsy revealed a diagnosis of mesangial proliferative glomerulonephritis. She developed end-stage kidney disease (ESKD) in 1982 and was started on intermittent hospital-based haemodialysis. She showed classic bone mineral metabolism abnormalities with hyperphosphataemia, hypocalcaemia and progressive rise in PTH levels consistent with a diagnosis of secondary/tertiary hyperparathyroidism. She was treated with phosphate binders and increasing doses of 1-alfacalcidol to suppress the PTH and eventually underwent parathyroidectomy for resistant hyperparathyroidism. Her other co-morbidities included hypertension and diabetes mellitus. She received a cadaveric renal transplant in 1982 and had lithotripsy for a renal transplant stone in 1993.

She was seen regularly in a renal transplant clinic with a stable graft function. Her immunosuppression consisted of cyclosporine A 50 mg twice a day and prednisolone 5 mg once a day. The blood pressure was well controlled on candesartan, atenolol and bendroflumethazide. Her other medications included atorvastatin, aspirin, omeprazole, alendronate, gliclazide and eprex (epoetin β).

Her renal allograft function remained stable with creatinine in the range 150–170 μ mol/l. She was found to have markedly raised PTH levels in the range 150–160 pmol/l (1.6–7.3 pmol/l). However, serum phosphate, calcium and alkaline phosphatase were within normal limits. She was started on 1-alfacalcidol 0.25 mg once a day to suppress her PTH levels. Her compliance to the medications was good. The PTH levels remained high in spite of progressive increase in the dose of 1-alfacalcidol (up to 1 μ g once a day). At one of her clinic visits, several venepuncture marks in right cubital fossa and a scar over the forearm alerted us to a possible cause of her raised PTH levels. Owing to the presence of an arteriovenous fistula in her left forearm, venous blood sampling was always performed in her right ante-cubital fossa. Further history taking and review of her notes confirmed that the scar over her right forearm was a surgical scar of a parathyroid gland implantation in the forearm. She has had

parathyroidectomy in 1987 with forearm implantation of one of the glands. We suspected that the high PTH levels are due to taking blood sample from the ante-cubital vein upstream of the parathyroid gland implant with a resultant sampling from the venous drainage of the parathyroid gland. To test this hypothesis, we performed simultaneous venous blood sampling from both the upper limbs. In addition, samples were also taken from above (ante-cubital fossa) and below (dorsum of the hand) the insertion of parathyroid gland implant in her right forearm. Table 1 summarises the PTH levels from blood samples taken from these sites.

These results demonstrate that markedly raised PTH levels in this patient were due to blood sampling upstream of the parathyroid gland implant site in right forearm with consequent sampling from one of the veins draining the parathyroid gland. We then reduced the dose of 1-alfacalcidol back to 0.25 μ g once a day and informed the patient that whenever a blood test for PTH is requested she should instruct the phlebotomists to take blood from dorsum of the right hand or from the left upper limb. Clear instructions have been recorded in patient's notes. She does indeed have a degree of secondary hyperparathyroidism but with true systemic PTH levels of 45–50 pmol/l.

DISCUSSION

This case highlights the importance of history taking and clinical examination during follow-up of patients with long-standing chronic illnesses such as the patient presented here. In a busy clinic it is not an uncommon practice to treat the blood results without making efforts to identify an underlying problem that could be revealed by

Table 1 PTH levels in blood samples taken from three different sites

Blood sampling site	PTH levels (pmol/l)
Right upper limb–ante-cubital fossa	153
Right upper limb–dorsum of the hand	47.2
Left upper limb–ante-cubital fossa	47.2

careful clinical assessment. In this patient, inappropriate increases in the dose of 1-alfacalcidol could have led to hypercalcaemia and development of adynamic bone disease due to over-suppression of parathyroid gland.¹ This was prevented by making correct decisions following history taking, notes review and physical examination.

Abnormalities of the bone mineral metabolism are common in patients with chronic kidney disease and renal transplant patients.² The UK renal association guidelines suggest that serum levels of PTH should be monitored in patients with CKD stages 3b-5 (eGFR<45), and therapeutic decisions made based on PTH levels and the levels of serum phosphate and calcium.³ The current recommendation suggests that treatment is considered in patients with CKD stages 3b-5 and patients on dialysis aiming for PTH levels of 3–9 times the upper limit of the normal range.

In our patient, venous drainage from the distal aspect of her right forearm (parathyroid gland implant site) contained high levels of PTH ($\times 3$ – 3.5 more than the true systemic PTH levels). This misled the clinicians leading to inadvertent prescription of increasing doses of 1-alfacalcidol to treat her pseudo-drug refractory secondary hyperparathyroidism.

Surgical options for the treatment of parathyroidectomy in renal patients include total parathyroidectomy, subtotal parathyroidectomy and total parathyroidectomy with forearm implantation in distal aspect of brachioradialis muscle or in subcutaneous tissue of the forearm.⁴ We suggest that all patients who undergo parathyroidectomy should have a clear documentation of the

parathyroid implant site (if any) in order to prevent errors in the interpretation of PTH levels.

Learning points

- Patients who have had parathyroidectomy in the past can have recurrent hyperparathyroidism.
- Parathyroid gland implantation in the forearm will lead to spuriously high PTH readings if the blood sample is taken from an upstream vein in ante-cubital fossa. This should be borne in mind while interpreting PTH levels in these patients.
- Over-suppression of parathyroid hormone could lead to adynamic bone disease.

Competing interests None.

Patient consent Obtained.

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