Cinacalcet in hyperparathyroidism management after pediatric renal transplantation

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Abstract Secondary hyperparathyroidism is often associated with end stage renal disease; even after renal transplantation, hyperparathyroidism may persist, and is responsible for hypercalcemia, hypophosphatemia and elevated parathyroid hormone (iPTH) levels. Parathyroid hyperplasia is frequently associated with persistent hyperparathyroidism, and may require a surgical treatment. Here, we report hyperparathyroidism along with parathyroid hyperplasia in a 7-year-old child, which persisted after renal transplant. Calcitonin and pamidronate failed to decrease serum calcium levels; clodronate was also inefficient. Cinacalcet therapy normalized serum calcium and phosphorus levels, and decreased iPTH levels in 3 months; a severe parathyroid hyperplasia was also corrected under calcimimetic therapy. In conclusion, we report in a child that hypercalcemia associated with secondary hyperparathyroidism can be corrected with cinacalcet after pediatric renal transplantation. We also show that parathyroid hyperplasia can regress under calcimimetic therapy in a transplanted child, making surgery unnecessary.

Keywords Kidney · Transplantation · Cinacalcet · Hyperparathyroidism

Introduction

Secondary hyperparathyroidism is often associated with end stage renal disease [1–3]. Even after renal transplantation, hyperparathyroidism may not resolve completely [4]. Persistent hyperparathyroidism after renal transplantation is responsible for hypercalcemia and increased parathyroid hormone (iPTH) levels; it also participates in hypophosphatemia, along with elevated FGF-23 levels [5]. It has been suggested that hypercalcemia and hypophosphatemia could effectively be corrected with cinacalcet in adult patients with persistent hyperparathyroidism after renal transplantation. Here, we report in a child that hypercalcemia and hypophosphatemia can be corrected, and that elevated iPTH levels can be decreased with cinacalcet after pediatric renal transplantation. We also show that parathyroid hyperplasia can completely regress after pediatric renal transplantation under calcimimetic therapy.

Case report

The patient was 18 months old when he was diagnosed with bilateral nephroblastoma; he had no previous medical history. He was initially treated by actinomycin and vincristine. At the age of 22 months, a right nephrectomy was performed, confirming a stage I nephroblastoma; chemotherapy was continued. Renal function was stable (serum creatinine was 54 $\mu\text{mol/l}$, Schwartz estimated GFR about 60 ml/min/1.73 m^2); neither calcium carbonate nor vitamin D3 was provided. At the age of 46 months, a relapse required a left nephrectomy; hemodialysis was started concomitantly. At that time, patient's weight was 15.6 kg, and size was 102.5 cm. Total serum calcium levels were increased (3.06 mmol/l or

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Fig. 1 Ionized calcemia, phosphatemia and iPTH levels during follow-up in a pediatric renal transplantation recipient. HD hemodialysis, Tx renal transplantation, C cinacalcet therapy, Mx number of months after beginning of associated event

12.24 mg/dl, normal range 2.2–2.7 mmol/l), ionized serum calcium levels were also increased (1.34 mmol/l or 5.36 mg/dl, normal range 1.2–1.3 mmol/l), as shown in Fig. 1. iPTH levels were high (529 ng/l, normal range for patients with normal kidney function 20–65 ng/l), serum phosphorus levels were increased (2.2 mmol/l or 6.81 mg/dl, normal range 1.3–1.85 mmol/l). Patient received sevelamer chlorhydrate 1600 mg twice a day; neither calcium carbonate nor vitamin D3 was provided. Renal transplantation was performed when the patient was 7 years and 7 months old; at that time, patient's weight was 17.9 kg, size was 115 cm. After renal transplantation, ionized serum calcium levels were still increased (1.6 mmol/l, 6.4 mg/dl), iPTH levels were high (348 ng/l), serum phosphorus levels were low (1.24 mmol/l, 3.83 mg/dl). At that time, the patient received phosphate salts, 788 mg twice a day. A renal biopsy showed traces of calcium deposits. A cervical ultrasonography showed a 9 mm × 4 mm parathyroid adenoma; a slight vascularization was identified on Doppler. A sestamibi parathyroid scintigraphy was inconclusive. Calcitonin and pamidronate failed to decrease serum calcium levels; clodronate was also inefficient. Cinacalcet was introduced 4 months after renal transplantation; the initial dose was 15 mg/day, increased every 15 days up to 60 mg/day. At 7 months after renal transplantation, total serum calcium levels were normal (2.37 mmol/l, 9.48 mg/dl), ionized serum calcium levels were also normal (1.24 mmol/l, 4.96 mg/dl), serum phosphorus was normal (1.42 mmol/l, 4.39 mg/dl), and iPTH had decreased (294 ng/l). The patient then received phosphate salts, decreased to 394 mg twice a day; neither calcium carbonate nor vitamin D3 was provided. A second renal biopsy performed as a control showed no traces of calcium deposits. A cervical ultrasonography performed 9 months after renal transplantation showed no visible parathyroid hypertrophy; this was confirmed by another ultrasonography performed 6 months later. Bone mineral density was normal throughout follow-up; renal function also remained stable (creatinine levels around 65 μ mol/l, Schwartz estimated GFR about 56 ml/min/1.73 m²).

Discussion–conclusion

Secondary hyperparathyroidism management after renal transplantation is often complex [6, 7]. It has been recently shown that hypercalcemia and hypophosphatemia could effectively be corrected with cinacalcet in adult patients with persistent hyperparathyroidism after renal transplantation [8]; however, there was no evidence of such efficiency in the pediatric population. Here we show that, after renal transplantation in a child, hypercalcemia, hypophosphatemia and elevated iPTH levels could be managed with adequate cinacalcet therapy, started at approximately half the initial dose used in adults, and progressively increased under clinical and biological monitoring until biological efficiency was reached. Moreover, a voluminous parathyroid hyperplasia regressed under calcimimetic treatment, as it could not be identified using ultrasonography anymore. These results suggest that cinacalcet may be used in the pediatric population suffering from secondary hyperparathyroidism after renal transplantation, with an efficiency probably comparable to that observed in adults.

Compliance with ethical standards

Conflict of interest None.

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