Tertiary Hyperparathyroidism in Children on Chronic Dialysis: Role of Surgery

H. A. Saafan, M. A. Salam, I. A. Elshafey, H. A. Kader, A. Fayez Hamza
Pediatric Surgery Unit, Ain Shams University, Egypt

Background/Purpose: Tertiary hyperparathyroidism is common in patients with renal disease. These patients may require operation for this disease if it cannot be controlled by medical therapy. Due to lack of renal transplantation in most of our patients they continue to have renal failure, so the risk of recurrence and re-operation is high.

Materials & Methods: Seventeen patients with tertiary hyperparathyroidism underwent parathyroidectomy in the paediatric surgery unit, Ain-Shams University. Serum parathyroid hormone concentrations were measured using either radioimmunoassay or chemo-illuminometric assay. Patients had preoperative localization studies with U/S, C-T scanning and radionuclide scanning. These patients were followed up by serum calcium, phosphorus and Serum parathyroid hormone concentrations.

Results: Fifteen patients, 6 to 16 years, had end-stage renal disease and two patients had undergone parathyroidectomy post renal transplantation. All 17 patients had elevated parathyroid hormone (PTH) levels. Fifteen patients had hyperplasia; 2 patients had single adenoma. Two patients required re-operation for recurrent hyperparathyroidism 24 months after his initial parathyroidectomy.

Conclusion: Patients with end-stage renal disease are prone to abnormalities of calcium metabolism. They frequently develop parathyroid hyperplasia. Recurrence can occur following operation because of missed gland or continuing renal failure.

Index Word: tertiary hyperparathyroidism, renal diseases

INTRODUCTION

Chronic renal failure results in a decrease in the excretion of dietary phosphorus. The resulting hyperphosphatemia leads to decreased plasma calcium concentration. There is also impaired renal conversion of 25-hydroxycalciferol to 1, 25-dihydroxycalciferol (vitamin D3), which results in decreased intestinal absorption of calcium. The decreased calcium, in serum, signals the parathyroid gland to release parathyroid hormone (PTH). 1,2

Other metabolic alterations associated with chronic renal failure also lead to hyperparathyroidism. Metabolic acidosis causes increased serum PTH and vitamin D concentrations. 1,3 The better understanding of these metabolic alterations has led to improved prophylactic treatment to decrease the incidence of parathyroid disease in patients with chronic renal failure. These treatments include better control of serum phosphate by: 1- decreasing absorption of dietary phosphate by oral administration of phosphate binders; 2- controlling the calcium concentration of the dialysate to prevent loss of calcium during dialysis; and 3- prophylactic administration of vitamin D or its bioactive metabolite, 1, 25 dihydroxycalciferol.

Despite these attempts at prevention, parathyroid disease is common in patients with renal failure, and approximately 5% to 10% of patients with renal failure require parathyroidectomy. 4,5 The renal failure can be corrected by kidney transplantation, and the parathyroid disease may be relieved as a result. The
parathyroid disease may become autonomous, however, and some patients will require parathyroidectomy even after transplantation re-establishes normal renal function.

This retrospective study was carried out to review the results of parathyroidectomy for patients with chronic renal failure at Ain Shams university hospitals.

**PATIENTS AND METHODS**

We performed parathyroidectomy in 17 patients with tertiary hyperparathyroidism during a 6-years period between, 2000, and 2006. The original pathology was obstructive uropathy in 8, glomerulonephritis in 6, haemolytic uremic syndrome in 2 and Alport syndrome in one. Two of our patients received renal transplants; they had parathyroidectomy 1 and 1.5 years after transplantation.

The indications for parathyroidectomy were intractable symptoms consistent with hyperparathyroidism that could not be controlled by medical management. Bone pain was the most common symptom leading to the operation. Many symptoms such as fatigue, emotional changes, and personality changes were also resent (Fig. 1). These symptoms were associated with elevated PTH level and inability to control serum calcium and phosphate concentrations by medical management.

Fig 1a,b. Bone disease.

Fig 2a,b. Radionuclide scanning.
Serum parathyroid hormone concentrations were measured in several ways. Early in this series the c-terminal or n-terminal radioimmunoassay was used to measure PTH concentrations. Most tests, however, measured intact PTH concentrations using a chemiluminometric assay. All patients had preoperative localization studies with U/S, C-T scanning and technetium Tc 99m sestamibi scintigraphy. (Fig2).

Parathyroidectomy was performed through a low cervical collar incision. Platysma flaps were raised, and the strap muscles were separated in the midline but were not divided in 13 patients (Fig.3). In the other 4 cases we approached the parathyroid glands through the medial border of the sternomastoids (Fig.4). An attempt was made to identify the four parathyroid glands in all patients. The thyroid gland was completely mobilized when needed to help facilitate identification of the parathyroid glands. Biopsies of all removed parathyroid glands were examined by frozen section to confirm the presence of parathyroid tissue. We generally performed complete excision of three parathyroid glands (Fig.5). The gland that appeared to be most normal was generally selected to be left and marked by a silk suture. We did not perform any re-implantation of the parathyroid gland into the brachioradialis muscle.

Recurrent hyperparathyroidism was diagnosed by an elevated serum PTH concentration and inability to control serum calcium and phosphorus concentrations by standard medical therapy (vitamin D3, phosphate binders, and supplemental calcium).

The mean standard deviation is given as the measure of central tendency for all data. The Chi-square test was used for statistical comparison.

RESULTS
Of the 17 patients, 8 were boys and 9 were girls. Their age ranged from 6 to 16 years (mean 11.0)

Parathyroidectomy was performed on an average of 4.2 years after beginning dialysis. Two patients who had undergone renal transplantation; one had parathyroidectomy 24 months after renal transplantation (The creatinine was 1.6 ± 0.4 mg/dL); the other was operated upon after 12 months. Bone pain was the most common symptom. Other symptoms included fatigue, joint pains, weakness, and renal stones

All patients had elevated PTH levels. The mean intact PTH level was 644± 894 pg/mL. The mean serum calcium was 11.2 ± 1.1 mg/dL and the mean phosphate was 5.8 ± 2.7 mg/dL.

Four glands were identified at surgery in 15 patients, three glands in two. The first 15 patients had three glands removed with biopsy from the normal remaining gland (which was the upper right in 7 patients; the upper left in five patients and the lower left in the remaining three). One of the remaining two patients required re-operation 2 years later because their calcium level did not fall. The remaining gland was identified at the second operation and excised. The last patient had only 2 glands removed, and the third one proved to be fatty tissue at pathology and the patient had recurrence and also needed re-surgery. Only in one patient; we had performed excision of 2 parathyroid glands from a mediastinal position but through the same neck incision.

Fifteen patients had been proved by histopathology to have hyperplasia. The remaining two patients had single adenoma (both were affecting the lower right gland). Four patients had transient hypocalcaemia (<8.0 mg/dL). One patient died after 1.5 year as a result of his end stage renal condition.

DISCUSSION
The metabolic derangements associated with chronic renal failure can lead to secondary hyperparathyroidism. Frequently, secondary hyperparathyroidism can be controlled by diet and administration of phosphate binders, and calcium and vitamin D3 supplements. Even with this medical regimen some patients ultimately require parathyroidectomy for this condition.

The indication for parathyroidectomy in our patients was documented PTH hypersecretion and symptoms consistent with hyperparathyroidism that could not be controlled by medical management. Bone pain was the most common symptom leading to operation. Many symptoms such as fatigue, emotional changes, and personality changes that can also be associated with hyperparathyroidism were also found in many patients with a variety of chronic diseases (and frequently in individuals without any apparent disease).
The great majority of patients who require operation had hyperplasia, as did 15 of our 17 patients. Hyperplasia can be treated by total parathyroidectomy with re-implantation of parathyroid tissue into the muscle or subtotal parathyroidectomy 6-7-8-10-13-17. We generally prefer,
even in adenoma, to perform subtotal parathyroidectomy. This highlights the importance of frozen sections during the surgery to minimize the incidence of recurrence. Should recurrent hyperparathyroidism occur, we believe it is feasible and safe to remove the remaining parathyroid gland from the neck with minimal risk of injury to the recurrent laryngeal nerve. In either case, one attempts to leave an adequate amount of tissue so that the patient will be neither hyper parathyroid nor hypo parathyroid. Nevertheless, the remaining parathyroid tissue is subject to the same metabolic aberrations as before the operation. Furthermore, the parathyroid tissue left behind is not normal, having been already stimulated by the abnormal metabolic state associated with renal failure. It may not be surprising, therefore, if followed up long enough, this left parathyroid tissue can hypertrophy and again cause hyperparathyroidism.

If one excludes the 2 patients who had recurrent hyperparathyroidism, none of the 13 patients with end stage renal disease required re-operation for recurrent or persistent hyperparathyroidism. Other studies have reported recurrence rates of hyperparathyroidism between 0% and 80%, and 8% to 14% require re-operation. In many series, however, the follow-up period is short (less than 7 years) and incomplete. Because recurrent hyperparathyroidism may take a long time to develop, short follow-up periods may not give the true rate of recurrence.

Successful renal transplantation corrects the renal failure and the metabolic aberrations that lead to hyperparathyroidism. It is advisable to wait 6 to 12 months after renal transplantation before performing parathyroidectomy to see whether correction of the renal failure will alleviate the hyperparathyroidism.

**REFERENCES**


