Parathyroidectomy after renal transplantation: a retrospective analysis of long-term outcome

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Abstract

Background. Advanced hyperparathyroidism refractory to active vitamin D continues to be a problem and frequently forces the nephrologist to resort to parathyroidectomy. One particular aspect is persisting hyperparathyroidism after renal transplantation. Published information on this point is fragmentary.

Design. Retrospective analysis.

Patients. Between 1983 and 1995 a total of 456 patients with renal secondary hyperparathyroidism were subjected to parathyroidectomy (PTX) of whom 103 were transplanted or had at least a history of renal transplantation. The present analysis concerns 37 patients who had a functional renal graft at the time of PTX and were followed for up to 13 years. PTX was performed after an average of 36.7 months after renal transplantation.

Outcome. Thirteen patients experienced rejection and became dialysis-dependent. Twenty-four patients had stable function of the renal graft. Seven patients died during follow-up. Hypoparathyroidism post-PTX developed in 4/37 patients, but could be overcome by replantation of cryoconserved parathyroid tissue.

Frequency estimate. A total of 2632 renal transplants were performed in the catchment area. As a minimum estimate 3.91% of patients with a functional graft required PTX.

Recommendation. Parathyroidectomy should be considered early in cases with advanced secondary renal hyperparathyroidism, since renal transplantation does not necessarily guarantee reversibility of parathyroid overactivity.

Key words: hyperparathyroidism; parathyroidectomy; renal transplantation; hypercalcaemia

Introduction

Even after successful renal transplantation, secondary hyperparathyroidism with hypercalcaemia and related complications is observed in a substantial number of patients.

Elevated PTH concentrations usually normalize after some time, but in a certain proportion of patients hyperparathyroidism persists, illustrating that even in the presence of normal graft function parathyroid overactivity is not necessarily reversible in each case. Most authors advocate to wait for at least 1 year after successful renal transplantation before parathyroidectomy is considered [1–3]. There has been no consensus concerning the optimal operative procedure, i.e. total or subtotal parathyroidectomy [4,5]. Most studies on PTX in transplanted patients report only the time period until PTH and calcium concentrations have normalized. We draw attention to the fact that long-term graft failure occurs in a substantial number of patients who become dialysis-dependent or require retransplantation. In view of the potential irreversibility of parathyroid overactivity and because of the often limited duration of sufficient renal graft function, renal transplantation is not necessarily the ‘ideal treatment’ [6] which solves the problem.

In order to work out rational recommendations with respect to the timing of parathyroidectomy and the choice of the surgical approach, well documented and thorough information is necessary. In order to provide such information, a retrospective analysis was carried out using the large local patient cohort.

Subjects and results

Total number of parathyroidectomies

Between 1983 and 1995, a total of 456 patients with secondary renal hyperparathyroidism were subjected to parathyroidectomy in our hospital (Figure 1). The patients came primarily from the Munich region. A small proportion came from other parts of Bavaria or Germany.

Parathyroidectomy in transplanted patients

A history of renal transplantation was present in 103/456 patients, i.e. 22.6%. Only 37 patients had a
Fig. 1. Patients subjected to parathyroidectomy with secondary renal hyperparathyroidism (1983–1995).

renal graft with adequate function at the time of parathyroidectomy, while 66 patients had become dialysis-dependent again at the time of PTX. The former patients are the subject of the present analysis.

During the same time interval (1983–1995), 2632 renal grafts were transplanted in the Munich region (Klinikum München Großhadern, Klinikum München Rechts der Isar, Zentralklinikum Augsburg). Approximately 4% of all patients with renal transplantation thus required parathyroidectomy.

Retrospective analysis of outcome after parathyroidectomy in patients with a functioning renal grafts

Description of the patient cohort. The present analysis concerns the 37 patients who had a renal graft with adequate function at the time of PTH. The average age was 44.3 years (24–63 years, 19 men, 18 women). Table 1 shows the underlying renal disease. The average duration of dialysis prior to transplantation was 71.1 months (3–150 months). Parathyroidectomy was performed on average 36.7 months (2–192 months) after renal transplantation. Sixteen patients were subjected to parathyroidectomy during 12 months following renal transplantation and 21 patients thereafter.

Indications for and selection optimal mode of parathyroidectomy. The indications to perform parathyroidectomy was based on laboratory values (1,84 PTH, alkaline phosphatase, and S-calcium), clinical symptoms (pruritus, bone pain) and in some cases bone biopsy.

The operative procedure was selected intraoperatively depending on the degree of macroscopically recognizable parathyroid gland changes. All patients had enlarged parathyroids which proved to exhibit nodular hyperplasia by histology. In 31 cases (84%), total parathyroidectomy was performed with transplantation of autologous parathyroid tissue into the m. brachioradialis of the arm that had been used for the AV shunt. In the six other patients (16%), subtotal parathyroidectomy was performed: in four patients classical three-and-a-half resection with marking the remaining residue with a clip; in one patient only three, in another only two parathyroid glands were identified. Parathyroid tissue was cryopreserved in all patients.

Long-term parathyroid function. Hypoparathyroidism (persisting hypocalcaemia despite substitution and a very low 1,84 PTH serum level) was noted postoperatively in four patients (11%). Normocalcaemia could be restored by replantation of cryopreserved parathyroid tissue 4, 5, 15 and 31 months after parathyroidectomy. There was no case of persisting or relapsing hyperparathyroidism.

Long-term graft function and patient survival. Twenty-four patients had a persisting good function of the renal graft with a mean follow-up of 65.7 (12–112)
months. Three patients required calcium (1–3 g/day) and two patients low-dose active vitamin D. Thirteen patients (35%) experienced rejection of the renal graft after an average of 26.4 (1–76) months after parathyroidectomy. Four patients underwent retransplantation, but this was successful only in two cases. Currently, 11 of the 13 patients are again on haemodialysis after an average of 59.8 (4–91) months following the rejection crisis. All 13 patients are normocalcaemic.

During follow-up, seven of the 37 patients (19%) died after an average of 43.1 (4–84) months following parathyroidectomy. At the time of death, six patients had a functioning renal graft. One patient had a rejection crisis 1 month prior to his death, which occurred 7 years after parathyroidectomy. Five patients died from myocardial infarction; in two cases, death was caused by septicemia.

Discussion

According to EDTA 1988 statistics, 2–3/1000 cases annually require parathyroidectomy after successful renal transplantation. Table 2 shows the communications which report on parathyroidectomy after successful renal transplantation. The majority of papers combine dialysis-dependent patients and patients living with a functioning graft without separating these two groups. The studies that report the number of patients living with a functioning graft and requiring parathyroidectomy show that this is higher than reported by the EDTA, on average 5.7% (1.3–20%). In the present study we find a proportion of 3.9% which is an underestimate because the figure was related to all renal transplantations and not the smaller number of successful renal transplantations. Furthermore, we report only parathyroidectomies performed in our hospital, while the total number of patients transplanted relates to all patients in the region (some of whom might also have parathyroidectomy outside our hospital). It is of interest that the much quoted papers [2,10] which report on lower proportions are based only on observations in five and seven patients, respectively. Almost all publications limit follow-up observations to when patients had been transplanted again. In contrast, the present study examines all 37 patients with parathyroidectomy and functioning transplants for a mean follow-up time of 66.7 months.

The indications which led to operation were persisting hypercalcaemia (n = 26) and symptomatic osteopathy (n = 27). Both problems were present in 19 patients and, in addition, soft tissue calcification, vascular calcification, and spontaneous fractures were observed [1]. The only preoperative method for localization was ultrasonography of the parathyroids, since other imaging procedures, e.g. CAT scan, MRT, or Sestamibi-scan are uncertain, expensive, and not indispensable prior to the first operation. In the 44% of the patients operated during the first year after renal transplantation, severe hypercalcaemia was present, which did not disappear despite good function of the renal graft. In 56% of the patients, parathyroidectomy was required after more than 1 year following successful renal transplantation; in one case even 16 years after successful transplantation. This observation documents that in advanced cases parathyroid overactivity is not always reversible after renal transplantation. As a consequence, increased PTH secretion and abnormal morphology of the glands may persist. During the follow-up, seven patients died from vascular causes; in all cases, renal transplantation and parathyroidectomy had been performed without any complications. Almost a third of our patients had a rejection crisis following parathyroidectomy. For such patients with chronic renal failure the problem of hyperparathyroidism is obviously not resolved by renal transplantation, even if the latter is successful for a prolonged period of time. We raise this point because many authors feel that whether the patient has been successfully transplanted or is on maintenance haemodialysis influences the decision of the operative procedure, i.e. total vs. subtotal parathyroidectomy [19]. Because good long-term renal function is never assured it is wise to base the operative procedure on the size of the glands and

Table 2. Listing of communications on parathyroidectomy after successful renal transplantation

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. of patients</th>
<th>Method of operation</th>
<th>NTXs (n)</th>
<th>PTXs (%)</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geis [7]</td>
<td>1973</td>
<td>18</td>
<td>subtotal/9 total</td>
<td>90</td>
<td>20.0</td>
<td>12</td>
</tr>
<tr>
<td>Malmaeus [9]</td>
<td>1982</td>
<td>12</td>
<td>subtotal</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Diethelm [10]</td>
<td>1982</td>
<td>5</td>
<td>total</td>
<td>368</td>
<td>1.3</td>
<td>72</td>
</tr>
<tr>
<td>Garvin [2]</td>
<td>1985</td>
<td>7</td>
<td>6 subtotal/1 total</td>
<td>100</td>
<td>7.0</td>
<td>2–44</td>
</tr>
<tr>
<td>D’Alessandro [14]</td>
<td>1989</td>
<td>15</td>
<td>10 subtotal/3 total</td>
<td>819</td>
<td>1.8</td>
<td>48</td>
</tr>
<tr>
<td>Vlcek [15]</td>
<td>1991</td>
<td>32</td>
<td>subtotal</td>
<td>534</td>
<td>5.9</td>
<td>228</td>
</tr>
<tr>
<td>Botha [16]</td>
<td>1992</td>
<td>37</td>
<td>35 subtotal/2 total</td>
<td>1100</td>
<td>3.3</td>
<td>120</td>
</tr>
<tr>
<td>Neonakis [17]</td>
<td>1995</td>
<td>21</td>
<td>subtotal/total</td>
<td>716</td>
<td>4.5</td>
<td>120</td>
</tr>
<tr>
<td>Own</td>
<td>1995</td>
<td>37</td>
<td>6 subtotal/31 total</td>
<td>2632</td>
<td>1.4</td>
<td>156</td>
</tr>
</tbody>
</table>
the degree of nodular transformation. If we perform total parathyroidectomy, transplantation of the parathyroid tissue into the shunt arm has always been successful and without complications [20].

Parathyroidectomy causes substantial amelioration of symptoms and signs. On the other hand, renal transplantation does not guarantee reversal of parathyroid overactivity. As a consequence, we advocate early parathyroidectomy in the patient for whom renal transplantation is considered or who has been transplanted, if this operative procedure is indicated.

References


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