SHORT MEDICAL REPORTS

Parathyroid hormone as a causative factor of primary non-function in renal transplants

Primary non-function of renal allografts, which continues to be a common early problem in transplantation, can be diagnosed when rejection and vascular problems have been excluded and biopsy findings are compatible with acute tubular necrosis. Early studies have defined factors affecting the donor kidney which are associated with primary non-function, and these include prolonged warm and cold ischaemia times.1 We sought to examine whether any non-immunological recipient factors play a part in primary non-function. There is substantial evidence that increased influx of calcium into the cell plays a role in cellular toxicity.1 Recent studies have suggested that parathyroid hormone causes increased levels of cytosolic calcium.2 The aim of this study was to review the immunoassayable parathyroid hormone (C terminal) concentrations immediately before transplantation in patients receiving a cadaveric renal transplant and their relation to the incidence of primary non-function.

Methods and results

We performed a retrospective analysis of 52 patients who underwent cadaveric renal transplantation during 1983-5 at this centre. The group included 27 men and 25 women aged 10 to 62 years. Twenty seven patients were undergoing haemodialysis and 25 chronic ambulatory peritoneal dialysis before transplantation. Forty five patients received their first transplant and seven their second or third transplant. Immunosuppression comprised prednisolone, 0-3-3 mg/kg body weight, and cyclosporin in doses tailored to maintain plasma trough concentrations at 50-150 μg/ml as measured by high pressure liquid chromatography. Blood was taken immediately before transplantation for measuring total calcium, phosphate, and C terminal immunoassayable parathyroid hormone concentrations.

The patients were divided into two groups according to whether their renal graft functioned immediately after transplantation or not. Primary non-function was diagnosed in those patients who required renal replacement treatment immediately after transplantation in the absence of rejection or a vascular cause.

<table>
<thead>
<tr>
<th>Mean (SEM) plasma calcium, phosphate, and immunoassayable parathyroid hormone concentrations before transplantation in renal allografts showing primary function and primary non-function</th>
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<tbody>
<tr>
<td><strong>Plasma calcium</strong> (mmol/l)</td>
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<tr>
<td>Primary function</td>
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<tr>
<td>Primary non-function</td>
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<td><em>p</em> Value</td>
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<td><em>Unpaired t test</em></td>
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<td>i-PTH <em>=</em> immunoassayable parathyroid hormone.</td>
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</table>

Twenty four patients within this period had primary non-function as defined. There were no differences in cyclosporin concentrations or HLA matching between these groups. The table shows that the primary non-function group had significantly higher parathyroid hormone concentrations, although the cold ischaemia time and total plasma calcium and phosphate values were not significantly different.

Comment

Parathyroid hormone has been postulated as a potential uraemic toxin, and recent studies have shown that it can cause an increase in proximal cell membrane calcium permeability,3 possibly through a similar mechanism to the calcium channels activated by parathyroid hormone that are found in an osteosarcoma cell line.4 These data would be compatible with the hypothesis that parathyroid hormone may have a nephrotoxic effect on the renal transplant. Parathyroid hormone concentration thus represents the first non-immunological recipient factor shown to affect primary non-function in the graft.5


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Use of acyclovir to treat chickenpox in pregnancy

Varicella, usually a fairly benign disease, may be severe and fatal—for example, in the immunosuppressed and in pregnancy.5 The only death from chickenpox in an adult admitted to this regional infectious diseases unit between 1984 and 1987 occurred in a pregnant woman. We describe this case together with three other cases of chickenpox in pregnancy in otherwise healthy women, all of whom were treated with intravenous acyclovir. A recent report suggests an association between smoking and varicella pneumonia.6 All four of our patients were smokers; three had pneumonia.

Case reports

Case 1—A 33 year old woman, 26 weeks pregnant, presented on the fourth day of illness with dyspnoea. She was feverish with a mild typical varicella rash. Despite minimal chest signs radiography showed widespread pneumonitis. Treatment with acyclovir (5 mg/kg eight hourly) stopped the development of skin lesions, but increasing hypoxia necessitated ventilation. The baby, delivered by caesarean section, died shortly after birth. Despite slow improvement in respiratory function the mother died a month later after an emergency laparotomy for intestinal obstruction. No necropy was permitted.

Case 2—A 22 year old woman, 25 weeks pregnant, presented with cough and dyspnoea at rest one day after the appearance of a chickenpox rash. She had minimal chest signs, hypoxia, and bilateral pneumonitis as shown by radiography. She received treatment with acyclovir (10 mg/kg eight hourly). The following day, despite oxygen treatment, she was more hypoxic and the dosage of acyclovir was increased to 18 mg/kg eight hourly with a good response. This was maintained for six days without apparent side effects. Despite transient premature labour pregnancy continued, and a normal baby was delivered at term.

Case 3—A 27 year old woman, 28 weeks pregnant, presented with a 24 hour history of dyspnoea on exertion six days after the onset of chickenpox. She had a widespread rash, with new vesicles still developing, and radiography showed extensive pulmonary damage. She was very hypoxic. Five days of treatment with acyclovir (15 mg/kg eight hourly) produced rapid improvement. Pregnancy proceeded, with term delivery of a normal baby.

Case 4—A 20 year old woman presented at 38 weeks’ gestation with the early stages of a varicella rash. There were no respiratory symptoms, and chest radiographs were normal. After five days of treatment with acyclovir (10 mg/kg eight hourly) her rash resolved rapidly. A healthy infant with no evidence of infection was delivered by caesarean section (breech presentation) eight days later.

Comment

In our patients there was little correlation between the severity of rash and life threatening disease. The consistent pointer to pneumonitis was tachypnoea. Varicella zoster immunoglobulin is about 50% effective in preventing chickenpox in susceptible contacts (trials have been carried out in the non-pregnant) or in modifying its course.7 It had not been given in the patients described despite all having histories of domestic contact.