Lack of correction of secondary hyperparathyroidism long term after kidney transplantation despite good graft function

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seen in young adults, males and Afro-American individuals. We recommend frequent monitoring of urine protein excretion and renal function for early detection of renal injury.

Conflict of interest statement. None declared.

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Table 1. Patients' characteristics according to pre-transplantation iPTH levels

<table>
<thead>
<tr>
<th>Variable</th>
<th>≥65 pg/mL (N = 95)</th>
<th>&lt;65 pg/mL (N = 55)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.8 ± 14.3</td>
<td>45.0 ± 15.5</td>
<td>0.08</td>
</tr>
<tr>
<td>Male gender, N (%)</td>
<td>54 (57)</td>
<td>20 (36)</td>
<td>0.02</td>
</tr>
<tr>
<td>African American, N (%)</td>
<td>45 (48)</td>
<td>20 (36)</td>
<td>0.19</td>
</tr>
<tr>
<td>Caucasian, N (%)</td>
<td>38 (40)</td>
<td>31 (56)</td>
<td></td>
</tr>
<tr>
<td>Other, N (%)</td>
<td>11 (12)</td>
<td>4 (8)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, N (%)</td>
<td>22 (24)</td>
<td>13 (26)</td>
<td>0.81</td>
</tr>
<tr>
<td>Hypertension, N (%)</td>
<td>66 (71)</td>
<td>42 (82)</td>
<td>0.13</td>
</tr>
<tr>
<td>Donor type, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cadaveric donor</td>
<td>70 (74)</td>
<td>36 (65)</td>
<td>0.29</td>
</tr>
<tr>
<td>Living donor</td>
<td>25 (26)</td>
<td>19 (34)</td>
<td></td>
</tr>
<tr>
<td>Time from transplant (months)</td>
<td>41.7 ± 40.5</td>
<td>49.5 ± 30.8</td>
<td>0.27</td>
</tr>
<tr>
<td>Time on dialysis (years)</td>
<td>4.6 ± 11.7</td>
<td>2.8 ± 2.9</td>
<td>0.41</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>74%</td>
<td>47%</td>
<td>0.001</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>21%</td>
<td>29%</td>
<td>0.49</td>
</tr>
<tr>
<td>Pre-emptive transplant</td>
<td>5%</td>
<td>24%</td>
<td>0.002</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>1.93 ± 1.68</td>
<td>1.51 ± 1.17</td>
<td>0.14</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>52.8 ± 22.4</td>
<td>56.6 ± 20.8</td>
<td>0.36</td>
</tr>
<tr>
<td>Most recent corrected serum calcium (mmol/L)</td>
<td>2.3 ± 0.3</td>
<td>2.3 ± 0.2</td>
<td>0.24</td>
</tr>
<tr>
<td>Pre-transplant corrected serum calcium (mmol/L)</td>
<td>2.3 ± 0.4</td>
<td>2.2 ± 0.3</td>
<td>0.68</td>
</tr>
<tr>
<td>Most recent serum phosphorus (mmol/L)</td>
<td>1.06 ± 0.42</td>
<td>1.16 ± 0.29</td>
<td>0.14</td>
</tr>
<tr>
<td>Pre-transplant serum phosphorus (mmol/L)</td>
<td>1.74 ± 0.58</td>
<td>1.77 ± 0.61</td>
<td>0.90</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>3.6 ± 0.5</td>
<td>3.5 ± 0.6</td>
<td>0.33</td>
</tr>
<tr>
<td>Pre-transplant iPTH pg/mL</td>
<td>191 ± 203 (range 65–1613)</td>
<td>42 ± 11 (range 3–62)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Follow-up iPTH pg/mL</td>
<td>239 ± 249 (range 28–1493)</td>
<td>107 ± 134 (range 13–739)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Change in iPTH category</td>
<td>17 (18%)</td>
<td>12 (24%)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Numbers are expressed as absolute values, percentages, mean ± SD and range where indicated.

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Lack of correction of secondary hyperparathyroidism long term after kidney transplantation despite good graft function

Sir,

Secondary hyperparathyroidism (SHPT) and its associated bone and vascular complications are highly prevalent in patients undergoing renal replacement therapy. Whether successful kidney transplantation corrects SHPT in the majority of patients with a functioning graft is unclear. In the context of an ongoing, randomized study on the effects of vitamin D therapy in post-transplant patients, we reviewed the clinical data of 150 consecutive kidney or kidney–pancreas transplant recipients with a functioning graft a minimum of 1 year after transplantation at our institution. Table 1 presents patients’ characteristics displayed according to a pre-transplantation iPTH level < or ≥65 pg/mL (upper limit of normal). As shown, despite a similar and acceptable post-transplant eGFR and optimal serum levels of calcium and phosphate, only 17% of the patients in the higher iPTH category regressed to normal, while 24% of the patients with low iPTH before transplantation moved to the higher category over time. In a multivariable model that included nine variables [age, gender, diabetes mellitus, iPTH< or ≥65 pg/mL at time of transplantation, most recent serum calcium (albumin corrected), most recent serum phosphorus, most recent creatinine, most recent eGFR and haemodialysis], we identified male gender [beta coefficient 2.67 (1.12–6.38); P < 0.03], pre-transplant haemodialysis
[beta coefficient 2.25 (0.95–5.30); P = 0.06] and iPTH ≥65 pg/mL prior to transplantation [beta coefficient 11.48 (4.79–27.53); P < 0.001] as independent variables predicting iPTH ≥65 pg/mL at follow-up (model \( X^2 = 46.56; P < 0.001 \)). The limited available literature suggests that the risk of persistent SHPT post-transplantation is associated with high serum levels of calcium and phosphorus prior to transplantation and sub-optimal graft function post-transplantation [1]. However, when we repeated our multivariable analyses including pre-transplantation serum calcium and phosphorus, the results did not change. Some investigators suggested that 25% [2] to 50% [3] of transplant recipients demonstrate elevated iPTH long term, although our data would suggest a much higher incidence. Potential explanations include adenomatous transformation of parathyroid nodules that may be only partially reversible, reduced intestinal absorption of calcium induced by steroid therapy and persistent relative vitamin D deficiency. Despite the known dissociation between iPTH levels and bone histology, early intervention to reduce the incidence of SHPT in post-transplantation with vitamin D receptor activators or calcimimetics may be very important to reduce the incidence of osteoporotic fractures and vasculopathy in these patients [4].

Conflict of interest statement. Dr. E. Rojas is supported by a training grant from Genzyme Therapeutics; Dr. Paolo Raggi has received research grants from and he is part of a Medical Advisory Board for Genzyme Therapeutics.

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Confirming high prevalence of human herpesvirus 8 infection in chronic kidney disease patients in São Paulo, Brazil

Sir,

Human herpesvirus 8 (HHV-8) is frequently associated with Kaposi’s sarcoma. It can be transmitted through organ transplantation or reactivated by immunosuppressive therapy. Chronic kidney disease (CKD) patients are at risk of this infection [1]. The present study aimed to determine the seroprevalence of HHV-8 in CKD patients in São Paulo, Brazil. The study was approved by the research ethics committees at participating institutions.

Blood samples collected from 805 CKD patients attended Hospital do Rim e Hipertensão and/or Santa Casa de Misericórdia de São Paulo (São Paulo, Brazil) were tested for latent and lytic HHV-8-specific antibodies using indirect immunofluorescence assays at Instituto Adolfo Lutz in São Paulo, Brazil, as previously described [2]. The chi-square test and/or Fisher’s exact test were performed for comparing categorical variables and HHV-8 serum status, using SPSS for Windows. Of the 805 CKD patients, 61.4% were males, 61.5% white, 35.5% black/pardum and 3.0% yellow. The mean age was 58 years (18–91). Two hundred ninety-five patients were on haemodialysis (HD), 54 on peritoneal dialysis (PD) and 456 not yet on renal replacement therapy (RRT).

One hundred forty-five (18.0%) CKD patients were found HHV-8-seropositive, of whom 56 (18.9%) were on HD, 8 (14.8%) on PD and the remaining 81 (17.7%) were not on any RRT. Examination of these different groups revealed no statistical significant differences (\( P = 0.963 \)). Further statistical analyses were conducted without this sub-grouping by RRT received. Table 1 discloses the comparison between HHV-8-seronegative and HHV-8-seropositive groups. Patients HHV-8-seropositive had a higher prevalence of previous transplant as well as higher prior exposure to sexually transmitted diseases. Of note, 57.0% of CKD patients who had syphilis also had HHV-8-seropositivity (\( P = 0.021 \)). Other variables showed lack of association with HHV-8 serological results.

High HHV-8 seroprevalence was observed in CKD patients in São Paulo, Brazil [3]. Interestingly, in the present study, similar proportions of HHV-8-seropositivity were observed in pre-dialysis and dialysis patients suggesting that dialysis proceedings were not related to HHV-8 transmission/acquisition. Another result was the strong association between HHV-8-seropositivity and previous transplant presenting another route of viral transmission as previously reported [4]. The association between HHV-8-seropositivity and syphilis could suggest that the syphilis lesions facilitate the entrance of the virus during sexual intercourse.

Finally, several studies conducted worldwide have attempted to find the best immunosuppressive therapy for use with HHV-8-seropositive transplant recipients [5]. It is not yet defined, but it is certain that these patients need an appropriated attendance to avoid iatrogenic KS and organ rejection, giving them perhaps a better quality of life after transplant. Therefore, due to the high HHV-8 seroprevalence found in the present study and the seriousness of the HHV-8-associated diseases, the authors suggest that screening for HHV-8 must be performed in CKD patients, even those in pre-dialysis.

Acknowledgements. This work was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Brazil, fellowship to ACA (PD #304372/2006-4) and to MCM. We thank Drs Pedro Jabur, Ivony Sens and José Ferraz Souza from Santa Casa de Misericórdia de São Paulo for data collection, and Drs Silvia R S Moreira and Silvia Manfredi from UNIFESP for samples collection.


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