Meningococcal vaccination and chronic kidney disease

Sir,

We read with great interest the editorial review about vaccination and chronic kidney disease by Janus et al [1]. Although this article is focused on end-stage renal disease patients, we think that it is possible to mention the meningococcal vaccine. This immunization is usually recommended for people exposed to a case of severe meningococcal infection, or for people travelling in endemic zones (sub-Saharan meningitis belt) in close contact with the local population. In some countries, this vaccine is incorporated in national vaccination programmes [2].

A few years ago, a risk of relapse of nephrotic syndrome was signalled, after meningococcal C conjugate vaccine [3]. However, that has been invalidated by a more recent study where no link was found between vaccination and a risk of relapse [4].

Thus the use of this vaccine, when necessary, can be recommended. However, there is a lack of data upon the degree of the immune response to this kind of vaccine in immunosuppressed patients. For asplenic individuals, for example, a double dose of vaccine has been proposed [5].

Conflict of interest statement. None declared.

Editorial Note: Dr Janus et al. had no further comments on this letter.

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Letter and Reply

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Regression of parathyroid gland swelling by treatment with cinacalcet

Sir,

Calcimimetic compounds, such as cinacalcet, reduce parathyroid hormone (PTH) secretion in patients with secondary hyperparathyroidism, as Fukagawa et al. demonstrated in the recent NDT article [1]. However, whether calcimimetic compound can reduce the size of an already-swollen parathyroid gland (PTG) is unclear. Here we report our observations of changes in the PTG size in a single case of secondary hyperparathyroidism treated with cinacalcet.

The patient was a 59-year-old woman who had been receiving haemodialysis since December 2003 for nondiabetic end-stage renal failure. In December 2006, elevated levels of serum intact PTH and alkaline phosphatase (ALP) were found (Table 1). Ultrasound examination revealed swelling of the right upper, right lower and left upper lobes of the PTG. Intravenous administration of the vitamin D analogue maxacalcitol (Oxarol®, Chugai Pharmaceutical Co., Ltd, Tokyo, Japan) reduced the levels of both intact PTH and ALP; however, the PTG (especially the left upper lobe) gradually enlarged, and the product of the serum levels of calcium and inorganic phosphorus (Ca × Pi) reached 100 mg²/dL².

In February 2008, cinacalcet tablets (Regpara®, Kirin Pharma Co., Ltd, Tokyo, Japan) were prescribed. A low dose of cinacalcet (25 mg/day; February through April 2008) shrank the right upper and lower lobes of the PTG but did not affect the size of the left upper lobe. The dose of cinacalcet was increased in March 2008 (50 mg/day), and, as a result, the size of all PTG lobes decreased (Table 1). The present observation suggests that (1) cinacalcet can reduce the size of PTG, and that (2) the sensitivity of the lobes of the PTG to cinacalcet can differ within a single patient. Regarding the first point, Mizobuchi et al. have reported that a high concentration of calcimimetic agent induces apoptosis in cultured hyperplastic parathyroid cells [2]. Regarding the second point, Kawata et al. have reported that the suppressive effect of cinacalcet on PTH secretion correlates negatively with the degree of calcium-sensing receptor expression in a rat model [3].

To our knowledge, this is the first report showing that cinacalcet can reduce the size of the PTG in a clinical setting. Considering the case report by Lazar and Stankus that cinacalcet can induce hungry-bone syndrome, as does parathyroidectomy [4], treatment with cinacalcet might be a curative treatment for secondary hyperparathyroidism, as is parathyroidectomy.

Conflict of interest statement. None declared.
Table 1. Clinical data including the size of parathyroid glands

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>December</td>
<td>September</td>
<td>April</td>
<td>August</td>
</tr>
<tr>
<td>Parathyroid glands</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right upper</td>
<td>331.7</td>
<td>331.1</td>
<td>437.7</td>
<td>443.3</td>
</tr>
<tr>
<td>Right lower</td>
<td>71.3</td>
<td>64.2</td>
<td>65.8</td>
<td>67.6</td>
</tr>
<tr>
<td>Left upper</td>
<td>9.8</td>
<td>25.4</td>
<td>79.1</td>
<td>168.5</td>
</tr>
<tr>
<td>Total</td>
<td>412.8</td>
<td>420.7</td>
<td>582.6</td>
<td>679.4</td>
</tr>
<tr>
<td>Intact PTH pg/mL</td>
<td>580</td>
<td>120</td>
<td>165</td>
<td>159</td>
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<tr>
<td>Intact osteocalcin</td>
<td>109.9</td>
<td>30</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>ALP IU/L</td>
<td>1068</td>
<td>153</td>
<td>168</td>
<td>163</td>
</tr>
<tr>
<td>Bone-type ALP IU/L</td>
<td>189</td>
<td>18.9</td>
<td>20.1</td>
<td>19.5</td>
</tr>
<tr>
<td>Ca mg/dL</td>
<td>9.4</td>
<td>10</td>
<td>10</td>
<td>10.1</td>
</tr>
<tr>
<td>Pi mg/dL</td>
<td>4.6</td>
<td>6.5</td>
<td>6.6</td>
<td>6.8</td>
</tr>
<tr>
<td>Ca × Pi mg2/dL2</td>
<td>43.24</td>
<td>65</td>
<td>66</td>
<td>68.68</td>
</tr>
<tr>
<td>PCR g/kg BW/day</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.3</td>
</tr>
</tbody>
</table>

PTH, parathyroid hormone; ALP, alkaline phosphatase; Ca, calcium; Pi, inorganic phosphorus; Ca × Pi, the product of Ca and Pi; PCR, protein catabolic ratio.

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Reply

Sir,

We would like to thank Dr Terawaki et al. for their interest in our article [1] and for the opportunity to comment on their case report [2]. As brought up by them, the effect of calcimimetics on the size of parathyroid hyperplasia has been an issue of concern, but still remains controversial [3]. In patients with chronic kidney disease, several factors, such as phosphate retention, hypocalcaemia and calcitriol deficiency, stimulate PTH secretion, and then induce hypertrophy and proliferation of parathyroid cells [4]. Theoretically, if such PTH secretion is pharmacologically suppressed for a long term, regression of gland mass could be induced, as previously shown in a study of calcitriol pulse therapy [5]. Such regression of parathyroid hyperplasia usually occurs in small glands with diffuse hyperplasia [6], while regression of nodular hyperplasia can be induced only by direct vitamin D injection therapy [7].

So far, several in vivo studies have shown that calcimimetics inhibit the development and progression of parathyroid hyperplasia [8,9], and also upregulate the expression of calcium-sensing receptor and vitamin D receptor (VDR) that were shown to be reduced in the setting of uraemia [10,11]. However, it is technically difficult to confirm the actual regression of parathyroid hyperplasia in rodent studies, and data on the effect of calcimimetics on the size of parathyroid hyperplasia are limited [12]. An in vitro study has shown that extremely high concentrations of calcimimetics induce apoptosis of parathyroid cells [13], but this study does not reproduce the actual setting of dialysis patients treated with calcimimetics.

In this regard, the case presented by Dr Terawaki et al. is of great interest. They indicated the possibility that calcimimetics may have a potential to regress the established parathyroid hyperplasia. Indeed, we also experienced a few similar cases in whom the size of parathyroid glands was reduced during cinacalcet treatment. In addition, we further experienced a case of severe hyperparathyroidism associated with a markedly enlarged parathyroid gland, which became hypovascularized during cinacalcet treatment (unpublished data); it is possible that such a hypovascularized gland may become smaller after longer cinacalcet treatment.

However, it is still unclear whether such regression of parathyroid hyperplasia can be induced universally in dialysis patients treated with cinacalcet. Furthermore, we