Pancoratic atrophy and low birth weight are also features of
HNF-1β mutations. Most importantly, patients with an
HNF-1β mutation may also be at risk of developing renal cell
carcinomas, since recent evidence suggests that HNF-1β is a
tumour suppressor gene [5].

In conclusion, patients with unexplained nephropathy
and/or renal cysts should be routinely screened for an
HNF-1β mutation in order to differentiate the RCAD
syndrome from diabetic nephropathy. Ultimately, these
patients are good candidates for combined kidney and
pancreas transplantation.

Conflict of interest statement. None declared.

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Marked hypercalcaemia in sepsis-induced multiple
organ failure

Sir,

A 58-year-old man was referred to our intensive care unit,
because of retropharyngeal abscess and Staphylococcus
aureus bacteraemia. On admission, he showed tachypnoea,
wheezing and oliguria. Laboratory examination revealed
hypoxia, cardiac failure, lung congestion, renal dysfunction
and marked inflammatory signs (Table 1). He was diagnosed
as having multiple organ failure due to sepsis, was intubated
on a ventilator, and started on treatment with inotropes and
antibiotics. This intensive treatment improved his clinical
condition and laboratory abnormalities; however, on day 10,
he showed marked hypertension (200/100 mmHg) and a new
rise of serum creatinine level. An intravenous infusion of a
calcium antagonist was thus initiated. On day 16, renal
function was improved, but marked hypercalcaemia was
noticed (Table 1). The patient was treated with a single dose
of intravenous pamidronate at 45 mg. Laboratory findings
included normocalciuria, a low level of intact-parathyroid
hormone (iPTH) and 1,25-dihydroxyvitamin D, an
undetected iPTH-related protein level and normal
thyroid and adrenal gland function. Six days after the dose
of pamidronate, the plasma ionized calcium levels were
reduced to normal ranges (1.27 mmol/l), and hypertension
was improved. On day 27, his clinical condition was
markedly improved, and he was transferred to the
general ward; after rehabilitation, the patient was discharged
on day 60.

We have described here, a patient with sepsis-induced
multiple organ failure who developed marked hypercalcae-
ia. The patient showed depressed PTH and vitamin D
levels, and his hypercalcaemia was effectively treated with
pamidronate. Critically ill patients have been reported to
have a high prevalence of bone hyper-resorption [1,2],
progressing to marked hypercalcaemia in some patients [2].
Urinary bone resorption markers (amino terminal
cross-linked telopeptide of type I collagen and deoxypyr-
idinoline) were increased in our case. These bone abnorm-
alities are thought to be caused by immobilization bone
hyper-resorption in a PTH-independent manner [1] and
biochemically responding to treatment with pamidronate [1,2].

In the present case, extremely high serum C-reactive protein
levels were observed on admission, indicating that levels
of circulatory pro-inflammatory cytokines were probably
markedly increased. Since these cytokines, particularly
interleukin-6, are known to enhance bone resorption via
increasing osteoclast activity and inhibiting osteoblast activity,
it is hypothesized that these inflammatory reactions may
have caused the alteration of calcium metabolism in this
patient.

Moreover, PTH levels were not completely suppressed
in spite of marked hypercalcaemia, and maximal tubular
reabsorption of phosphorous per glomerular filtration rate
(TmP/GFR) was decreased, suggesting that our patient
might have been in a mild hyperparathyroid state. During
acute oliguric renal failure, low ionized calcium levels,
1.09 mmol/l, could, in our case, stimulate PTH secretion;
this parathyroid hyperactivity might persist even after
recovery of renal function. Jeffries et al. [3] have described
this type of hyperparathyroid state after recovery

Fig. 1. Magnetic resonance imaging of glomerulocystic kidneys.
from multiple organ failure as a life-threatening tertiary hyperparathyroidism.

We speculate that several factors, i.e. immobilization, the sepsis-induced marked inflammatory reactions and the parathyroid hyperactivity, might have contributed to the development of hypercalcaemia in our case. Unrecognized hypercalcaemia in critically ill patients is thought to be very dangerous, as it can cause cardiovascular dysfunction [3]. Indeed, also in our case, renal dysfunction and marked hypertension occurred during developing hypercalcaemia. Our study suggests that nephrologists should be alert for this type of hypercalcaemia during the course of multiple organ failure with sepsis.

Conflict of interest statement. None declared.

Table 1. Changes in the laboratory data in the present case

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 6</th>
<th>Day 10</th>
<th>Day 16</th>
<th>Day 27</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein (g/dl)</td>
<td>5.5</td>
<td>5.4</td>
<td>5.9</td>
<td>6.2</td>
<td>6.4</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.2</td>
<td>2.4</td>
<td>2.5</td>
<td>2.8</td>
<td>3.4</td>
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<tr>
<td>Sodium (mEq/l)</td>
<td>136</td>
<td>140</td>
<td>140</td>
<td>143</td>
<td>140</td>
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<tr>
<td>Chloride (mEq/l)</td>
<td>98</td>
<td>107</td>
<td>105</td>
<td>108</td>
<td>106</td>
</tr>
<tr>
<td>Potassium (mEq/l)</td>
<td>3.9</td>
<td>4.5</td>
<td>4.1</td>
<td>4.5</td>
<td>4.2</td>
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<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>65</td>
<td>26</td>
<td>43</td>
<td>32</td>
<td>25</td>
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<tr>
<td>Creatinine (mg/dl)</td>
<td>3.27</td>
<td>1.21</td>
<td>2.67</td>
<td>1.1</td>
<td>0.81</td>
</tr>
<tr>
<td>Total calcium (mg/dl)</td>
<td>8.5</td>
<td>9.6</td>
<td>9.8</td>
<td>12.1</td>
<td>9.2</td>
</tr>
<tr>
<td>Ionized calcium (mmol/l)</td>
<td>1.09</td>
<td>1.36</td>
<td>ND</td>
<td>1.71</td>
<td>ND</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>3.3</td>
<td>3.8</td>
<td>4.8</td>
<td>4.2</td>
<td>4.5</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>2.1</td>
<td>ND</td>
<td>ND</td>
<td>1.7</td>
<td>1.7</td>
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<tr>
<td>C-reactive protein (mg/dl)</td>
<td>52.88</td>
<td>15.3</td>
<td>19.2</td>
<td>12.91</td>
<td>3.4</td>
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<td>Urine volume (ml/day)</td>
<td>470</td>
<td>1702</td>
<td>1200</td>
<td>2100</td>
<td>2500</td>
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<tr>
<td>Creatinine clearance (ml/min)</td>
<td>ND</td>
<td>95.7</td>
<td>29.4</td>
<td>77.1</td>
<td>121.6</td>
</tr>
<tr>
<td>Fractional excretion of calcium (%)e</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>2.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Tubular reabsorption of phosphorus</td>
<td>ND</td>
<td>ND</td>
<td>0.83</td>
<td>0.7</td>
<td>0.8</td>
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<tr>
<td>TmP/GFR (mg/dl)f</td>
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<td>ND</td>
<td>1.2</td>
<td>1.8</td>
<td>2.6</td>
</tr>
<tr>
<td>iPTH (pg/ml)g</td>
<td>ND</td>
<td>ND</td>
<td>21</td>
<td>40</td>
<td></td>
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<tr>
<td>1,25-dihydroxyvitamin D (pg/ml)h</td>
<td>ND</td>
<td>ND</td>
<td>11.1</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

*Reference range, 8.6–10.32 mg/dl; breference range, 1.13–1.28 mmol/l; crefference range, 2.4%; dreference range, 2.5–4.5 mg/dl; ereference range, 10–65 pg/ml; freference range, 10–55 ng/ml; ND, not determined.

Advance Access publication 30 November 2006

Anti-carbonic anhydrase II antibody in autoimmune pancreatitis and tubulointerstitial nephritis

Sir,

Autoimmune pancreatitis (AIP) has been characterized by diffuse enlargement of the pancreas, irregular narrowing of the pancreatic duct, high levels of serum IgG4, and lymphoplasmacytic infiltration in the pancreatic parenchyma [1]. Accumulating evidence suggests that this autoimmune disease could present with diffuse infiltration of IgG4-positive plasmacytes in multiple organs, resulting in sclerosing cholangitis, sialadenitis and retroperitoneal fibrosis [1]. In 2004, tubulointerstitial nephritis (TIN) associated with AIP was independently reported by two groups [2,3]. Renal biopsy revealed tubulointerstitial inflammatory infiltrates with IgG4-positive plasma cells. However, it remains unknown to which antigenic peptides in the kidney these antibodies bind.

A 66-year-old male was referred to our department because of a rise in serum creatinine concentrations from 0.83 to 1.75 mg/dl during the previous 6 months. The diagnosis of AIP had been made a year previously by high serum IgG4 level of 670 mg/dl, and by the findings of imaging studies such as computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic retrograde cholangiopancreatography (ERCP). On admission, his laboratory data showed serum IgG4 of 1830 mg/dl. Renal biopsy demonstrated TIN with plasma-cell infiltration, although the glomeruli appeared almost normal (Figure 1A). Immunohistochemistry revealed that IgG4 was positive in the infiltrating plasma cells and also in the distal tubular cells (Figure 1B). After 8 weeks of treatment with oral prednisolone, his serum creatinine and IgG4 levels decreased to 0.87 mg/dl and 694 mg/dl, respectively.

This case showed clinical findings characteristic of AIP-associated TIN, such as plasma-cell infiltration in the interstitium, high serum level of IgG4, and a favourable response to steroid therapy. Moreover, renal biopsy demonstrated IgG4...