corticotherapy she was switched to pulse i.v. dexamethasone. Four days later (after 3 weeks of complete anuria) diuresis started to resume. Urinalysis revealed proteinuria (4.12 g/24 h), lambda light chains (2.41 g/l) and microhaematuria. Subsequently, complement normalized and urinalysis became negative. Creatinine dropped to 106 μmol/l and no paraprotein was detectable in neither serum nor urine. In conclusion, this report describes one of the oldest patients with ITG. ITG has been associated with haematologic malignancies, hepatitis C, cryoglobulinaemia or autoimmune disease [1–3]. All these were excluded. The presentation by acute renal failure with an improvement of renal function after therapy has not been reported previously. Patients with ITG usually present with proteinuria, microhaematuria, hypertension and renal insufficiency, that may gradually progress to end-stage renal disease [3,5]. In this case the illness started with dehydration. However, there were no features of acute tubular necrosis in the biopsy, and we assume that initial dehydration was a cause of accelerated fibrillogenesis. Successful treatment with steroid pulse therapy has been reported previously [4,6]. Our patient showed a dramatic response to pulse steroids, although a lower continuous dose was ineffective. At present, 13 months after the diagnosis, the patient is still in complete remission.

Conflict of interest statement. None declared.

Acute tubulointerstitial nephritis associated with celecoxib

Sir,

The selective cyclooxygenase-2 inhibitors (COX-2 inhibitors) cause renal syndromes that parallel those of the traditional non-selective non-steroidal anti-inflammatory drugs (NSAIDs). Celecoxib promotes haemodynamic acute renal failure (ARF) via inhibition of vasodilatory prostaglandins synthetized by the COX-2 enzyme [1,2]. Another potential cause of ARF associated with celecoxib is acute tubulo-interstitial nephritis (ATIN).

A 34-year-old male with HIV infection presented complaining of weakness, anorexia and decreased urine output. Medications included lamivudine 150 mg bid, lopinavir 3 mg bid, tenofovir 300 mg qd and prevacid 30 mg qd. The patient was on a stable regimen of these drugs for ~10 months. Celecoxib 200 mg bid was added 3 weeks prior to admission. Serum creatinine concentration measured 5 weeks prior to celecoxib therapy was at baseline (114 μmol/l).

Physical examination revealed a blood pressure of 115/70 mmHg and pulse of 85/min without orthostasis. The rest of the exam was benign. Laboratory data demonstrated blood urea nitrogen (16.4 mmol/l) and serum creatinine (292 μmol/l). Urinalysis had 2+ protein on dipstick, while the urine sediment contained a few granular casts, 3–5 red blood cells and 4–6 white blood cells/high power field. Ultrasound revealed large echogenic kidneys.

The patient received i.v. normal saline (2 l). Celecoxib and antiretroviral medications were discontinued. Renal function worsened over the next 3 days; creatinine increased to 521.6 μmol/l. Renal biopsy demonstrated a diffuse interstitial infiltrate with lymphocytes, eosinophils, marked tubulitis and interstitial oedema. The glomeruli and vessels were unremarkable. Oral prednisone 60 mg/day for 2 weeks was administered. Serum creatinine declined from 521 to 106 μmol/l over the next 3 weeks.

ARF, hyperkalaemia, hyponatraemia, oedema formation and hypertension have all been noted with the selective COX-2 inhibitors [1,2]. Haemodynamic ARF develops in patients treated with NSAIDs who depend on vasodilatory prostaglandins to maintain blood flow and glomerular filtration. Based on this known effect, celecoxib-associated inhibition of vasodilatory prostaglandins was considered as a possible cause of haemodynamic ARF in this patient. However, despite discontinuation of celecoxib and volume repletion, renal function continued to deteriorate making haemodynamic ARF unlikely.

The temporal association of celecoxib administration and development of ATIN suggests that this drug was the culprit. Like traditional NSAIDs, ATIN complicates therapy with this new class of drugs (Table 1). Since these drugs block COX, arachidonic acid may be shunted into the lipoxygenase pathway, favouring production of proinflammatory leukotrienes. This may promote the development of ATIN.

Physicians should be aware that selective COX-2 inhibitors have the potential to cause ATIN. Clinicians should be suspicious of this diagnosis when renal function does not improve within 48–72 h of drug discontinuation. Haemodynamic renal failure should be questioned and renal biopsy undertaken to clinch the correct diagnosis.

Conflict of interest statement. None declared.


DOI: 10.1093/ndt/gfh046
Enzyme replacement in the treatment of Fabry’s disease. Is there a point-of-no-return?

Sir,

We read with interest the recently published article by De Schoenmakere et al. [1] on enzyme replacement therapy in Fabry’s disease and the Editorial Comment by Breunig and Wanner [2] in the same issue of NDT. In both papers the question raised is whether there is or not a point-of-no-return beyond which organ damage cannot be reversed in spite of correct enzyme replacement treatment. Our experience with a patient may help to answer to this question.

A young man, 29 years old, presented in our outpatient clinic with ankle oedema and was diagnosed with nephrotic syndrome with microhaematuria. The serum creatinine at that time was 1.1 mg/dl. The clinical exam discovered angiotensinomas in pelvic localization. He had suffered acroparaesthesias, hypohidrosis and dizziness for years. Kidney and skin biopsies suggested Fabry’s disease. Very low levels of alpha-galactosidase were demonstrated in the patient and in his mother. He received treatment with enzyme replacement with agalsidase beta 1 mg/kg every 14 days. The necropsy found that cerebral haemorrhage was the cause of death. Cardiac hypertrophy persisted and there were multiple deposits of globotriaosylceramide particularly in endothelial cells (Figure 1).

Enzyme replacement therapy was unable to stop the progression of Fabry’s disease in our patient. This treatment was initiated when the renal function was very low and probably the organ damage was very advanced. We think that in our patient the kidney fibrosis and the damage in other organs like heart, vascular endothelium, etc., had reached a point beyond which the treatment was not useful. The conclusion is that enzyme replacement therapy in Fabry’s disease patients must be initiated as soon as possible to avoid reaching that point-of-no-return.

Conflict of interest statement. None declared.

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Extracellular fluid volume and EPO dose in haemodialysis

Sir,

Erythropoietin (EPO) requirements vary in haemodialysis patients. The most commonly recognized causes of EPO resistance are iron deficiency and chronic inflammation. We have previously noted a correlation between serum albumin and extracellular fluid volume (Vecf) in HD patients [1]. If serum albumin is lower in subjects with an increased Vecf, then haemoglobin may be too. However, unlike albumin,


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Table 1. Cases of ATIN associated with the selective COX-2 inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Author</th>
<th>Peak SCr</th>
<th>Treatment</th>
<th>Final SCr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib</td>
<td>Alper [3]</td>
<td>186 µmol/l</td>
<td>Steroids</td>
<td>97 µmol/l</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>Brewster a</td>
<td>522 µmol/l</td>
<td>Steroids</td>
<td>124 µmol/l</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>Rocha [5]</td>
<td>769 µmol/l</td>
<td>Haemodialysis, steroids</td>
<td>115 µmol/l</td>
</tr>
</tbody>
</table>

SCr, serum creatinine concentration.

*Current case.