Acute renal failure with severe loin pain and patchy renal ischaemia after anaerobic exercise (ALPE) (exercise-induced acute renal failure) in a father and child with URAT1 mutations beyond the W258X mutation

Sir,

ALPE is defined as (i) acute renal dysfunction or failure due to (ii) anaerobic exercise, accompanied by (iii) loin pain and (iv) normal or only slight elevation of creatine phosphokinase or serum myoglobin [1,2]. It has been reported that 51% of ALPE cases involve patients with renal hypouricaemia [1]. After cloning of the SLC22A12 gene (URAT1: uric acid transporter 1) [3], seven renal hypouricaemic patients with exercise-induced acute renal failure were analysed for mutations of URAT1 [3–6]. Five patients were homozygotes for W258X, one patient was a heterozygote for W258X and one patient was a compound heterozygote for W258X,Q297X [3–6].

We describe a father and son who both developed ALPE with renal hypouricaemia beyond the W258X mutation of URAT1.

Case 1. One day after performing a 150 m dash at a neighbourhood athletic meeting, a 40-year-old male (father) developed severe loin pain and consulted our clinic. His serum creatinine and uric acid levels were 2.9 and 2.1 mg/dl. Fractional Excretion of Uric Acid (FEUA) was 49.7% at that time. Delayed computed tomography (CT) scans after administration of contrast media demonstrated patchy wedge-shaped enhancement. He recovered from ALPE in 4 weeks, and serum creatinine and uric acid decreased to 1.0 and 0.6 mg/dl, respectively.

Case 2. Five years later, the 14-year-old son of case 1 developed acute renal failure after performing the 400 m dash twice. Three hours after the race, severe loin pain developed and he consulted a local doctor (serum creatinine 1.45 mg/dl). Fractional Excretion of Uric Acid (FEUA) was 49.7% at that time. Delayed computed tomography (CT) scans after administration of contrast media demonstrated patchy wedge-shaped enhancement. He recovered from ALPE in 4 weeks, and serum creatinine and uric acid decreased to 1.0 and 0.7 mg/dl, respectively.

As shown in Figure 1, the father was an R90H homozygote and the son was a compound heterozygote for R90H/W258X. The mother was a heterozygote for W258X with a normal serum uric acid level, and the daughter was a compound heterozygote for R90H/W258X with renal hypouricaemia, but there was no history of ALPE in this subject. There is no previous report of a homozygous R90H mutation among 32 previously reported patients with renal hypouricaemia [4]. Therefore, this is the first report that ALPE developed in a patient with R90H homozygous mutation and in a patient who was a compound heterozygote for R90H/ W258X mutation.

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Statins and progression of renal failure: is a reconsideration of clinical practice guidelines justified?

Sir,

In the 2002 and 2003 clinical practice guidelines (CPG) [1], it is stated that there is ‘insufficient evidence to recommend lipid-lowering therapy for the purpose of slowing the progression of chronic kidney disease (CKD)’. Recently, these guidelines were questioned on the basis of post hoc...
analyses of several large clinical trials, with cardiovascular disease (CVD) end-points, in the general population [2].

In the above-mentioned post hoc analyses, apart from the increased risk for type I errors [2], there are several limitations. Renal failure patients were excluded [1] and results regarding CKD progression are often based on fewer patients than initially included in the study [3]; glomerular filtration rate is indirectly estimated; adjustment for main factors influencing CKD progression is often incomplete and, when it is, changes the initial results [4], while data for albuminuria or microalbuminuria are frequently absent [5]. If the negative results of the ASCOT-LLA [6], VA-HIT [7] and ALERT [8] studies are added to these limitations, a motivated, based on post hoc analyses, reconsideration of the CPG seems, up to now, less urgent.

On the other hand, considering the impressive results achieved by statin treatment in studies with CVD end-points in the general population and taking into account the dyslipidaemia patterns in CKD patients, a few points of interest in this particular population are worth highlighting.

The main target, regarding lipids, in the majority of the studies in the general population, was elevated low-density lipoproteins (LDL) and total cholesterol (tChol). At initial stages of CKD, a similar dyslipidaemic pattern—due to nephrotic syndrome or to common causes of CKD such as diabetes, atherosclerosis, etc.—is frequently observed. Results based on studies in the general population can potentially be extrapolated (regarding hypolipidaemic treatment for CVD prevention) in CKD patients with a similar dyslipidaemic profile. The improvement of cardiovascular status—at least the haemodynamic benefit—should also be important for the stabilization or retardation of CKD progression. Furthermore, the pleiotropic effects of these drugs and specifically their actions on endothelial function, oxidative stress, inflammation, etc. might also be beneficial in slowing progression of CKD in this subgroup of patients.

In contrast, in patients with severe CKD in whom the dyslipidaemic pattern approaches that of patients with end-stage renal failure (ESRF) in renal replacement treatment (who usually have elevated triglycerides, low high-density lipoproteins and normal or low tChol and LDL), extrapolation of the general population study results might no longer be appropriate (mainly because this dyslipidaemic profile does not exist in the populations included in these studies). Furthermore, hypertriglyceridaemia is better treated with fibrates or hypolipidaemic drugs other than statins, which do not seem to have any beneficial effects on CKD progression [7]. Moreover, cholesterol lowering in this subgroup of CKD patients might even be inappropriate, especially if the ‘reverse epidemiology’, regarding the detrimental role of low tChol in ESRF patients’ morbidity and mortality, is valid and also extended to the pre-dialysis population. Finally, malnutrition and aggravation of micro-inflammation, frequently observed in these late CKD stages, might be inter-related with dyslipidaemia and also have to be taken in consideration.

In any case, only studies in CKD populations (such as SHARP and PREVEND-IT [1]), with end-points related to renal function in time, can eventually give a definite answer to the question of whether lipid-lowering treatment is beneficial for the progression of CKD.

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Bedside testing of CAPD fluid for bilirubin to aid diagnosis of visceral perforation

Sir,

Peritonitis is a major complication of continuous ambulatory peritoneal dialysis (CAPD). Visceral perforation accounts for 1–10% of such complications and can be a difficult diagnosis to make [1,2]. The delay in diagnosis has a significant impact on mortality and morbidity [1]. We would like to highlight a case of CAPD peritonitis that was associated with visceral perforation.

A 47-year-old patient presented to a district general hospital with abdominal pain and was originally treated for CAPD peritonitis. He had been on CAPD for 2 years having reached end-stage renal failure due to immunoglobulin-A nephropathy. There was no history of peptic ulcer disease nor was there steroid, proton pump inhibitor or H2 antagonist use. Initial clinical examination revealed diffuse tenderness across the abdomen without rebound or guarding and he was started on antibiotics for CAPD peritonitis. He was transferred to the regional renal unit and his clinical