We present a case of a 39-year-old woman with polycystic kidney disease who started peritoneal dialysis in 2000. Four years later, the patient received a cadaver donor transplant from a 52-year-old woman. Surgery was performed without technical difficulties and good initial graft perfusion was observed. An immunosuppressive regimen consisting of tacrolimus, mycophenolate mofetil and steroids was initiated.

The post-operative course showed persistent anuria with dependency on dialysis every 48 h. Isotopic renogram demonstrated a vascular pattern with an almost flat excretion curve. Renal biopsy showed broad ischaemic necrosis of the tissue sample.

Detailed screening for thrombosis risk factors revealed increased prothrombin immunoreactivity and molecular genetic analysis identified a heterozygous point mutation at position 20210 of the prothrombin gene.

Recently, a clinical study reported the potential for inherited hypercoagulability due to the V Leiden factor or prothrombin G20210A, to predispose to acute graft thrombosis [1].

The G20210A prothrombin mutation occurs in 1–2% of the population and represents a frequent cause of inherited thrombophilia.

Our patient developed RCN in the early post-transplant period. Organ transport, storage and transplantation problems and haemodynamic instability or rejection in the early post-transplant period were ruled out. Only the G20210A mutation of the prothrombin gene was found.

The G20210A prothrombin mutation is a risk factor for graft loss and is linked to a high frequency of acute vascular rejection due to the broad antigen exposure triggered by vascular wall injury and induced by the prothrombotic state [1,2].

The first case series of patients heterozygous for the G20210A prothrombin mutation and unsuccessful kidney transplantation was published in 1999 and included three renal transplant recipients who experienced graft loss due to thrombosis in the peri-operative period [3]. The G20210A mutation is also associated with a 2.95-fold increased risk for allograft loss, an observation that provides the basis for screening recipients before renal transplantation [4]. In contrast, screening of 562 transplant recipients found a prevalence of 2% and no significant differences were reported in the 30 day and 1 year graft survival rates among patients with or without the G20210A mutation [5].

It seems reasonable to believe that endothelial injury and ischaemic-reperfusion syndrome were related to transplantation in a woman with no previous history of thrombophilia, but with a heterozygous point mutation at position 20210 of the prothrombin gene, could trigger RCN.

New research is required to elucidate the role of this mutation in the course of kidney transplantation.

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A puzzling case of high serum creatinine in a healthy woman

Sir,

A 42-year-old woman with a history of recurrent urinary tract infection presented to the emergency room with acute malaise and abdominal pain. On physical examination, the patient was febrile and the right kidney was painful on percussion. Blood tests showed moderate leukocytosis, high C-reactive protein (>200 mg/l) and a serum creatinine and serum urea in the normal range. A dipstick analysis of the urine revealed leukocyturia and bacteriuria and the abdominal ultrasound showed normal kidneys. An acute pyelonephritis was diagnosed and after a 3-day course of intravenous antibiotics the patient was discharged afebrile and in good condition with a prescription of levofloxacin for another 7 days.

Ten days later, the patient was seen by the general practitioner. At that time, the patient appeared healthy with normal body temperature and an unremarkable abdominal examination. Surprisingly, the serum creatinine was considerably elevated (400 μmol/l; normal range: 45–102 μmol/l). The blood test was repeated by a second general practitioner and confirmed the previous results. A computerized tomography scan of the abdomen was performed and revealed no pathological findings. Acute renal failure was suspected and the patient was admitted to our hospital for further examination. The physical examination was still unremarkable (i.e. no signs of uraemia). The blood tests were repeated and serum creatinine (82 μmol/l) and serum urea (3.3 mmol/l; normal range: 2–8 mmol/l) values were in the normal range.

How can the highly pathological serum creatinine measured by both general practitioners in this obviously healthy woman be explained? The general practitioners used the enzymatic method (Reflotron® Creatinine; Roche Diagnostics, Switzerland) for serum creatinine analysis, whereas the Jaffé method was applied in our hospital. In the enzymatic assay, the non-proteinogenic amino acid sarcosine is formed in the course of the reaction (Table 1). Sarcosine, an intermediary of one-carbon metabolism, is usually undetectable in human blood and, therefore, does not interfere with the test. To support the diagnosis of sarcosinaemia, the patient's serum creatinine level was measured on a single blood sample level using both the enzymatic and the Jaffé method simultaneously. The serum

Table 1. The Reflotron® creatinine assay

Substrates	Enzymes	Products
Creatinine + H_2O	Creatinine iminohydrolase	*N*-Methylhydantoine + NH_3
N-Methylhydantoine + $2H_2O$ + ATP	*N*−Methylhydantoine amidohydrolase	*N*-Carbamoylsarcosine + ADP + P
N-Carbamoylsarcosine + H_2O	*N*−Carbamoylsarcosine amidohydrolase	Sarcosine + CO_2 + NH_3
Sarcosine + H_2O + O_2	Sarcosine oxidase	Glycine + HCHO + H_2O_2
H_2O_2 + indicator	Peroxidase	Dye + H_2O

creatinine level was 403 μmol/l (enzymatic method) and 79 μmol/l (Jaffé method), respectively. The diagnosis was confirmed in our patient by an amino acid analysis (HPLC ion-exchange chromatography) that revealed substantial sarcosinaemia of 460 μmol/l. The high concentration of sarcosine interfered with the enzymatic test method used by the practitioners.

Sarcosinaemia is caused by a deficiency of sarcosine dehydrogenase [1] and was originally described in 1966 in a brother and sister with mild mental retardation [2]. Later on, newborn screening programmes revealed that this inherited defect of amino acid metabolism occurs in about 1:350 000 (New England) and reflects mainly a benign metabolic state [3]. The gene for human sarcosine dehydrogenase is localized on chromosome 9q34 and genetic data are consistent with an autosomal recessive mode of inheritance.

The Jaffé method is known to be rather unspecific and to interfere with a number of compounds, but not with sarcosine. Thus, in the presence of sarcosinaemia, the serum creatinine concentration is more accurately determined by the not specific Jaffé than by the specific enzymatic method.

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