Isotope dilution mass spectrometry (IDMS) may replace conventional assays of serum creatinine in the future and the MDRD formula has recently been re-calibrated to IDMS-traceable serum creatinine values [4]. Until there is widespread adoption of IDMS creatinine analysis, we believe the four-variable MDRD formula represents an improvement compared with serum creatinine alone for detection of chronic kidney disease. As with any first order screening test, there is a trade-off of higher sensitivity for lower specificity. Thus, whilst the MDRD GFR is imperfect, we would prefer to choose a relative over-estimation of low-GFR, rather than risk missing a significant number of patients who do have established CKD, but who would be overlooked when using conventional biochemical parameters.

Conflict of interest statement. None declared.

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doi:10.1093/ndt/gfl181

Letters

Advance Access publication 18 January 2006

Fatal relapse of thrombotic thrombocytopenic purpura after surgery in a patient with congenital absence of vWF-cleaving protease activity

Sir,

Thrombotic thrombocytopenic purpura (TTP) is a relatively rare disorder, commonly described with the pentad of thrombocytopenia, microangiopathic haemolytic anaemia, mental status deterioration, renal failure and fever. Although it is well known that virtually every organ may be affected by TTP, cardiac involvement is rarely reported in the TTP literature [1–6]. With the present case we would like to highlight two significant and neglected problems in patients with TTP: cardiac involvement and postoperative relapse of disease.

A 29-year-old male was diagnosed with a TTP in 1990 at the age of 14. At that time he suffered from the cerebrovascular insult with residual discreet left-sided haemiparesis. His father died at the age of 41 from a brain haemorrhage. After achieved remission with plasma exchange, he was stable until August 1996 when he relapsed and developed the chronic form of TTP. Since that time, he had been treated with plasma exchanges every 3 weeks. He experienced six relapses, all responding to intensified plasma exchange treatment. Congenital deficiency of von Willebrand factor-cleaving protease (ADAMTS13) activity was diagnosed in 2002. In January 2003, the patient developed end-stage renal disease and started with haemodialysis.

A heart ultrasonography, performed in February 2005 as a part of the routine pretransplantation examinations, demonstrated severe mitral insufficiency (grade IV) with dilative left-side cardiomyopathy. Heart indices were as follows: LVIDd 8.0 cm, LA 8.0 cm, Ao 3.0 cm, IVS and SSLV 1.0 cm. Ejection fraction of the left ventricle was 30%. There were no pathologic changes on coronarography. Electrocardiogram showed atrial fibrillation. The patient had never complained of either chest pain or stress intolerance.

He underwent biological mitral valve replacement in July 2005. Preoperative platelets were 178 × 10^9/l (normal range 150–350 × 10^9/l), with other laboratory measurements within the normal range except for serum BUN and creatinine. There were no signs of haemolysis. The operation and early postoperative course were uneventful. He was dialyzed in the evening of day 0 due to hyperkalaemia. On the first postoperative day, platelet count fell to 80 × 10^9/l, with mild anaemia. Both findings were attributed to the mechanical destruction in the bypass circuit. Next morning platelets dropped to 20 × 10^9/l. A nephrologist was consulted and ordered urgent plasma infusion. However, the patient suddenly developed cardiorespiratory arrest and died. Postmortem examinations were concordant with the diagnosis of TTP. The heart was enlarged, with enormously dilated left atrium and ventricle. Histology revealed widespread myocardial thrombotic involvement, without signs of myocardial haemorrhage or necrosis.

Data on the clinical presentation of cardiac involvement in patients with TTP are scarce, probably due to ‘silent’ myocardial damage. Although some form of chest pain was reported in 6% of TTP/HUS patients [4], postmortem examinations revealed myocardial thrombotic involvement in all patients [3]. Our case demonstrates that severe, life-threatening changes may be present in the heart of an asymptomatic patient. It seems possible that extensive thrombotic changes in myocardial small vessels may promote development of dilatative cardiomyopathy.

Another problem that arises in our case is the postoperative relapse of TTP. Although most cases of heart surgery-associated TTP were demonstrated in patients after coronary artery bypass grafting associated with treatment with clopidogrel or ticlopidine [7–9]. Anstadt et al. recently reported the case of a patient with decreased vWF-cleaving protease activity who relapsed after cardiac surgery [10]. Considering deficient vWF-cleaving protease activity as a
risk factor for relapse of TTP. Lactate dehydrogenase and markers of haemolysis are not routinely ordered in our intensive care unit; this fact, together with the not unusual fall of platelets in patients after cardiac surgery, resulted in delayed recognition of TTP relapse. This case clearly demonstrates that every postoperative decrease in the number of platelets in a patient with TTP should be considered as a relapse and calls for intensive medical supervision. Relapse may become fatal without the prompt institution of plasma exchange.

Cardiac involvement in TTP demands more extensive research, and patients should regularly be screened for the presence of heart abnormalities (ECG, ultrasonography), even when asymptomatic. Relapse of TTP after cardiac surgery is unpredictable, but our report supports the observation of Anstadt et al. that deficient vWF-cleaving protease activity increases the risk of relapse [10].

Conflict of interest statement. None declared.

(See related article by Patschan et al. NDT Advance Access publication March 30, 2006. doi:10.1093/ndt/gfl127.)

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Is oxidative stress implicated in high bone turnover in end-stage renal disease (ESRD)?

Sir,
End stage renal disease (ESRD) is a condition in which oxidative stress is much enhanced and implicated in a variety of uremic complications [1,2]. Oxidative stress influences bone turnover [3,4] and in theory may also play a role in bone disease in ESRD. To explore this hypothesis, we investigated the relationship between an oxidative stress marker such as oxidized LDL (ox-LDL) and a specific biomarker of bone turnover [5] alkaline phosphatase (AlkPhos) in the cardiovascular risk extended evaluation in dialysis (CREED) database [6]. We excluded from the study all conditions that may independently influence bone turnover (diabetes, parathyroidectomy, treatment with aluminium hydroxide or beta-blockers). Thus, from an original cohort of 283 individuals, 161 dialysis patients (age 62 ±16 years, 93 males and 68 females) were included in this analysis.

As shown in Figure 1, there was a graded increase in serum levels of AlkPhos across tertiles of ox-LDL and this association also held true when ox-LDL and AlkPhos were analysed as continuous variables (r = 0.31, P < 0.001). Such an association remained highly significant (β = 0.21, P = 0.005) even after adjustment for a series of potential confounders such as age, sex, duration of dialysis, treatment modality, use of calcium carbonate or calcium acetate, serum calcium and phosphate, body mass index and serum C-reactive protein.

In patients with ESRD, serum levels of AlkPhos are directly related to ox-LDL and this association is independent of a series of potential confounders. We believe that our observation is hypothesis-generating in that it suggests that the effects of oxidative stress in ESRD may also encompass bone disease. Further studies, considering more refined markers of bone turnover and of oxidative stress and interventions in experimental models, represent useful areas to further explore the link between bone turnover and oxidative stress in ESRD.