Acute renal failure due to tumor lysis syndrome in a HIV seropositive patient with Castleman’s disease

Sir,

Castleman’s disease (CD), a rare lymphoproliferative disorder, is characterized by histological features of lymph node hyperplasia and capillary proliferation. Conditions such as minimal-change, membranous, mesangiproliferative, membranoproliferative glomerulonephritis, thrombotic microangiopathy and renal amyloid have been reported with CD [1]. Acute renal failure (ARF) due to tumour-lysis syndrome (TLS) has not been reported in these patients.

Case. A 34-year-old Caucasian male was admitted to the Houston VA medical center with nausea, right upper quadrant and epigastric pain. His past medical history was significant for the diagnosis of HIV infection 11 years previously. He had refused therapy until 6 months prior to this admission when he developed constitutional symptoms and cervical lymphadenopathy. Lamivudine, Didanosine and Nevirapine were started since he had a low CD4 count (105 cells/l.) and a high viral load (> 75 000 HIV RNA copies/ml). An abdominal CT scan at that time revealed extensive lymphadenopathy. The diagnosis of a plasma-cell variant of multicentric CD was made from a cervical lymph node excision biopsy.

During this admission, initial blood tests were as follows: serum creatinine 5.4 mg/dl, uric acid 12.9 mg/dl, phosphorus 3.1 mg/dl and serum LDH 361 U/l. Acute pancreatitis was also noted. Baseline serum creatinine and uric acid were not elevated. Renal ultrasound showed normal renal sizes with no evidence of hydronephrosis. Microscopic urinalysis showed granular casts without crystals or pyuria. Given this constellation of lab findings, the possibility of ‘spontaneous’ TLS from CD was included in our differential diagnosis of ARF.

Introduction of cyclophosphamide and prednisone resulted in rapid destruction of tumour cells and worsening of TLS, manifested by a dramatic rise in the serum levels of creatinine, phosphorus (12 mg/dl), uric acid (20 mg/dl) and LDH enzyme (550 U/l). Cervical lymphadenopathy and pancreatitis improved. Haemodialysis was continued for 10 days along with allopurinol. With the resolution of TLS, renal function slowly improved over 6 weeks.

Comment. CD has hyaline-vascular and plasma cell variants and clinically could be localized or multicentric. While localized CD is a benign lymphoproliferative disorder, the multicentric type is associated with infections, multi-organ failure and malignancies [2]. It is postulated that Kaposi’s sarcoma associated virus (HHV-8) could play a crucial role in producing IL-6 and releasing angiogenic factors resulting in lymphoplasmacytic proliferation [2]. Renal involvement in CD has clinical presentations that vary from nephrotic syndrome to antimonyperoxidase-antibody-positive rapidly progressive glomerulonephritis [3] and end-stage renal disease from renal amyloidosis [4].

Even though TLS is common in haematologic malignancies after chemotherapy, in rapidly growing tumours hyperuricaemia could be seen even without the introduction of chemotherapy or radiotherapy, an entity recognized as ‘spontaneous’ TLS. We postulate that our patient initially may have had spontaneous TLS and that subsequent renal recovery was hampered by chemotherapy-induced TLS.

Conflict of interest statement. None declared.

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Molecular forms of adiponectin in uraemic plasma

Sir,

Adiponectin is a recently found anti-atherogenic plasma protein secreted by adipocytes. Plasma adiponectin level is reduced in patients with coronary artery disease [1], type 2 diabetes mellitus [1] and obesity [2]. In contrast to these high-risk groups, plasma adiponectin has been reported to be elevated in haemodialysis patients [3]. Since uraemic plasma is known to contain not only intact forms but also fragments of some peptide hormones such as parathyroid hormone, it is an important question whether adiponectin in uraemic plasma is intact or not. To answer the question, we analysed its molecular forms.

Plasma samples were taken from two patients (patients A and B) on maintenance haemodialysis and a healthy volunteer; both 42-year-old men without diabetes, obesity or coronary artery disease. Fresh plasma was fractioned by gel filtration using a 10 x 300 mm column of Superose 6 HR (Amasham Biosciences, Tokyo) and 31 mM Tris–HCl buffer (pH 7.2). An aliquot of each 0.5 ml fraction was assayed for adiponectin by ELISA [2]. Subsequently, another aliquot of the fractioned plasma was subjected to SDS–polyacrylamide gel electrophoresis (PAGE) in reducing condition. Western blotting was done using anti-adiponectin monoclonal
antibody ANOC 4908 (a generous gift from Dr Funahashi, Osaka University Graduate School of Medicine) as the first antibody and peroxidase-labelled rabbit anti-mouse IgG polyclonal antibody as the second antibody. Plasma adiponectin levels of the haemodialysis patients and the healthy subject were 25.1, 9.1 and 5.1 µg/ml, respectively. Reference range of adiponectin was 5.5 ± 2.0 µg/ml (mean ± SD, n = 51) for healthy men in our laboratory.

Upon gel filtration chromatography of plasma from the healthy subject, immunoreactive adiponectin migrated as macromolecules larger than IgG (150 kDa) showing three peaks. A similar gel filtration pattern was found for the uraemic plasma samples. No adiponectin immunoreactivity was detected in fractions corresponding to monomeric adiponectin or smaller fragments.

Western blotting of the fractioned healthy plasma (Figure 1) showed one major band at 30 kDa and another faint band at 80 kDa in reducing condition. In contrast, the 80 kDa band predominated in non-reducing condition. The extra band noticed at 28 kDa was non-specific staining for IgG light chain due to the known cross-reactivity of the second antibody (labelled polyclonal rabbit anti-IgG antibody) with human IgG light chain [2]. No other bands corresponding to adiponectin fragments were detected. These results agreed well with a previous report [2], and fit the corresponding to adiponectin fragments were detected in fractions corresponding to monomeric adiponectin or smaller fragments.

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Aldosterone and potassium balance in dialysis patients

Sir,

The article by Hussain et al. [1], showing that spironolactone, even at dosages as low as 25 mg/day, may cause dangerous hyperkalaemia in some dialysis patients (two out of 15 patients) reminds us of the importance of aldosterone-driven potassium (K) secretion in extrarenal sites (among others, the colon, salivary and sweat glands) in uraemia [2,3]. Though extrarenal K excretion is <10% of total K excretion in subjects with normal renal function, it increases (at least in the colon) in the course of chronic renal failure, up to 30 mmol/day [2]. Aldosterone exerts in the colon the same effects as in the collecting tubule, by interacting with a specific mineralocorticoid receptor (MR) [3]. Thus, inhibition or stimulation of MRs are expected to result in corresponding changes in faecal K secretion. Stimulation of MRs in anuric patients on chronic haemodialysis with either fludrocortisone [4] or glycyrrhetinic acid (which allows direct activation of MRs by endogenous cortisol in aldosterone-sensitive cells) [5] is associated with significant reductions in plasma K levels. However, there has been little appreciation so far of the clinical relevance of colonic K secretion in dialysis patients. There is a general belief that colonic K secretion does not consistently affect K balance and that in

Fig. 1. Western blotting of plasma adiponectin. Healthy (top) and uraemic (bottom) plasma samples were fractioned by gel chromatography, and an aliquot of each fraction was subjected to SDS–PAGE in reducing condition. Adiponectin was visualized by western blotting using anti-adiponectin antibody. Pre-stained SDS–PAGE molecular standards included lysozyme (21.4 kDa), soybean trypsin inhibitor (28.8 kDa), carbonic anhydrase (35.5 kDa), ovalbumin (50.3 kDa), bovine serum albumin (93 kDa) and phosphorylase B (113 kDa). The gel filtration fraction numbers and molecular size markers for gel filtration (IgM, 900 kDa; IgG, 150 kDa; albumin, 67 kDa) are indicated below each lane. The major bands of 30 kDa correspond to adiponectin monomer.