Letters
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Renal extraction of cystatin C

Sir,

Cystatin C is considered as a new marker of glomerular filtration rate (GFR). However, studies on its renal physiological handling are lacking [1], making the study of van Rossum et al. interesting [2]. Nevertheless, we have some comments. Firstly, as contrast injection may induce acute variation in intrarenal haemodynamics, it would be of interest to know the timing of the sampling procedure in relation to iodine injection [3]. Secondly, the authors have described large absolute and relative variations in cystatin extraction compared with iothalamate extraction. No systematic bias could be detected, and opposite ratios are observed in both kidneys of individual patients. This could be explained in part by the high analytical coefficient of variation (CVa) reported for the cystatin measurements (11.3% for 1.4 mg/l). This CVa must still be higher in the patient samples (and not the controls given by the manufacturer DAKO). The use of sodium citrate tubes is also questionable as it is never recommended in immuno-assays. Performing the cystatin in triplicate will not change this limiting fact. Thirdly, the authors confirm the tubular variation (CVa) reported for the cystatin measurements (11.3% for 1.4 mg/l). This CVa must still be higher in the patient samples (and not the controls given by the manufacturer DAKO). The use of sodium citrate tubes is also questionable as it is never recommended in immuno-assays. Performing the cystatin in triplicate will not change this limiting fact. Thirdly, the authors confirm the tubular secretion of iothalamate [4]; however, iothalamate has been used as a GFR ‘reference’ measure in most important studies [5]. We would be interested in the authors’ opinion on this topic.

Conflict of interest statement. None declared.

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Successful treatment of severe/active cryoglobulinemia membranoproliferative glomerulonephritis associated with hepatitis C virus infection by means of the sequential administration of immunosuppressive and antiviral agents

Sir,

Membranoproliferative glomerulonephritis (MPGN) associated with type II mixed cryoglobulinaemia is the principal renal manifestation of hepatitis C virus (HCV) infection [1]. The management of HCV-related cryoglobulinemic MPGN is difficult; HCV eradication by antiviral therapy with interferon-α and ribavirin can lead to clinical remission [2], but severe/active renal disease may be resistant to antiviral therapy [1–3]. In such cases, corticosteroids in combination with cytotoxic agents and plasmapheresis have been used to decrease cryoglobulin production and improve vasculitic manifestations, but long-lasting remission of the renal disease is uncommon. We report a case of severe/active HCV-related cryoglobulinemia MPGN which was successfully treated by means of the sequential administration of immunosuppressive and antiviral agents.

A 50-year-old man presented with a 5-week history of arthralgia and ankle oedema. The physical examination on admission showed hypertension (180/100 mmHg), pleural effusion and oedema of the legs. The laboratory findings were haemoglobin 118 g/l, serum albumin 25 g/l, blood urea nitrogen 49 mg/dl and creatinine 1.6 mg/dl with creatinine clearance of 52 ml/min. Alanine (ALT) and aspartate aminotransferases (AST) levels were within the normal range. Urinalysis showed heavy proteinuria (10.5 g/24 h) and active urine sediment. The patient was positive for HCV antibodies and serum HCV RNA; the genotype was 1 and the viral load 7.6 × 10^6 copies/ml. The other laboratory results were rheumatoid factor (RF) 871 IU/ml (0–15), complement factor C4 0.19 g/l (0.20–0.50) and cryocrit 20%, with type II (IgG-IgM-k) cryoglobulins. A liver biopsy showed mild chronic hepatitis (grade A1, stage F1 according to the METAVIR Cooperative Study Group) [4], and a kidney biopsy a cryoglobulinemic MPGN with marked endocapillary proliferation, intraluminal thrombi, cellular crescents and vasculitis with fibrinoid necrosis; immunofluorescence microscopy revealed granular capillary wall and mesangial deposits and intraluminal masses of IgM, IgG and C3. Immunosuppressive treatment was started with corticosteroids (methylprednisolone pulses of 1.0 g/day for 3 days, followed by oral prednisone 1.0 mg/kg/day slowly tapered to a maintenance dose of 0.2 mg/kg/day) and oral cyclophosphamide 2 mg/kg/day. After 3 months, serum creatinine and creatinine clearance had normalized, proteinuria had decreased to 800 mg/24 h and cryocrit to 5%, and the clinical signs of the disease (pleural effusion, ankle oedema, arthralgia) had disappeared. ALT and AST levels remained unchanged, whereas HCV RNA levels had increased (38.3 × 10^6 copies/ml). As the nephrotic syndrome was in clinical remission, cyclophosphamide and prednisone were discontinued, and antiviral treatment was started with once-weekly injections of peginterferon α-2a 100 µg

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