fetoprotein) were normal. There were no pathologic findings on CT thoracic-abdominal scan and barium enema. On upper gastrointestinal series there was deformity of the duodenal bulb; the patient refused gastroscopy. Symptomatic treatment plus antiplatelet agents were given.

Ten months later, he presented with upper gastrointestinal bleeding. On gastroscopy an ulcer was seen in the gastric antrum and the biopsy was compatible with adenocarcinoma. A subtotal gastrectomy was carried out and the pathological study showed an intestinal-type adenocarcinoma with invasion of the muscularis and metastases to two intrapleural lymph nodes. A search for distant metastases was negative.

In the subsequent evolution, the most significant facts were: irregular blood pressure control, progressive deterioration of renal function, proteinuria below the nephrotic range and increase in the fractional excretion of the protein to 0.15–0.21%. Also the patient had a cerebrovascular accident and exacerbation of tumor-related nephrotic syndrome with treatment of the neoplasm. Cancer 1984; 54: 1082–1084.

In the subsequent evolution, the most significant facts were: irregular blood pressure control, progressive deterioration of renal function, proteinuria below the nephrotic range and increase in the fractional excretion of the protein to 0.15–0.21%. Also the patient had a cerebrovascular accident and exacerbation of tumor-related nephrotic syndrome with treatment of the neoplasm. Cancer 1984; 54: 1082–1084.

Comment. The prevalence rate of neoplasia in patients over 50 with membranous glomerulonephritis and nephrotic syndrome (NS) is increased; because the glomerulonephriti

Sir,

Cases of acute renal failure with the use of rifampicin are rare and are usually attributed to tubulointerstitial lesions [1], three cases [2–4] with glomerular involvement and crescentic disease have been reported. We present a case of acute renal failure secondary to mesangiocapillary glomerulonephritis type I in a patient taking rifampicin as antitubercular therapy for open tuberculosis. This case presented a therapeutic dilemma regarding the use of immunosuppressive therapy in conjunction with continuation of antibiotic treatment and supports a causal relationship between rifampicin and glomerular disease.

A 69-year-old lady presented with a 6-month history of weight-loss, night sweats, and haemoptysis. She had been treated for pulmonary tuberculosis twice in the past; in 1955 and in 1964 with streptomycin, PAS andisoniazide but had never received rifampicin.

A chest radiograph showed a cavity at the left apex and consolidation at the right base; sputum microscopy was positive for acid fast bacilli, sputum culture grew M. tuberculosis and the gastric carcinoma. To establish a causal relationship between rifampicin and glomerular disease.

In the present case there is a temporal association between MPGN and the gastric carcinoma. To establish a causal relationship between glomerulonephritis and neoplasia, some authors consider necessary for the nephropathy to remit on treatment of the tumour and to relapse when the tumour recurs [1]. In our patient, following gastrectomy renal failure continued to worsen and proteinuria persisted although it decreased. In fact, the increase in the fractional excretion of protein indicates that probably the reduction in proteinuria is related to deterioration of renal function. This unfavourable course does not exclude a causal association, because residual tumour, presumably, remained after operation. There were also other poor prognosis features, such as advanced age, arterial hypertension, renal failure and glomerular sclerosis, which might have led to progression of the glomerulonephritis by non immunological mechanisms. Besides, it has been reported in literature that treatment of the tumour is not always followed by remission of the NS [2,3].

It is a debatable issue whether all adult patients with MPGN and NS should undergo an extensive evaluation, looking for an occult cancer. In any case, MPGN should be kept in mind as a possible forerunner of carcinoma.

Nephrology1 and Pathology2 Sections
Hospital General de Elche Spain
R. Enriquez1 A. E. Sirvent1 J. B. Cabezuelo1 M. Perez-Ramos2 F. Amoros3 A. Reyes1


Therapeutic dilemma: crescentic mesangiocapillary glomerulonephritis type I in a patient on antitubercular therapy with rifampicin.

Sputum microscopy was positive for acid fast bacilli, sputum culture grew M. tuberculosis. Her renal function at the time was normal with urea of 3.2 mmol/l and creatinine of 82 µmol/l, albumin was 30 g/l. Therapy was started with rifampicin 600 mg, isoniazid 300 mg and pyrazinamide 2 g once daily. Three days after commencing therapy she started feeling unwell with gastrointestinal upset and diarrhoea. Ten days later she was admitted with increasing shortness of breath and ankle swelling. On examination she was normotensive, afebrile, in a sinus tachycardia and in biventricular failure.

Investigations showed: full blood count; Hb 10.7 g/dl; WBC 10.3 × 10⁹/l; neutrophils 8.05 × 10⁹/l; platelets 596 × 10¹²/l. ESR was 94 mm/h.

Biochemistry: sodium 115 mmol/l; potassium 5.2 mmol/l; urea 19.2 mmol/l; creatinine 553 µmol/l; liver enzymes were normal. Serum albumin was 25 g/l. Her 24-h urinary protein excretion was 13.39 g and creatinine clearance was 10 ml/min. Immunology: ANA, ANCA and anti-GBM antibodies were negative. Complement levels including C3, C4 and C1 inhibitor as well as complement function (CH50 and circulating immune complexes) were unremarkable.

CRP was 64 mg/l (0–10). Serum immunoglobulins and serum electrophoresis were normal. IgG subclasses were normal. ASO titre, hepatitis B and C serology, blood and urine cultures were all negative. Sputum microscopy and culture were still positive for M. tuberculosis. Renal ultrasound showed normal sized kidneys with slight reduction in

© 1999 European Renal Association–European Dialysis and Transplant Association
corticomedullary differentiation. A chest radiograph showed previously noted changes and pulmonary oedema.

A renal biopsy showed features in keeping with mesangio-capillary glomerulonephritis type I with cellular crescents. Three days after admission her creatinine had reached 714 μmol/l with clinical deterioration. Her rifampicin was discontinued and immunosuppressive therapy was commenced (methylprednisolone i.v. 1 g daily for 3 days followed by a tapering course of oral prednisolone beginning with 60 mg o.d.). Simultaneously, clarithromycin 250 mg b.d. was introduced as a third anti-tuberculous drug. Over the following 7 months her creatinine fell to 172 μmol/l with a reduction of proteinuria to 5.31 g/24 h. She continued on a combination of antitubercular treatment and steroids, clarithromycin was stopped after 2 months, isoniazid and pyrazinamide after 6 months. The dose of prednisolone was reduced slowly to 20 mg o.d.

There is a debate in the literature regarding the pathogenesis of renal damage with rifampicin since the first report in 1971 [5]. A review of 36 reported cases in 1976 [1] found that the renal failure only occurred in treatment of tuberculosis and seemed to be more frequent and severe in intermittent or discontinuous use of the drug.

Renal biopsies had been performed in 13 of the reported cases of which 12 showed tubulointerstitial lesions.

The observation of two cases with glomerular involvement [6,7] in addition to interstitial and tubular changes plus positive immunofluorescence raised the question whether a pathomechanism similar to Heymann nephritis [8] or the model of Sugisaki [9] was involved. In these models altered tubular antigens act as a trigger for an autoimmune response which then causes glomerulonephritis via immune complex deposition. Hirsch et al. [3] suspected but did not prove an interaction of different anti-mycobacterial drugs.

Three cases of crescentic glomerulonephritis associated with rifampicin have been reported [2–4]. One author [3] withdrew rifampicin but with little improvement in renal function. Murray et al. [4] demonstrated a good result with the use of steroids and cyclophosphamide, the same regimen used by Chan et al. [2]. In this latter case rifampicin was not withdrawn and the patient died having refused dialysis.

We chose to discontinue rifampicin and use steroids as an immunosuppressive agent plus introduction of an alternative third anti-tubercular drug to ensure the severe infection remained well controlled, with favourable results regarding renal function, however the patient remains nephrotic.

The small number of cases reported plus, the persisting question about the exact pathomechanism behind the renal damage makes it difficult to give recommendations. The limited published evidence strongly supports both the withdrawal of rifampicin and the use of immunosuppressive drugs (either high dose steroid alone, or in combination with cyclophosphamide). Careful consideration however must be given to the fact that the risks of overwhelming infection precipitated by immunosuppression might outweigh the benefits for renal function.

Department of Renal Medicine
Royal Preston Hospital
Preston, UK

A. Kistler
D. W. P. Lappin
R. A. Coward


The heterogeneity of glomerulonephritis associated with HIV

Sir,

HIV-associated nephropathy (HIVN) has been considered the most specific renal lesion in patients with HIV infection. This entity is clinically characterized by heavy proteinuria, varying degrees of renal insufficiency and rapid development of end-stage renal disease. Findings on microscopy consist of a focal ‘collapsing’ glomerulosclerosis with severe tubulo-interstitial disease and intratubular atypical inclusions on electron microscopy [1]. However, several immunocomplex glomerulonephritis (ICGN) complicating AIDS have been reported [2–8], both in clinical and autopsy series.

It is now well established that cryoglobulinemic glomerulonephritis is a hepatitis C virus associated glomerular disease [9,10]. HIV patients are often coinfected with hepatitis C (HCV) and B viruses. However, information concerning renal clinical and pathologic abnormalities in this coinfected population is scarce.

We observed four patients with HIV disease coinfected with HCV who underwent a renal biopsy after presenting clinically with a glomerulonephritic syndrome.

**Cases.** We performed percutaneous renal biopsy on four HIV patients. All were white caucasian men, with a mean age of 29.7 years (range 25–33 years). Three had been intravenous drugs abuser and one had a transfusion-associated HIV. Renal presenting symptoms were proteinuria in three cases and acute renal failure in the fourth (Table 1). All four were normotensive. The three ex-addicts patients were anti-HCV positive by RIBA-2. Serologic studies for hepatitis B markers revealed the following: hepatitis B surface antigen (HBsAg) was negative in all of them, antibody to hepatitis B antigen (HBeAb) was negative in two and positive in two, and antibody to hepatitis B core antigen was positive in four. Renal biopsy showed a membranous nephropathy in two patients, focal segmental glomerulosclerosis in one and diffuse proliferative endocapillary in one.

The follow-up of the patients was total recovery in one, moderate renal failure in two and end-stage renal disease in one.

**Discussion.** We report four patients suffering from HIV infection with glomerular disease, three of them were coinfected with HCV. Although HCV/HIV co-infection is found...