Letters

Focal sclerosis with tip lesions secondary to polycythaemia vera

Sir,

Secondary erythrocytosis due to increased erythropoietin production is occasionally associated with renal disease such as renal neoplasia, renal artery stenosis, cysts, IgA nephropathy, focal sclerosis, nephrosclerosis, and chronic glomerulonephritis. However, renal impairment secondary to true polycythaemia vera (PV) has been reported only in very few cases. We observed a patient with a glomerulopathy with symptomatic proteinuria after a 4-year history of PV who showed marked clinical regression after consistent therapy by regular phlebotomy.

Case. A 52-year-old male presented with new-onset frothy urine and lower-leg oedema and was admitted for investigation of proteinuria of 4 g in 24 h. Four years ago a high haematocrit (61%) was found during routine investigations and the diagnosis of PV was made after bone-marrow aspiration. At that time urine examination and serum creatinine
were normal. PV had been treated by occasional venesections (total of five in 4 years). There was no family history of renal disease and no known heart or lung disease.

On examination the patient was plethoric with pedal oedema, the spleen was enlarged, blood pressure was 160/90 mmHg. Fundus examination revealed a hyperemic disc and tortuous vessels. Laboratory results were as follows: haemoglobin (Hb) was 18.2 g/dl, haematocrit 54.6%, red blood cell count 59 x 10^6, total leucocyte count 10.3 x 10^9 with a normal differential count, platelets 4.1 x 10^12. Leucocyte alkaline phosphatase was elevated to 140 (normal 20–95). Serum erythropoietin determined by radioimmunoassay was 12 mU/ml (normal 10–39 mU/ml). Serum creatinine was 1.1 mg/dl, serum protein 65 g/l with albumin 35 g/l, BUN 15 mg/dl, and 24-h protein revealed glomerular proteinuria of 1.2 g with transferrin 30.0 mg/l, albumin 393 mg/dl, ß-1-microglobulin 5.5 mg/l. The bone marrow was hypercellular and showed proliferation of all three cell lines. Arterial blood gas analysis showed pO₂ 95 mmHg. Fundus examination revealed a hyperaemic disc and tortuous vessels. Laboratory results were as follows: described a patient who presented with new-onset proteinuria 4 years after the diagnosis of PV. The marked regression of proteinuria indicates resolution of the renal disease and no known heart or lung disease. Arterial blood gas analysis showed pO₂ 93.6 mmHg prognosis; however, inframembranous hyalinosis or progression to global sclerosis may also evolve. Consistent phlebotomy for lowering the haematocrit in the asymptomatic and stable patient, proteinuria was markedly reduced after 6 months of maintaining haematocrit consistently below 50% by venesection, and serum creatinine remained normal. After 18 months, the patient remains asymptomatic with only low-grade proteinuria. Long-term follow-up of this patient will be required to show whether the remission of proteinuria indicates resolution of the renal changes and a good prognosis. We suggest regular screening for renal impairment in patients with PV as renal complications can be prognostically important and may be prevented by consistent lowering of haematocrit.

Consistent phlebotomy for lowering the haematocrit approached clinically beneficial to the course of renal disease in our patient. Although for ethical reasons we did not perform a second renal biopsy to establish histological regression in the asymptomatic and stable patient, proteinuria was markedly reduced after 6 months of maintaining haematocrit consistently below 50% by venesection, and serum creatinine remained normal. After 18 months, the patient remains asymptomatic with only low-grade proteinuria. Long-term follow-up of this patient will be required to show whether the remission of proteinuria indicates resolution of the renal changes and a good prognosis. We suggest regular screening for renal impairment in patients with PV as renal complications can be prognostically important and may be prevented by consistent lowering of haematocrit.

Comment. Very few cases of renal complications of PV are reported in the literature [1–4]. Our patient developed nephrotic range proteinuria 4 years after the diagnosis of PV; the histology of a renal biopsy showed focal segmental glomerulosclerosis with tip lesion. Tip lesions are an abnormality of the glomerulo-tubular junction probably due to prolapse of visceral epithelial cells into the tubular origin that have been described as early segmental lesions and are typical of secondary glomerulopathies [5]. Tip lesions are associated with a relatively good prognosis [6]. A secondary glomerular impairment due to PV was diagnosed, given the onset of renal symptoms 4 years after the diagnosis of PV and the histological findings. The marked regression of symptoms and proteinuria after consistent PV therapy by venesection supports this diagnosis.

PV associated with parenchymal renal disease has been occasionally reported; however, only five cases developed renal impairment after a history of PV [1–4]. Factors associated with polycythaemia such as hyperperfusion of glomeruli, hyperviscosity-induced circulatory disturbance, and especially vascular thrombosis might contribute to the pathogenesis and progression of renal disease in PV. Sharma et al. [3] described a patient who presented with new-onset proteinuria 2 years after PV had been diagnosed. As in our patient, they found a marked reduction in proteinuria after normalization of haematocrit. Renal biopsy in their patient revealed focal sclerosis and they suggested altered renal haemodynamics in PV as pathogenic factors. Other authors described diffuse mesangial proliferation and focal tubular atrophy with interstitial fibrosis in patients with PV [2,3]. In our patient demarcated segmental lesions of the glomerular tuft were noted and electron microscopy revealed marked vacuolization of podocytes typical of glomerular tip lesions. Early glomerular tip lesions are thought to have a relatively good prognosis; however, inframembranous hyalinosis or progression to global sclerosis may also evolve.

Consistent phlebotomy for lowering the haematocrit appeared clinically beneficial to the course of renal disease in our patient. Although for ethical reasons we did not perform a second renal biopsy to establish histological regression in the asymptomatic and stable patient, proteinuria was markedly reduced after 6 months of maintaining haematocrit consistently below 50% by venesection, and serum creatinine remained normal. After 18 months, the patient remains asymptomatic with only low-grade proteinuria. Long-term follow-up of this patient will be required to show whether the remission of proteinuria indicates resolution of the renal changes and a good prognosis. We suggest regular screening for renal impairment in patients with PV as renal complications can be prognostically important and may be prevented by consistent lowering of haematocrit.