Sir,

Renal failure occurring during administration of recombinant interleukin-2 (rIL-2) for advanced cancer has been attributed to pre-renal factors such as rIL-2-induced capillary leak syndrome or cardiac dysfunction and to the inhibitory effect of rIL-2 on the synthesis of renal prostaglandins [1-3]. The induction of proteinuria is dependent on the commercial source of rIL-2 [4]. Renal function usually returns to normal after discontinuation of rIL-2. Structural damage to the kidneys has not been reported.

We describe a case of acute interstitial nephritis during continuous intravenous administration of rIL-2 in a 58-year-old Caucasian male with metastatic renal carcinoma. Five weeks after a left-sided nephrectomy, treatment with continuous intravenous infusion of rIL-2 9 × 10^6 IU/m^2/h (EuroCetus, Amsterdam) was started through a central venous catheter with an implanted subcutaneous reservoir. Influenza-like symptoms were treated with paracetamol throughout the treatment period. After 2 weeks, a transient erythematous rash and persistent leukocytosis and eosinophilia (up to 64%) developed. At 3 weeks, a thrombosis of the central venous line was treated with streptokinase (5,000 U/h for 20 h). During the entire period of rIL-2 administration, weight gain was minimal and blood pressure remained within the normal range. No other drugs were administered.

At the end of the 6th week of treatment, oliguria developed and plasma creatinine concentration rose from a baseline of 130 to 1,280 μmol/L. By courtesy of Dr. J.G. van de Tweel, ultrasound examination, no dilatation of the collecting system of the right kidney was found. Renal failure persisted after treatment of the urinary tract infection prompting renal biopsy on the 14th day of renal failure. It showed essentially normal glomeruli, but a dense interstitial infiltrate consisting of lymphocytes, plasma cells, neutrophilic and eosinophilic granulocytes. The infiltrate extended into the tubules (fig 1). There was no evidence of tumor in the biopsy.
specimen. Renal function was restored after a period of hemodialysis and methylprednisolone pulse therapy (fig. 2).

818 µmol/l. Renal function deteriorated despite discontinuation of rIL2, and infusion of blood and crystalloids had no effect other than inducing overhydration. Laboratory investigations at that time showed WBC 19.2 x 10^7/l and creatinine 1,109 µmol/l. Urine analysis yielded only slight proteinuria, the fractional sodium index was 13% (normal < 1%). The sediment showed many WBC and RBC per high-power field but no cellular casts. Urine culture yielded Streptococcus agalactiae sensitive to amoxicillin probably related to the bladder catheter that had been introduced at the start of renal failure. On

Fig. 2. Time course of acute renal failure during treatment of metastatic renal carcinoma with interleukin-2.

Urine volume l/d

Acute interstitial nephritis is usually related to exposure to drugs or systemic infections. It is probably immune-mediated but the precise etiology is not known [5]. The time course of the renal injury in this patient indicates that rIL2 is the most likely cause of the acute interstitial nephritis.

Acute renal failure during rIL2 treatment is not always prerenal. In the absence of the vascular leak syndrome or hypotension, the possibility of interstitial nephritis should be taken into account and confirmed by renal biopsy. Treatment with corticosteroids should be considered [6].

References


