Acute Interstitial Nephritis and Idiopathic Cranial Diabetes Insipidus

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was 134 mmol/l and potassium 4.9 mmol/l. Serum creatinine was raised to 149 μ mol/l (1.68 mg/dl), urea 4.4 mmol/l (29.7 mg/dl), and they continued to increase to 540 μ mol/l (6.1 mg/dl) and 17 mmol/l (103 mg/dl), respectively, over 1 week. There was type IV renal tubular acidosis with serum bicarbonate 17 mmol/l, chloride 112 mmol/l, potassium 5.5 mmol/l and a simultaneous urine pH of 7. The globulin level was increased to 48 g/l, with polyclonal increase in serum immuno-globulin G to 2,100 mg/dl (normal 700-1,850).

Dear Sir,

We present here a case of idiopathic acute interstitial nephritis (AIN) in a patient with idiopathic cranial diabetes insipidus (DI). The possibility of both conditions having an auto-immune pathogenesis is discussed.

A 27-year-old Chinese female presented to the University Medical Unit, Queen Mary Hospital, in August 1982 with polydipsia and polyuria for 2 years. Physical examination was normal. Her blood pressure was 110/70 mm Hg. Her serum sodium was 141 mmol/l, potassium 3.9 mmol/l, chloride 110 mmol/l, bicarbonate 23 mmol/l, glucose 5.0 mmol/l (90.2 mg/dl), urea 3.4 mmol/l (20.6 mg/dl), creatinine 72 μ mol/l (0.81 mg/dl), albumin 46 g/l and globulin 33 g/l. Complete blood picture, serum calcium, phosphate, urate transaminases and alkaline phosphatase were normal. Antinuclear antibody (ANA) was absent. Urinalysis was normal. Simultaneous serum and urine osmolalities were 290 and 93 mosm/kg, respectively. X-rays of the chest and pituitary fossa were normal. The water deprivation test showed impaired urinary concentration capacity responsive to exogenous 1-deamino-8-D-arginine vasopressin, compatible with partial cranial DI. Computerized tomography showed no abnormality in the hypothalamic-pituitary region. Her DI was satisfactorily controlled with nasal 1-deamino-8-Z-arginine vasopressin.

She remained stable until May 1988, when she developed malaise and oliguria. There was normochromic normocytic anaemia with haemoglobin 7.4 g/dl and reticulocyte count 0.5%. White cell count was normal; eosino-philia was absent. Erythrocyte sedimentation rate was elevated to 149 mm. Serum sodium

Fig. 1. Light micrograph of renal biopsy, showing heavy cortical infiltration by lymphocytes, polymorphs and plasma cells. There is marked interstitial oedema. The tubules contain cellular

debris, and the central dilated tubule is focally ulcerated with exudation of fibrin- and necrotic material. HE. $\times 150$.

Serum albumin was 30 g/l, and the levels of urate, calcium, phosphate, transaminases and alkaline phosphatase were normal. There was no eosinophiluria or glycosuria. Proteinuria amounted to 0.25 g/24 h, and creatinine clearance was 12 ml/min. ANA became slightly positive at 1:50, anti-DNA and anti-extractable nuclear antigen (including anti-SSA and anti-SSB) were absent. Serum immunoglobulin E, complement components C3 and C4 were normal, and cryoglobulin was absent. Schirmer's test demonstrated normal tear

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production. There was no evidence of mycobacterial or viral infection. Renal biopsy showed acute interstitial nephritis with prominent interstitial infiltration by lymphocytes, plasma cells, polymorphs, and tubular ulceration and infiltration by polymorphs (fig. 1). There was no eosinophilic infiltration or granuloma formation. Immunofluorescence was negative. No drug or herb intake could be incriminated. Prednisolone 40 mg daily was started. Serum creatinine, renal tubular dysfunction, and erythrocyte sedimentation rate normalized within 4 weeks.

Haemoglobin rose to 12.1 g/dl, and ANA titre decreased to 1:10. Prednisolone was tapered off after 16 weeks. Two months later, the disease relapsed with creatinine rising to 280 $\mu\text{mol/l}$ (3.2 mg/dl), erythrocyte sedimentation rate 140 mm and haemoglobin 8.9 g/dl. There was proximal renal tubular acidosis, renal glycosuria and raise of amino acid excretion to 23.2 mmol/24 h (normal 3.6-14). Fractional phosphate excretion was normal. ANA titre increased to 1:250; anti-DNA and anti-extractable nuclear antigen were absent; the immunoglobulin G level was 1,750 mg/dl. Prednisolone was restarted. Renal impairment and proximal tubular dysfunction resolved in 6 weeks, and ANA became negative. She is currently in remission, taking prednisolone 5 mg daily, 20 months after the relapse.

An association between idiopathic AIN, uveitis and idiopathic hypoparathyroidism has been recognised [1, 2]. This is the first report of an association between idiopathic AIN and idiopathic cranial DI. The pathogenesis of AIN is complex, but the predominance of T lymphocytes in the renal intersti-

tium suggests a role for cell-mediated immunological injury [3]. In our patient, the elevated ANA titre and immunoglobulin G level, and their decrease following immunosuppression, pointed towards an auto-immune pathogenesis. There has also been evidence that both uveitis and idiopathic hypoparathyroidism were of probable auto-immune origin [4]. Furthermore, auto-antibodies to vaso-pressin-producing cells have been demonstrated in idiopathic cranial DI [5]. We therefore postulate that idiopathic AIN, cranial DI, uveitis and hypoparathyroidism may all be manifestations of an underlying auto-immune diathesis.

The clinical and histological presentations of AIN in our patient were typical. Eosinophilia and eosinophilic infiltration of the renal interstitium had been found in only a minority of cases [1]. Eosinophiluria, reported in 40-100% of patients, could be masked by the release of cytoplasmic granules upon eosinophil activation [6]. Proximal renal tubular dysfunction is a frequent manifestation of idiopathic AIN [1]. In contrast, the sequential appearance of distal and proximal tubular dysfunction has not been described previously.

Following reports of spontaneous recovery from AIN, the genuine therapeutic efficacy of steroids was doubted [7]. However, the rapid relapse of AIN in our patient following cessation of

the steroid and the prompt and sustained improvement with reinstitution of immunosuppression lend strong support to the beneficial effect of steroids in this disorder.

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