Immu-no-allergic interstitial nephritis related to fluindione: first biopsy proven cases

Sir,

Drug-induced acute interstitial nephritis (AIN) can cause end stage renal failure. Withdrawal of imputable drugs is the best treatment, and requires early recognition. We report the first two biopsy-proven cases of fluindione-related AIN indicating that fluindione must be included in the list of imputable drugs.

Case 1. A 72-year-old man was admitted to our unit for acute renal failure (serum creatinine 353 μmol/l vs 107 μmol/l at baseline). He had started fluindione for atrial fibrillation five weeks before. Clinical examination was normal. There was no eosinophilia. Urine protein/creatinine ratio was 25 mg/mmol, containing low molecular weight protein without albumin. There was no haematuria or pyuria. Renal ultrasonography was normal. Fluindione was stopped at admission. Transjugular renal biopsy disclosed interstitial lymphocytic infiltration with severe tubulitis. Immunofluorescent studies revealed no immune deposits. The renal function returned to baseline level 2 weeks after fluindione was stopped, without corticosteroid therapy.

Case 2. An 80-year-old woman, who had experienced a phlebitis treated with fluindione 4 months earlier, was admitted to the medical unit for contralateral ilio-femoral phlebitis. Her baseline serum creatinine level was 100 μmol/l due to nephrosclerosis. After initial heparin treatment, fluindione was reintroduced. Twelve days later, serum creatinine level was 181 μmol/l, and then rose to 374 μmol/l. She was transferred in our renal unit, and her clinical examination was normal. There was no eosinophilia. Proteinuria was 0.5 g/day without albuminuria or immunoglobulin light chain: there was no haematuria or pyuria. At ultrasound exploration, kidneys appeared normal, and vena cava and renal veins were free of thrombus. Fluindione was stopped and substituted by heparin. Renal biopsy revealed a marked diffuse interstitial infiltration with mostly lymphocytes and a few polynuclear cells and mild tubulitis. Immunofluorescent studies were negative. Soon after, the patient died of pulmonary embolism despite intensive medical care.

In these two cases, fluindione was implicated as the likely causative agent. In Case 1, the renal function improved after fluindione was withdrawn without corticosteroid treatment. No follow-up was possible in Case 2. As no other new drug was introduced, we consider these cases as fluindione-induced immuno-allergic AIN. Only two cases have previously been reported [1,2], but none was biopsy-proven. In contrast with our report, these cases presented extra-renal involvement including hyperthermia associated with cutaneous manifestations. Delays between fluindione introduction and disease onset were 3 and 8 weeks, which is comparable with the 5-weeks delay observed in Case 1, but longer than the usual 10 days delay in drug-induced AIN [3]. In Case 2, the delay was 12 days, but as the patient had already been exposed to fluindione, it is compatible with a re-exposure immuno-allergic side-effect.

Physicians should be aware of this severe side-effect and of its potential clinical latency.


Fluoroquinolone-induced acute interstitial nephritis in immunocompromised patients: two case reports

Sir,

Nephrotoxic side effects related to the use of fluoroquinolones (FQ) are relatively rare, and only four cases were reported with the newer fluoroquinolones (levofloxacin and norfloxacin) [1]. The risk factors and mechanisms were largely unknown. We described two biopsy-proven cases of levofloxacin and ciprofloxacin induced acute interstitial nephritis (AIN) in immunocompromised patients.

Case 1. A 41-year-old Chinese female with known history of systemic lupus erythematosus was treated with levofloxacin 200mg twice a day for 10 days because of urinary tract infection. At the first presentation, biochemical tests were normal except lymphopenia (lymphocyte count, 1067/μl) and bacteriuria. However, fever developed after 1 week of levofloxacin treatment. Physical examination revealed excessive extracellular fluid volume. Laboratory studies showed serum creatinine 5.4 mg/dl, serum urea nitrogen (BUN) 27 mg/dl, WBC count 8610/μl with 60.4% neutrophils, 22.9% lymphocytes and 2.4% eosinophils. Urinalysis revealed WBC 2–5/hpf without bacteria. Immunoglobulin, complement and ANA were all normal. A renal biopsy showed normal glomeruli with mild hypercellularity, interstitial infiltration with mononuclear cells, no immunofluorescent expression, and no electron dense deposits. A diagnosis of AIN was made.