Sir,

Fungal peritonitis is a rare but serious complication of peritoneal dialysis (PD) and is associated with significant mortality. Observational studies suggest that it accounts for approximately 2–7% of PD related peritonitis, but it can be difficult to clear, can result in catheter loss and can frequently lead to conversion to haemodialysis [1–3].

Case. A 65 year-old male patient on automated peritoneal dialysis (APD) for almost two years was admitted with a 24h history of dysuria and fever. He had a history of recurrent urinary tract infections during the last 3 months. He had received multiple antibiotic regimes for different pathogens and was carrying an indwelling urinary catheter. He had no prior episodes of PD-related peritonitis.

On admission, his temperature was 38.5°C, pulse 100 bpm and blood pressure 120/70 mmHg. His abdomen was slightly distended and he had pain on the pubic area with no rebound or guarding and normal bowel sounds. The PD catheter exit site did not show any evidence of infection. Laboratory investigation was remarkable for leucocytosis. Urine examination revealed severe pyuria. A urine culture was taken and he was empirically started on i.v. ciprofloxacin, as pyelonephritis was suspected. However, during the first 24 h after admission, he started complaining for abdominal pain and distension, a cloudy peritoneal fluid was noticed and the diagnosis of peritonitis was made. He was transferred to continuous ambulatory peritoneal dialysis and was put on intraperitoneal administration of cefuroxime and tobramycin, according to our PD-related peritonitis treatment protocol.

However, on the third hospital day, fungi were isolated from his urine, blood and peritoneal fluid cultures. The previous regimen was stopped and he was started on fluconazole i.p. and i.v. and liposomal amphotericin B i.v. The patient remained febrile, complained of severe abdominal pain and became hypotensive. As the patient was becoming septic, the PD catheter was surgically removed and a right internal jugular venous catheter for haemodialysis was placed. The isolated pathogen was *Candida albicans* resistant to all azoles and sensitive only to amphotericin B. The patient remained febrile, even after six days of amphotericin B administration. The addition of caspofungin to the initial regimen seems to have contributed to the favourable outcome in a way, but the patient did not improve and remained febrile, even after six days of amphotericin B administration. The diagnosis of peritonitis was made. He was transferred to continuous ambulatory peritoneal dialysis and was put on intraperitoneal administration of cefuroxime and tobramycin, according to our PD-related peritonitis treatment protocol.

The patient remained febrile, complained of severe abdominal pain and distension, a cloudy peritoneal fluid was noticed and the diagnosis of peritonitis was made. He was transferred to continuous ambulatory peritoneal dialysis and was put on intraperitoneal administration of cefuroxime and tobramycin, according to our PD-related peritonitis treatment protocol.

In conclusion, we report a case of fungal peritonitis due to *Candida albicans* resistant to azoles, with signs of systemic candidiasis (candidaemia) that responded to a combination therapy with caspofungin and amphotericin B without adverse effects. We do not suggest the routine empirical use of caspofungin for fungal peritonitis in PD as the available data are very limited, but our favourable outcome might indicate the addition of a new antifungal agent in our armamentarium against severe and life-threatening fungal infections in patients undergoing peritoneal dialysis.

**Conflict of interest statement.** None declared

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**Comments.** Fungal peritonitis is uncommon, but by no means rare (2–7%). It is associated with significant mortality (20–30%). Prior use of antibiotics, the immunosuppressed state, diabetes mellitus and malnutrition (low serum albumin levels) are risk factors for fungal peritonitis [2–4].

Our patient had received multiple antibiotic regimens in the past three months for recurrent urinary tract infections without any antifungal prophylaxis and he was carrying an indwelling urinary catheter. He also had evidence of candidaemia and systemic candidiasis, as *Candida albicans* was isolated from the urine specimens, blood cultures and peritoneal fluid. A possible explanation for the peritonitis episode might be the urinary tract colonization with fungus, as the patient had received many antibiotics without antifungal prophylaxis, resulting in candidaemia and peritonitis through the haematogenous route. Early removal of the PD catheter might have contributed to our patient’s favourable outcome in a way, but the patient did not improve and remained febrile, even after six days of amphotericin B administration. The addition of caspofungin to the initial regimen seems to have contributed to the favourable outcome, as the patient became afebrile only after three days of combination therapy.

There is no established therapy for fungal peritonitis and most centres use combination therapies with variable success. Most authorities suggest early PD catheter removal, because the catheter is usually contaminated with fungi [4]. Echinocandins is a new class of antifungal agents and caspofungin was the first of the class been licensed. There is only one report in the literature regarding caspofungin use in peritoneal dialysis, but no report of combination of caspofungin with amphotericin B. Madariaga et al. have described a patient intolerant to amphotericin B who presented peritonitis due to *Trichosporon inkin* and had a favourable outcome by caspofungin administration [5].
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. Transjugal 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 examination was normal. Fluindione was stopped and substituted by heparin. Renal biopsy examination was normal. Fluindione was stopped at admission. Transjugal 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.

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 200 mg 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) which had been noted for 2 years. Urinalysis demonstrated WBC 25–50 per high-power field (hpf) and bacteriuria. However, fever developed after 1 week of levofloxacin treatment. Physical examination revealed excessive extra-cellular 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.