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LETTERS TO THE EDITOR

Chronic bacterial prostatitis and relapsing *Enterococcus faecalis* bacteraemia successfully treated with moxifloxacin

Chronic bacterial prostatitis (CBP) caused by *Enterococcus* spp is difficult to treat because the registered antimicrobial agents to treat CBP that penetrate the prostate sufficiently, fluorquinolones and trimethoprim—sulfamethoxazole, are less effective for enterococcal infections.[1—3] Here we report a case of recurrent *Enterococcus faecalis* bacteraemia due to underlying CPB which was eventually cured with moxifloxacin.

A 47-year-old man was admitted to undergo a cadaveric kidney transplantation. Two weeks postoperatively, he developed signs of septicaemia from a urinary tract infection which were confirmed by blood and urine cultures that both grew *E. faecalis*. The patient was treated with amoxicillin (1000 mg q.i.d i.v. for 1week, then oral 750 mg t.i.d for 3 weeks). During the second week of treatment, a double J ureteral catheter and a bladder catheter were removed. Ultrasonography showed a normal kidney transplant and a normal bladder. The patient recovered and repeated cultures of urine were sterile. Two weeks after finishing his antibiotic treatment, the patient was readmitted because of fever and chills. Urosepsis was suspected because urine sediment contained leucocytes and streptococci. Again blood and urine cultures grew *E. faecalis*. There were no stigmata of endocarditis. The patient was treated with amoxicillin (1000 mg q.i.d for 2 weeks) and he quickly recovered. The urine became sterile. Two weeks after this antibiotic course, the patient yet again was readmitted with a similar clinical picture. Cultures of blood and urine grew *E. faecalis*. Repeated urologic work-up revealed no abnormalities. The prostate was soft and tender. By exclusion, chronic bacterial prostatitis was diagnosed.

Qualified by *E*-test, the organism was susceptible to amoxicillin, nitrofurantoin and moxifloxacin (MIC 0.19 mg/l) and intermediate susceptible to linezolid (MIC 3 mg/l). The MIC for ciprofloxacin was 1.5 mg/l. After treatment of bacteraemia with amoxicillin (1000 mg q.i.d. i.v. for 10 days) the patient was treated for chronic bacterial prostatitis with moxifloxacin (400 mg o.d. for 6 weeks). The patient recovered and repeated urine and semen cultures remained negative. During 6-month follow-up there has been no recurrence of fever, bacteraemia or urinary tract infection. The patient developed a severe graft rejection with irreversible renal insufficiency requiring haemodialysis. During this episode asymptomatic bacteruria with *E. faecalis* was once recognized but not treated. The patient became anuric and during further 6-month follow-up he remained well on haemodialysis without episodes of infection.

Drugs that are lipid-soluble, non-ionized, small molecules and not bound to plasma proteins are the most effective in penetrating the prostatic gland.[1,2] Based on these pharmacokinetic characteristics, fluoroquinolones remain the treatment of choice in CPB. Water-soluble agents, as amoxicillin, might be used in acute prostatitis because the prostatic barrier against antimicrobial penetration is disrupted by severe inflammation but this not recommended for treatment of CBP.[4]

Moxifloxacin has greater efficacy against *Enterococcus* spp compared to ciprofloxacin with comparable pharmacokinetics.[5] Therefore moxifloxacin was likely to be the most effective in this patient. Based on the successful outcome of this first case we conclude that moxifloxacin is a potential treatment option in CPB patients with susceptible *E. faecalis*.

Conflict of interest

The authors have no conflict of interest.

References

1. Barza M. Anatomical barriers for antimicrobial agents. *Eur J Clin Microbiol Infect Dis* 1993;**12**(Suppl. 1):S31—5.
2. Charalabopoulos K, Karachalios G, Baltogiannis D, Charalabopoulos A, Giannakopoulos X, Sofikitis N. Penetration of antimicrobial agents into the prostate. *Chemotherapy* 2003 Dec;**49**(6):269—79.
3. Pronk MJ, Pelger RC, Baranski AG, van Dam A, Arend SM. Cure of chronic prostatitis presumably due to *Enterococcus* spp and gram-negative bacteria. *Eur J Clin Microbiol Infect Dis* 2006 Apr;**25**(4):270—1.
4. Wagenlehner FM, Naber KG. Current challenges in the treatment of complicated urinary tract infections and prostatitis. *Clin Microbiol Infect* 2006 May;**12**(Suppl. 3):67—80.
5. Aktas Z, Gonullu N, Salcioglu M, Bal C, Ang O. Moxifloxacin activity against clinical isolates compared with the activity of ciprofloxacin. *Int J Antimicrob Agents* 2002 Sep;**20**(3):196—200.

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Invasive fungal sinusitis in patients treated with fludarabine

Sir

The majority of patients with invasive fungal sinusitis (IFS) are immunocompromised at the time of disease onset. Stem cell transplantation, prolonged neutropenia, immunosuppression following solid organ transplantation, diabetes mellitus, HIV infection and high-dose corticosteroids are risk factors.[1] IFS is historically associated with a mortality of >50%.[2] *Aspergillus* spp. and zygomycetes are the commonest causative organisms.[1] We performed a service review to determine the clinical features, risk factors and outcome of patients with invasive fungal sinusitis at our institution.

Potential cases of IFS were retrospectively identified from histopathology, microbiology, radiology and discharge coding databases for the period from 1st January 2003 to 30th September 2006 and case notes were reviewed. Addenbrooke's hospital has specialist services including haematology—oncology, stem cell and solid organ transplantation and otorhinolaryngology. IFS was classified as proven, probable or possible.[3] Antigen detection (e.g. galactomannan) and molecular techniques (e.g. PCR) were not available in the study period. The study was approved by the local ethics committee and all patients had given written informed consent to be included in the study.

Five proven and one probable case of IFS were identified in the study period (Table 1). The age ranged from 7 to 62 (median 53.5 years); and four were female. All were haematology patients with acute myeloid leukaemia (AML, five patients) or myelodysplasia (MDS, one patient). *Aspergillus* spp. was responsible for five cases (*Aspergillus fumigatus* (1), mixture of *A. fumigatus*/*Aspergillus flavus* (1), three culture negative) and one case was due to the zygomycete *Rhizopus* spp. (culture positive).

With the exception of one patient with facial paraesthesia, all patients presented with facial pain and all had additional symptoms (rhinorrhoea or facial swelling). All had been neutropenic for <14 days (mean 10 days). All affected patients had received fluconazole prophylaxis and all but one patient were hospitalized in HEPA-filtered positive pressure side rooms.

All patients with IFS were treated with liposomal amphotericin B (LAB, AmBisome®, Gilead), initiated empirically after 72 h of fever despite broad-spectrum antibiotics. All cases required ≥5 mg/kg/day to control the infection. Four underwent surgical debridement. The total cumulative per kilogram dose and duration of treatment varied considerably (108—305 mg, 24—63 days). No patients died due to IFS. However, three patients had persisting neurological dysfunction, four had significant disruptions to chemotherapy and one had treatment abandoned. Two patients who had treatment disruptions died (7 and 8 months later) of relapsed disease. All five patients who underwent further chemotherapy were given secondary prophylaxis with systemic antifungal therapy and IFS did not recur.

Notably, no cases occurred in patients following stem cell or solid organ transplantation and no patient had acidosis, diabetes or high-dose corticosteroid use, despite there being 253 stem cell transplants (89 allogeneic, 164 autologous) and >500 solid organ transplants (243 liver, 285 kidney) in the study period. Furthermore, all patients developing IFS had received fludarabine-based chemotherapy and, in 5/6 cases, IFS developed within 21 days of receiving fludarabine. Thirty-nine of 121 (32%) patients treated for myeloid malignancy in the study period received fludarabine-based regimens compared to none of the 82 patients who received an alternative regimen. This was highly significant (Chi square analysis $p < 0.001$). Whilst myeloid leukaemia is a recognized risk factor,[2] the association with fludarabine has not been previously described. Fludarabine causes T-helper cell depletion which is important in defending against invasive fungal infection.[4] Fludarabine has been suggested to increase risk of invasive pulmonary aspergillosis in leukaemia patients.[5]

IFS is a serious complication of intensive chemotherapy though our experience indicates that mortality may be lower since the introduction of lipid-associated preparations of amphotericin B. Our findings support recent studies with mortality rates of approximately 20%.[1,6] None of our patients died. Haematology patients had a lower mortality than diabetic patients in one study.[1] The same study found infection with *Aspergillus* spp. rather than zygomycetes to be another favourable prognostic indicator.[1] All our patients had early therapy with LAB, which we have previously found to be associated with a lower mortality than treatment with conventional amphotericin in invasive pulmonary aspergillosis.[7] Culture is required in all cases to direct antifungal chemotherapy. Initial therapy should be broad-spectrum. Currently available parenteral echinocandins and azoles have limited activity against zygomycetes, although posaconazole, currently available in oral formulation only, will broaden therapeutic options.

Specialists in infection should be aware that novel risk factors for IFS are emerging with the development of aggressive chemotherapeutic regimens. At our institution,