didemia persisted for 9 days and disappeared only after therapy with fluconazole, liposomal amphotericin B, caspofungin, and nystatin (figure 1). All 3 patients fully recovered after resolution of leukopenia.

Resistance to amphotericin B but not to fluconazole has been reported among some *C. kefyr* isolates [2, 3]. Antifungal susceptibility testing revealed MICs for fluconazole of 0.19 μg/mL for the isolate from patient 2 and 0.25 μg/mL for the isolate from patient 3, indicating microbiologic susceptibility. Caspofungin is at least as effective as amphotericin B for the treatment of candidemia [4, 5]. Our results indicate that caspofungin is also effective against *C. kefyr* fungemia.

The unusual occurrence of *C. kefyr* bloodstream infections in patients with neutropenia may be linked to dietary habits, because patients 2 and 3 had a history of ingesting dairy products containing live *C. kefyr.* This organism has been isolated from multiple milk products (e.g., bovine milk contains 16 different species of yeast, including *C. kefyr*) [6–8]. Because prophylactic fluconazole treatment (100–200 mg/day, orally) in stem cell transplant recipients has been associated with emergence of infection due to fluconazole-resistant non–*albicans* species of *Candida,* our patients did not initially receive fluconazole prophylaxis [9]. However, recently, higher doses of fluconazole (400 mg/day) given for 75 days after stem cell transplantation have been reported to provide clinically important protection against invasive yeast infection [10]. The occurrence of *C. kefyr* fungemia reflects the growing diversity of *Candida* species responsible for disseminated infections in neutropenic patients.

Acknowledgments

Financial support. Deutsche Krebshilfe (10-1801-Re1 to C.R.); and the International Myeloma Foundation (to M.M.).

Potential conflicts of interest. All authors: no conflicts.

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Clinical Infectious Diseases 2005; 41:1365–6

Anti–BK Virus Activity of Ciprofloxacin and Related Antibiotics

SIR—I read with interest the recent article by Leung et al. [1] on the use of ciprofloxacin to decrease the polyoma BK virus load. The authors determined the inhibitory concentrations for the virus using an assay that inhibits the cytopathic effects of the polyoma BK virus. This is a slow and laborious assay that requires an incubation period of 28–35 days. I have used the Gardner strain of the polyoma BK virus to determine the 50% virus inhibitory concentrations of ciprofloxacin and related antibiotics using a faster assay, which employs PCR to measure virus replication directly over a period of 7 days. At the same time, this assay measures the drug concentration that causes a 50% reduction in host cell replication as a measure of drug toxicity. Technical details of this assay have been published [2]. The antiviral activities of different antibiotics measured by this assay are presented in table 1.

These data show that, although the 50% virus inhibitory concentrations of different antibiotics vary from 79.7 to 266.6 μg/mL, the toxicity profile as measured by the 50% reduction in host cell replication also changes proportionately, so that the selectivity index (defined as the ratio of the 50% reduction in host cell replication value to the 50% virus inhibitory concentration value) never exceeds 3.6. To put this in perspective, the pharmaceutical industry generally does not pursue clinical development of antimicrobial drugs that have a selectivity index of <10.0. Thus, these data show that ciprofloxacin and related antibiotics have only a modest anti–polyoma BK virus effect. There is no evidence that any of these compounds are

Table 1. Antiviral activity of ciprofloxacin and related antibiotics against polyoma BK virus.

Drug	No. of experiments	Mean value ± SE		
		IC^{50}, μg/mL	EC^{50}, μg/mL	Selectivity index[a]
Ciprofloxacin	3	216.67 ± 16.7	66.67 ± 16.7	3.6 ± 0.8
Levofloxacin	3	283.3 ± 16.6	266.6 ± 120.2	1.7 ± 0.7
Gatifloxacin	3	283.3 ± 16.6	233.3 ± 16.6	1.2 ± 0.07
Norfloxacin	3	125.0 ± 25.0	137.5 ± 12.5	0.9 ± 0.2
Moxifloxacin	3	108.3 ± 22.1	183.3 ± 16.7	0.6 ± 0.2
Ofloxacin	3	86.7 ± 36.9	79.7 ± 40.6	1.1 ± 0.4
Novobiocin	2	266.8 ± 53.1	240 ± 80.0	1.3 ± 0.7
Coumermycin	3	10.6 ± 3.9	13.6 ± 2.6	0.7 ± 0.2

NOTE. EC^{50}, 50% virus inhibitory concentrations; IC^{50}, 50% reduction in host cell replication.

[a] The selectivity index is defined as the ratio of the 50% reduction in host cell replication to the 50% virus inhibitory concentration.

likely to be significantly more effective than others in clinical use.

Leung et al. [1] have made an interesting observation in that these drugs can have a prophylactic role by virtue of their ability to effectively blunt the peak urinary viral load in bone marrow transplant recipients. However, the low selectivity index makes it uncertain how effective these compounds will be in patients with full-blown hemorrhagic cystitis or polyoma BK virus nephropathy, who typically have extremely high viral loads. Continued efforts to discover drugs with a higher selectivity index are warranted.

Acknowledgments

Financial support. Supported by NIH, NIAID contract #N01-AI-3044.

Potential conflicts of interest. P.S.R.: no conflicts.

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Clinical Infectious Diseases 2005; 41:1366–7

Reply to Randhawa

The data by Dr. Randhawa [1] showed that ciprofloxacin was only modestly active in vitro against polyoma BK virus. The findings, indeed, confirmed our laboratory and clinical data previously reported in [2]. We showed that ciprofloxacin prophylaxis significantly decreased the severity of BK viruria in patients after hematopoietic stem cell transplantation. Furthermore, ciprofloxacin achieved a high urinary concentration, which was comparable to the concentration needed in vitro to suppress polyoma BK virus replication. We also cautioned that the anti–polyoma BK virus activity of ciprofloxacin in vitro was not strong. This implies that ciprofloxacin might be more effective as prophylaxis against hemorrhagic cystitis. In clinically overt cases of hemorrhagic cystitis in which the polyoma BK virus load has already peaked, ciprofloxacin may not be efficacious. However, the prevention of hemorrhagic cystitis is a more important clinical goal, because established hemorrhagic cystitis is notoriously difficult to treat. This is where we think the significance of our results lies. Finally, further screening and study of chemically modified fluoroquinolone derivatives may yield more potent anti–polyoma BK virus agents with better selectivity.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

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Clinical Infectious Diseases 2005; 41:1367