Combination Antibiotic Therapy for Severe Melioidosis

Sir—We read with interest the article by Dorman et al. [1] concerning a case of melioidosis in chronic granulomatous disease. We would like to comment on the therapeutic regimens used in this case.

The authors state that combination therapy is recommended for severe disease. While it is true that some investigators have recommended intravenous combination therapy for treatment of severe disease [2], there is no evidence to support its use. There are only four reported randomized comparative trials of antibiotic therapy for severe melioidosis. The first two trials compared ceftazidime alone [3], or ceftazidime plus trimethoprim-sulfamethoxazole (TMP-SMZ) [4], with a combination of chloramphenicol, doxycycline, and TMP-SMZ. The results of both trials demonstrated a substantial reduction in mortality with use of the ceftazidime-containing regimens. We do not know whether use of TMP-SMZ provides additional benefit. The results of two further trials of β-lactamase inhibitor–containing regimens (amoxicillin/clavulanate or cefoperazone/sulbactam) vs. ceftazidime alone [5] or ceftazidime plus TMP-SMZ [6], did not show significant differences in mortality. Imipenem has also been evaluated as therapy for melioidosis and appears to be effective as a single-agent therapy (A. Simpson, unpublished data).

The combination of imipenem and doxycycline for therapy for melioidosis has never been the subject of clinical investigation. Doxycycline has been shown to antagonize the cidal action of ceftazidime against *Burkholderia pseudomallei* in vitro [7], and it is possible that doxycycline may antagonize imipenem. We recommend caution in the use of untested, potentially antagonistic regimens in treatment of a disease associated with high mortality and relapse rates. This same point applies to the combination of oral cefixime and doxycycline used for maintenance treatment in this case.

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References


Community-Acquired Pneumonia in Human Immunodeficiency Virus–Infected Patients

Sir—Recently I read with interest the article by Baril and colleagues [1] regarding bacterial pathogens causing community-acquired pneumonia (CAP) in HIV-infected patients. Baril et al. reported the predictably high incidence of CAP due to *Streptococcus pneumoniae* and *Haemophilus influenzae* in patients with HIV. However, the authors reported a single case of *Staphylococcus aureus*–related CAP and six cases of CAP due to *Pseudomonas aeruginosa* in HIV-infected patients. The report does not clearly indicate how these cases were diagnosed, but the table suggests that specimens were obtained bronchoscopically, although a semi-quantitative protected specimen brush (PSB) technique was not used. Interpretation of the data is difficult because demographic data on these patients are not provided (e.g., prior antibiotic therapy might have selected out *P. aeruginosa* and *P. aeruginosa* colonized the lower respiratory tract).

It has been my experience and that of others that the bacterial pathogens that cause CAP in patients with HIV are the same as those in the normal population, with a few important exceptions [2–7]. Bacteremic CAPs due to *S. pneumoniae* and *H. influenzae* should alert clinicians to the possibility of HIV infection. Because HIV infection results in decreased cell-mediated immunity, it is not surprising that in addition to the usual respiratory pathogens found in normal hosts, in HIV-infected patients with CAP there is an increased incidence of intracellular bacterial pathogens (i.e., *Salmonella* and *Legionella* species). Other nonbacterial intracellular pathogens that cause pneumonia in HIV-infected patients (e.g., *Pneumocystis carinii* and cytomegalovirus [CMV]) were not the focus of the article.

In normal hosts CAP is due almost exclusively to *S. pneumoniae*, *H. influenzae*, or *Moraxella catarrhalis*. *Klebsiella pneumoniae* is found almost exclusively in patients with chronic alcoholism. CAP due to *S. aureus* almost always occurs in the setting of postviral influenza. *S. aureus* is a cause of CAP only in HIV-infected individuals who have a history of intravenous drug abuse (IVDA) or use of PCP [8, 9]. Similarly, *P. aeruginosa* is not a cause of CAP in normal or nonleukopenic immunocompromised hosts [10].

On the basis of their findings, the authors suggest that clinicians should include antipseudomonal coverage in their empirical cover-