SHORT REPORT: DISEASE SEVERITY AND OUTCOME OF MELIOIDOSIS IN HIV COINFECTED INDIVIDUALS

WIRONGRONG CHIERAKUL,† VANAPORN WUTHIEKANUN, WIPADA CHAOWAGUL, PREMJIT AMORNCHAI, ALLEN C. CHENG, NICHOLAS J. WHITE, NICHOLAS P. J. DAY, AND SHARON J. PEACOCK

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Medical Department, Sappasitiprasong Hospital, Ubon Ratchathani, Thailand; Menzies School of Health Research, Charles Darwin University, Darwin, and The Geelong Hospital, Barwon Health, Geelong Australia; Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford, United Kingdom

Abstract. This study examined whether coinfection with HIV and Burkholderia pseudomallei leads to altered disease severity or outcome associated with melioidosis. Coinfection was detected in only 8 of 524 (1.5%) adults with melioidosis in northeast Thailand. Clinical presentation and acute outcome were similar in HIV-positive and HIV-negative patients.

Melioidosis, an infection caused by the bacterium Burkholderia pseudomallei, is a major cause of community-acquired septicemia in northeast Thailand. A wide spectrum of disease presentations is recognized; septicemia is clinically similar to that caused by other major pathogens, whereas subacute and chronic disease may mimic tuberculosis clinically.1 There may be prolonged latency between presumed exposure and disease, and recurrence after apparent cure is relatively common. Given the clinical features, the intracellular survival of B. pseudomallei, and the lack of protective humoral immunity, it has been suggested that cell-mediated immunity may be important in controlling infection with B. pseudomallei.2,3 However, in contrast with the well-described association between HIV and tuberculosis, the proportion of patients with melioidosis who are coinfected with HIV is low and not significantly different to that in apparently healthy blood donors.4,5 In this case series, we describe the clinical manifestations of patients with melioidosis coinfected with HIV.

A retrospective study was performed of patients presenting to Sappasitiprasong Hospital, Ubon Ratchathani, northeast Thailand, between 1995 and 2001 with culture-proven melioidosis. These patients had been prospectively recruited by our study team through active ward surveillance as part of screening for inclusion into treatment trials. Data were recorded prospectively and admission sera taken in all cases. The patients were followed-up long-term by one of the coauthors (Wipada Chaowagul). Before HIV testing, a clinical database containing a subset of clinical information minus patient hospital or other identifying numbers was created and linked to an anonymous serum sample bank. Seven patients were known to be HIV-positive on presentation with melioidosis, none of whom had a recorded history of an AIDS defining illness. Ethical approval for this study was obtained from the Faculty of Tropical Medicine, Mahidol University, and the Oxford Tropical Research Ethics Committee.

HIV serology testing was performed according to the World Health Organization guidelines. All serum samples were evaluated using a screening test (Serodia-HIV1/2 kit, Fujirebio, Tokyo, Japan). A negative result was interpreted as negative. A positive result was confirmed using a second test (Determine HIV-1/2 kit, Abbott Laboratories, Illinois). Discordant results were repeated in parallel. For these repeat samples, two negatives were classified as negative, two positives as positive, and discrepant results as indeterminate.

A total of 524 patients were evaluated. Of these, 15 were positive for HIV on the screening test, but only 8 were positive for HIV by the second test. All indeterminate test samples were negative on both tests when retested in parallel. Thus, 8 of 524 patients (1.5%) were considered to be infected with HIV. Clinical details for patients who tested as HIV-positive are shown in Table 1. Bacteremia was present on admission in 5 of 8 (63%) coinfected patients, compared with 291 of 561 (52%) patients who were HIV-negative (P = 0.73). The total number of body sites culture positive for B. pseudomallei was not different in the two groups (P = 0.96). No patients were known to have tuberculosis. The duration of hospital stay was shorter for coinfected patients; admission ranged from 1 to 35 days (median, IQR 8 [2 to 9.5] days) for coinfected patients compared with 0 to 324 days (median, IQR 14 [7 to 22] days) for HIV-negative patients (P = 0.047). There was no significant difference between the two groups in mortality (1 of 8 [13%] HIV-positive patients versus 150 of 516 [29%] HIV-negative patients) or recurrent disease (1 of 8 [13%] HIV-positive patients versus 50 of 516 [10%] HIV-negative patients).

Our finding of a low prevalence of HIV infection in patients with melioidosis is consistent with a previous small study in Ubon Ratchathani, where no cases of HIV were found in 121 patients with melioidosis in 1992.6 Additionally, we did not observe a rise in melioidosis rates at our institution coincident with the rise of HIV prevalence in the province, in contrast to rates of other HIV-associated pathogens such as non typhoidal Salmonella spp.7 These figures are similar to those in Darwin, Australia, where only one patient with HIV/AIDS has been noted in 419 melioidosis patients between 1989 and 2005 (Currie BJ, personal communication). The reasons for the lack of interaction between HIV and melioidosis, and indeed the specific immunologic responses that may be protective against B. pseudomallei generally, are poorly understood.

There are several limitations to this study. The number of HIV-positive patients was small. We do not have CD4 count data for the HIV-positive patients; lymphocyte counts were not used as a surrogate as these are likely to be affected by acute illness and are not reliable. Information regarding stage of HIV infection is limited by the anonymous nature of the database, although the 7 patients already known to be HIV-positive did not have advanced disease.
A specific cell-mediated response against *B. pseudomallei* antigens has been noted in immunocompetent survivors of melioidosis when compared with healthy controls and asymptomatic seropositive patients, suggesting that cell-mediated immunity may be important in determining resistance to and the outcome of melioidosis. However, in contrast to diabetes, thalassemia, and renal disease, HIV infection does not appear to be a major risk factor for melioidosis. We conclude that HIV infection does not influence the presentation or outcome of disease due to *B. pseudomallei*.

Reprint requests: Dr. Wirongrong Chierakul, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, 420/6 Rajivithi Road, Bangkok, 10400, and Center for Clinical Vaccinology and Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Churchill Hospital, Oxford OX3 7LJ, United Kingdom.

References: