Bacteremia due to *Helicobacter cinaedi* in two patients with human immunodeficiency virus infection

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AE SIMOR, JL BRUNTON. Bacteremia due to *Helicobacter cinaedi* in two patients with human immunodeficiency virus infection. Can J Infect Dis 1992;3(3):139-141. *Helicobacter cinaedi* (formerly *Campylobacter cinaedi*) has been associated with enteric disease in homosexual men. The authors report two cases of *H cinaedi* bacteremia occurring in patients with human immunodeficiency virus (HIV) infection. These cases illustrate that *H cinaedi* may act as an opportunistic pathogen in patients with HIV infection or the acquired immune deficiency syndrome.

Key Words: *Helicobacter cinaedi* bacteremia, HIV infection

Bactériémies dues à *Helicobacter cinaedi* chez deux patients porteurs du virus de l'immunodéficience humaine

RESUME: *Helicobacter cinaedi* (anciennement *Campylobacter cinaedi*) est associé aux maladies entériques chez les hommes homosexuels. Les auteurs rapportent deux cas de bactériémies à *H cinaedi* chez des patients porteurs du virus de l'immunodéficience humaine (VIH). Ces cas illustrent le fait que *H cinaedi* pourrait agir à titre d'agent pathogène opportuniste chez les patients porteurs du VIH ou atteints du syndrome d'immunodépression acquise.

CAMPYLOBACTER SPECIES ARE FREQUENTLY ISOLATED from homosexual men and have been recovered from patients with the acquired immune deficiency syndrome (AIDS) (1-3). Most patients have symptoms of enterocolitis, although occasionally systemic illness with bacteremia has also been reported. The majority of these infections have been due to either *Campylobacter jejuni* or *Campylobacter fetus* subspecies *fetus*. Two newly recognized and related bacterial species, *Helicobacter cinaedi* and *Helicobacter fennelliae* (formerly

Campylobacter cinaedi and *Campylobacter fennelliae*) (4), have recently been associated with enteric disease in homosexual men (5,6).

The authors report two cases of bacteremia due to *H cinaedi* occurring in patients with human immunodeficiency virus (HIV) infection. These cases provide further information regarding the spectrum of illness associated with this organism and serve to illustrate that *H cinaedi* may act as an opportunistic pathogen in patients with HIV infection.

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CASE PRESENTATIONS

Case 1: A 38-year-old homosexual male with AIDS was admitted to hospital in June 1990 for investigation of fever, cough and dyspnea. The patient had first been found to be HIV antibody positive in 1988 when he developed Kaposi's sarcoma and *Pneumocystis carinii* pneumonia. Subsequently, he developed pulmonary involvement with Kaposi's sarcoma and was started on chemotherapy with adriamycin, bleomycin and vinblastine. Other medications were zidovudine, acyclovir and ketoconazole. Ten days prior to admission the patient developed fever, chills, increasing cough and shortness of breath. He also had mild diarrhea but no abdominal pain.

On examination, the patient was cachectic, febrile, tachycardic and dyspneic. Blood and stool cultures obtained on admission yielded no significant growth. No opportunistic pulmonary infections were identified and the respiratory failure was attributed to progressive pulmonary Kaposi's sarcoma. A colonoscopy revealed edematous mucosa involving the transverse colon. Histopathological examination of a colonic biopsy revealed cytomegalovirus inclusions identified by in situ DNA hybridization. Treatment with ganciclovir was started and continued for three weeks. The diarrhea resolved, but the patient remained febrile. Repeat blood cultures, obtained two months following admission to hospital, yielded *H cinaedi* after five days of incubation. During treatment with erythromycin the patient became afebrile and was subsequently discharged from hospital. Three months later, the patient died of respiratory failure; there was no evidence of recurrent bacteremia.

Case 2: A 35-year-old homosexual male presented to the emergency department in July 1990 with a one day history of fever, chills, myalgias and arthralgias. In the previous two weeks, the patient had also noted mild diarrhea and a cough productive of scanty amounts of sputum. The patient had first been found to be HIV antibody positive in 1987. In the following year, he was hospitalized with bacteremic pneumococcal pneumonia. The patient had had oral candidiasis for several years, but no other opportunistic infections had been identified. Medications included zidovudine, acyclovir and ketoconazole.

On examination in the emergency department, the patient was afebrile and did not appear to be acutely ill. There was oropharyngeal candidiasis, but no other focus of infection was apparent. Cardiopulmonary and abdominal examinations were normal. A chest x-ray was also normal. Blood and urine specimens were obtained for culture and the patient was discharged home from the emergency department with no specific treatment. He continued to complain of intermittent fever, myalgias and diarrhea. Empiric treatment with ciprofloxacin was started and the patient became afebrile with resolution of the diarrhea 48 h later. After five days of incubation, the blood cultures grew *H cinaedi*. Treatment with ciprofloxacin was continued for

10 days, and there has been no recurrence of symptoms after four months of follow-up.

Isolation of *H cinaedi* from the present two patients occurred approximately one month apart. The patients were not sexual partners and had no other known common contacts. Neither of them had a significant history of animal contact or travel. Their isolates were identified as *H cinaedi*-like organisms by accepted criteria (4,5); the identities were confirmed by the National Laboratory for Enteric Pathogens (Laboratory Centre for Disease Control, Ottawa, Ontario).

DISCUSSION

There are now several *Campylobacter* and *Helicobacter* species known to be associated with human disease. *C. jejuni* and *Campylobacter coli* are important causes of infectious diarrhea, whereas *C. fetus* subspecies *fetus* is recognized as a cause of bacteremia and sepsis in debilitated or immunocompromised hosts. *Helicobacter pylori* has been associated with chronic active gastritis (7), although patients with AIDS appear to have lower than expected rates of infection with this organism (8). The name *H cinaedi* has been proposed to denote a new species within the genus *Helicobacter* based on phenotypic characteristics, biochemical tests and DNA homology studies (4). The organisms are fastidious and slow growing, typically requiring several days of incubation in a microaerophilic environment for growth to be detected. The source and natural reservoir of *H cinaedi* are not known, although the organism has been recovered from the feces of healthy hamsters (9). Whether colonized hamsters serve as a reservoir for human *H cinaedi* infection has not been determined. The organism appears to be transmitted sexually within male homosexual populations, and had initially been isolated only from homosexual or bisexual men; no isolates were recovered from 150 heterosexual men or women sampled by Quinn and co-workers (1). More recently, however, Vandamme et al (10) reported the isolation of *H cinaedi* from two female adults and three children.

The spectrum of illness associated with *H cinaedi* infection includes asymptomatic gastrointestinal carriage, proctitis, enterocolitis and bacteremia (1). The present report adds to the seven previously reported cases of *H cinaedi* bacteremia (10-13). Six cases (including the two reported here) have occurred in homosexual or bisexual men, four of whom were known to be infected with HIV. The other two male patients presented with *H cinaedi* bacteremia prior to the availability of HIV serological testing (1). Interestingly, they both had concurrent pulmonary tuberculosis, suggesting that they may also have had HIV infection. *H cinaedi* bacteremia occurring in two adult women and one child were reported by Vandamme et al (10), but no other clinical information is provided. All six of the patients for whom clinical data are available presented

with a nonspecific febrile illness; only two patients had preceding gastrointestinal symptoms. In each of the reports, blood cultures were processed using the Bactec system (Johnston Laboratories, Maryland). The blood cultures were incubated for two to six days before bacterial growth was detected. Patients were treated with a variety of antimicrobial agents, including erythromycin, tetracycline, chloramphenicol, ciprofloxacin, gentamicin and antituberculous drugs. All of the patients survived their episode of bacteremia and there were no reported relapses, although one HIV-infected patient subsequently had bacteremia due to *H fennelliae* (13).

Susceptibility testing of *H cinaedi* to a variety of antimicrobial agents suggests that isolates are generally susceptible to ampicillin, tetracycline, chloramphenicol, aminoglycosides and quinolones, although 28% of 43 isolates were found to be resistant to 8 µg/mL erythromycin (14). Susceptibility testing for these slow-growing organisms has not been standardized, and optimal therapy for *H cinaedi* infection has not been determined. However, based on in vitro susceptibility test results, appropriate therapy for bacteremic infections may include tetracycline, ciprofloxacin or an aminoglycoside.

In HIV-infected patients, bacterial enteric pathogens such as salmonella, campylobacter and shigella may cause chronic relapsing and/or bacteremic infection. Both humoral and cell-mediated immunity may be important in host defence against infection due to bacterial enteropathogens. Sera from HIV-infected subjects

with persistent and severe *C jejuni* infection had abnormally low campylobacter-specific antibody responses compared to otherwise healthy volunteers, and specific humoral immunity was found to be important in preventing campylobacter bacteremia (2). Changes in mucosal secretory antibody production have also been noted in HIV-infected patients. Kotler et al (15) found a reduction in the number of IgA-containing plasma cells in the intestinal lamina propria of patients with AIDS. Not surprisingly, changes in mucosal cell-mediated immunity have also been reported. Rodgers and co-workers (16) have documented abnormalities in the distribution of T-lymphocyte subsets in the intestinal mucosa of AIDS patients. The number of CD4 helper-inducer T cells in the lamina propria was found to be reduced, paralleling the depletion of circulating lymphocytes. These defects have been related to direct infection of intestinal mucosal cells by HIV. Combined local and systemic defects in cell-mediated and humoral immunity may render the HIV-infected patient susceptible to enteric infections that subsequently become bacteremic or chronic and relapsing.

In summary, *H cinaedi* is a recently recognized enteric pathogen that may cause proctocolitis or bacteremia. Most cases have been reported in homosexual men, and the organism is believed to be transmitted sexually in these patients. Bacteremic illness is more likely to occur in patients with HIV infection, possibly because of intestinal mucosal and systemic defects in humoral and cell-mediated immunity.

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