Fatal *Bacillus cereus* Endocarditis Masquerading as an Anthrax-like Infection in a Patient with Acute Lymphoblastic Leukemia: Case Report

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A 38-year-old male farm worker with relapsing acute lymphoblastic leukemia spontaneously developed an ulcerating ulcer on his anterior thigh which was surrounded by a non-tender area of erythema. *Bacillus cereus* was isolated from the ulcer and blood, and the patient received intravenous penicillin and vancomycin for one week. When sensitivity studies were returned he was treated with gatifloxacin orally. After two weeks of combined antimicrobial therapy and negative blood cultures, the patient received combination chemotherapy with vincristine, prednisone, doxorubicin and cyclophosphamide. He was hospitalized a day after completing chemotherapy with neutropenic sepsis due to *B. cereus*. He received similar antimicrobial therapy as previously, but died three days later. At autopsy, the patient was found to have acute mitral valve endocarditis and bilateral brain abscesses. This was the first case of *B. cereus* endocarditis reported in a patient with acute lymphoblastic leukemia.

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Bacillus cereus infection has been described for more than a century (1). Initially thought to be a contaminant, it has been definitely recognized as a human pathogen since Ferrar's landmark review in 1963 (2). Clinical infections resulting from *B. cereus* can be classified as local and confined to the skin and eye, bacteremic and septic, central nervous system infections including meningitis and brain abscess, respiratory involving both the lung and pleural space, endocarditis and food poisoning (1). Herein, a fatal case of *B. cereus* endocarditis that presented with an ulcerating cellulitis of the leg and bacteremia is reported. While receiving adequate antimicrobial therapy, this male patient developed an acute endocarditis and multiple brain abscesses and died. He was also receiving combination chemotherapy for acute lymphoblastic leukemia (ALL).

Case report

A 38-year-old Hispanic-American male farm worker was diagnosed two years previously with ALL for which he received chemotherapy with vincristine, prednisone and L-asparaginase. He experienced a complete remission. In February 2004, the patient developed weakness and anorexia and was found to have relapsed. Because of fever and a right thigh ulcer surrounded by a 5×5-cm area of a brawny, non-tender erythema, he was hospitalized at the Eisenhower Medical Center on February 15th, 2004. The physical examination was otherwise within normal limits.

The peripheral smear and bone marrow examination was diagnostic of relapsed ALL. Blood cultures and cultures of the thigh wound grew out *B. cereus* which was sensitive to penicillin, vancomycin, clindamycin and ciprofloxacin. The patient received a one-week course of penicillin (12×10^6 units per day in six divided doses) and 2 g vancomycin per day in two divided doses. Subsequently, the leg ulcer and surrounding erythema almost completely resolved. Follow up blood cultures were sterile, and the patient was discharged afebrile on 750 mg ciprofloxacin orally twice daily.

A week later, and after two weeks of appropriate antimicrobial therapy, he was readmitted for combination chemotherapy with vincristine, prednisone, cyclophosphamide and doxorubicin. He remained on ciprofloxacin during treatment and additionally received trimethoprim/sulfamethoxazole and ganciclovir for antimicrobial prophylaxis. He was hospitalized for five days and discharged on the same antimicrobial prophylaxis regimen.

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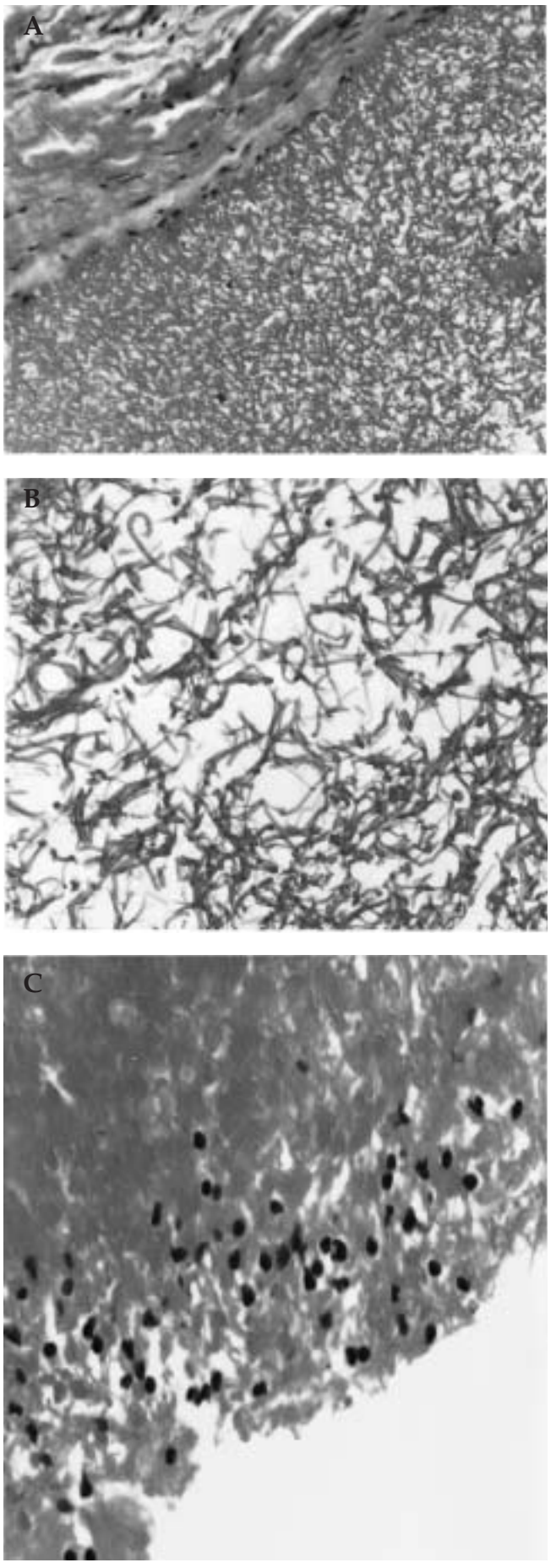

At 24 h after discharge the patient was re-hospitalized with fever and confusion. The physical examination was unremarkable, but he quickly became comatose and hypotensive. A small, shallow ulcer without a surrounding brawny edema was cultured as well as blood. Only the latter grew *B. cereus*. A lumbar puncture was not performed, despite multiple necrotic areas being identified in the brain by magnetic resonance imaging, because of a persistent and severe thrombocytopenia which was uncorrectable with platelet transfusions. The patient was also severely neutropenic. He was declared brain dead after three days of therapy with penicillin, vancomycin and ciprofloxacin.

An autopsy revealed endocarditis of the mitral valve due to Gram-positive rods which, at post-mortem culture, grew *B. cereus*, as did one of several brain abscesses. The histology of the mitral valve is shown in Figure 1.

Discussion

To date, only 12 cases of *B. cereus* endocarditis have been reported in the English literature. Ten cases were reviewed, and an additional case report was presented by Steen et al. (3), since when an additional case report has been published (4). Of the 12 previously reported cases of endocarditis, none had concomitant leukemia.

The present patient presented as a typical *B. cereus* bacteremia, which is usually transient and not clinically significant (1). Clinically significant bacteremias ordinarily occur in patients who are neonates, intravenous drug abusers, those receiving hemodialysis or continuous intravenous infusions, or those with an underlying neoplasm (1,5). The initiation of combination chemotherapy at two weeks after effective antimicrobial therapy for an indolent bacteremia, subsequently was associated with an overwhelming sepsis with bacteremia, endocarditis and multiple brain abscesses and death within three days.

It must be assumed that this patient with ALL was probably more vulnerable to *B. cereus* bacteremia, and the use of effective antimicrobial(s) for two weeks also failed to eradicate the organism. With worsening of his neutropenia by cancer chemotherapy, an overwhelming sepsis, endocarditis and multiple brain abscesses ensued. Of the 12 reported cases of *B. cereus* endo-

Figure 1: Mitral valve vegetations. A, B) Masses of fibrin and other blood elements deposited on the valve leaflet. The thrombus is only loosely attached at one edge and there is virtually no inflammation in the valve cusp. C) Few degenerating leukocytes were present at the thrombus edge.

carditis, none has had an underlying neoplastic disorder.

Among the previously treated patients with endocarditis, 10 of 12 recovered when treated with either clindamycin, vancomycin, penicillin, aminoglycosides and erythromycin. Cardiac surgery was also performed in four patients. Most isolates of *B. cereus* in patients with endocarditis produce beta-lactamases that render the organism resistant to penicillin and the cephalosporins. Although most strains of *B. cereus* are capable of producing penicillinases and cephalosporinases, the organism in the present patient displayed in-vitro sensitivity to penicillin, and that agent was used in conjunction with vancomycin for a week until the sensitivity studies were completed. At that time, treatment was changed to ciprofloxacin - to which the organism was sensitive in vitro - and this was continued until the patient's final hospitalization. At that time, *B. cereus* was again isolated from the blood, and all three antimicrobials were administered until the patient's death. Recent studies (6) have shown a high degree of efficacy of clinafloxacin as well as other quinolones in the antimicrobial management of bacterial endocarditis.

Meningoencephalitis and brain abscesses are rarely associated with *B. cereus* infection. It is of interest to note that most have been reported in conjunction with adult lymphocytic leukemia (7-11) and myelodysplasia (12). In the present patient the onset of encephalitis and brain abscess formation appeared to follow chemotherapy as the patient was well and afebrile prior to that treatment. It is of interest to note that breakthrough bacteremia and fungemia in patients administered prophylactic antimicrobials and receiving chemotherapy occur more frequently with acute leukemia (9,13).

In conclusion, this case report of a young adult with acute lymphoblastic leukemia and an indolent skin ulcer with surrounding, non-tender brawny edema and *B. cereus* bacteremia was treated with two weeks of effective antimicrobial therapy against that organism. He then received chemotherapy with vincristine, prednisone, cyclophosphamide and doxorubicin. A week later, while still receiving antimicrobial therapy, he apparently developed recurrent bacteremia accompanied by multiple brain abscesses and acute mitral valve endocarditis that led to his death within three days.

References

1. Drobniewski FA. *Bacillus cereus* and related species. Clin Microbiol Rev 1993;6:324-338
2. Farrar WE. Serious infections due to "non-pathogenic" organisms of the genus *Bacillus*. Am J Med 1963;34:134-141
3. Steen MK, Bruno-Murtha LA, Chaux G, Lazar H, Bernard S, Sulis C. *Bacillus cereus* endocarditis: Report of a case and review. Clin Infect Dis 1992;14:945-946
4. Castedo E, Castro A, Martin P, Roda J, Montero CG. *Bacillus cereus* prosthetic valve endocarditis. Ann Thorac Surg 1999;68:2351-2352
5. Colpin GGD, Guiot HFL, Simonis RFA, Zwaan FE. *Bacillus cereus* meningitis in a patient under gnotobiotic care. Lancet 1981;ii:694-695
6. Levine DP, Holley HP, Eiseman I, Willcox P, Tack K. Clinafloxacin for the treatment of bacterial endocarditis. Clin Infect Dis 2004;38:620-631
7. Funada H, Uotani C, Matachi T, et al. *Bacillus cereus* bacteremia in an adult with acute leukemia. Jpn J Clin Oncol 1988;18:69-74
8. Jenson HB, Levy SR, Duncan C, McIntosh S. Treatment of multiple brain abscesses caused by *Bacillus cereus*. Pediatr Infect Dis J 1989;8:795-798
9. Marley EF, Saini NK, Venkatraman C, Orenstein JM. Fatal *Bacillus cereus* meningoencephalitis in an adult with acute myelogenous leukemia. South Med J 1995;88:969-972
10. Sakai C, Iuchi T, Ishii A, Kumagai K, Takagi T. *Bacillus cereus* abscesses occurring in a severely neutropenic patient: Successful treatment with antimicrobial agents, granulocyte colony-stimulating factor and surgical drainage. Intern Med 2001;40:654-657
11. Strittmatter M, Hammann G, Sahin U, Feiden W, Kohl K, Schimrigk K. Intrazerebrale Blutung and multiple Hirnabszesse durch *Bacillus cereus* im Rahmen eine akuten lymphatischen Leukaemie. Nervenarzt 1995;66:785-788
12. Mori T, Tokuhira M, Takae Y, et al. Successful nonsurgical treatment of brain abscess and necrotizing fasciitis caused by *Bacillus cereus*. Intern Med 2002;41:671-673
13. Spanik S Trupl J, Kunova L, et al. Risk factors, aetiology, therapy and outcome in 123 episodes of breakthrough bacteraemia and fungaemia during antimicrobial prophylaxis and therapy in cancer patients. J Med Microbiol 1997;46:517-523

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