Candida arthritis treated with amphotericin B

This report describes a patient with acute lymphoblastic leukemia who developed arthritis of the knee caused by Candida tropicalis. Systemic therapy with amphotericin B apparently suppressed but did not eliminate the infection. Resolution of the arthritis occurred only after three intra-articular injections of amphotericin B. Intra-articular administration of amphotericin B may be a useful adjunct to systemic antifungal therapy in the treatment of these infections.

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Candidiasis is the most frequently occurring fungal infection in patients with hematologic malignancies. Although superficial colonization and localized infections are most common, invasive visceral infections are often encountered. The complications of endocarditis, suppurative thrombophlebitis, esophagitis, pyelitis, and endophthalmitis are well known. Joint infection with Candida, however, is extremely rare and to our knowledge has not been reported previously in patients with malignancy. The following is a case report of Candida arthritis in a patient with acute lymphoblastic leukemia.

CASE REPORT

An 11-year-old white female was referred to the National Cancer Institute with the diagnosis of acute lymphoblastic leukemia. She had been in good health until one week prior to admission, when she complained of abdominal pain, nausea, vomiting, and fever.

On admission the patient appeared acutely ill; oral temperature was 39.2°C. She was jaundiced and had multiple petechiae and ecchymoses over the lower extremities. Cervical, axillary, and inguinal lymph nodes were enlarged and the patient had hepatosplenomegaly. No other abnormalities were noted. Funduscopic examination was normal.

Initial laboratory data included a hemoglobin concentration of 11 gm/dl; white blood cell count of 1,900/mm³ (60% lymphocytes, 27% lymphoblasts, 3% neutrophils), and a platelet count of 13,000/mm³. A bone marrow biopsy specimen was hypercellular with approximately 90% lymphoblasts. Total serum bilirubin concentration was 5.8 mg/dl with a direct fraction of 4.2 mg/dl, serum glutamic oxalacetate transaminase 49 IU, serum glutamic pyruvic transaminase 39 IU, alkaline phosphatase 123 IU, and lactic dehydrogenase 720 mg/dl. Additional diagnostic studies including a chest roentgenogram were normal.

Following cultures of the blood, urine, stool, nose, and throat, the patient was treated with intravenous oxacillin (8 gm/day) and gentamicin (150 mg/day). Therapy was discontinued after three days when culture results were negative. The patient received induction therapy with prednisone and vincristine (day 1). On the eighth day, she developed a persistent fever for which no source was found. On day 16, she developed a persistent fever for which no source was found. On day 16, the platelet count was 16,000/mm³. She complained of arthralgias in both upper and lower extremities, particularly in the left knee. Physical examination revealed ecchymosis above the left knee and suprapatellar fullness; the other joints were normal. Roentgenogram of the knee showed soft tissue swelling but no bony abnormalities.

During the second course of induction chemotherapy (days 18-21) the signs and symptoms of arthritis disappeared. On day 27 she again became febrile and the left knee became swollen, warm, and tender. Arthrocentesis yielded 6 ml of cloudy, yellow serosanguinous fluid; the leukocyte count was 9,640/mm³ with 98% neutrophils and 2% mononuclear cells. The mucin clot test was normal; no crystals were seen. The glucose concentration was 93 mg/dl. Gram stain revealed no organisms. Culture of the joint fluid grew Candida tropicalis, which was isolated subsequently from sputum, urine, stool, and multiple blood cultures. Roentgenograms of the knee showed minimal osteoporotic changes.

Intravenous therapy with amphotericin B was begun and within one week the patient’s knee had clinically improved. She
became afebrile and cultures of blood, urine, and stool revealed no pathogens.

On day 50, the patient was discharged in complete remission. Maintenance chemotherapy was instituted (prednisone, vincristine, methotrexate, and 6-mercaptopurine) and the patient was treated with systemic amphotericin B for a period of seven weeks to a cumulative dose of 480 mg, at which time all signs of arthritis had disappeared and antifungal therapy was discontinued.

Three and one-half months later, while in hematologic remission, the patient again developed arthritis in the left knee. Arthrocentesis yielded 11 ml of cloudy yellow fluid; the leukocyte count was 33,700/mm³ (86% neutrophils and 14% mononuclear cells), Gram stain was negative, and culture of the fluid again grew Candida tropicalis. The organism was resistant to 5-fluocytosine in vitro. Blood cultures were sterile. Intravenous amphotericin B was begun at a dose of 10 mg every other day, and was increased to a maximum of 30 mg every other day.

Seven weeks later, following a total dose of 525 mg of amphotericin B, the left knee remained swollen, warm, and tender. Intra-articular injections of amphotericin B at doses of 1 mg, 5 mg, and 3 mg, respectively, were administered at 14-day intervals. Each of these injections was associated with increased joint swelling and tenderness accompanied by fever, nausea, and vomiting which subsided within three days. Two weeks following the last intra-articular injection, the knee appeared normal, and she was asymptomatic. Systemic therapy with amphotericin B was continued for seven additional weeks until a total dose of 1,535 mg had been given. The patient has had subsequent bone marrow relapses and has successfully undergone bone marrow transplantation without further evidence of Candida infection.

DISCUSSION

Arthritis is an unusual manifestation of Candida infection; only nine cases have been reported in the literature.1,2,4,5 Five occurred in neonates; the remainder were in adults, all but one of whom were receiving immunosuppressive therapy. None of the reported patients had an associated malignancy. All had knee involvement as the major site of arthritis. With one exception, in which C. guilliermondii was isolated, C. albicans was the pathogenic species responsible.

The diagnosis of Candida arthritis in our patient was based on isolation of the organism from the blood, urine, and joint fluid. Similar to other cases described, Gram stain of the infected joint fluid revealed many neutrophils but no organisms. Roentgenograms demonstrated only subtle changes in the joint architecture, which improved with resolution of the infection.

Both systemic and intra-articular therapy with amphotericin B have been used successfully to treat Candida arthritis. 2, 4, 5, 9 Despite prolonged intravenous amphotericin B treatment, the infection described in this patient did not resolve. Because of this apparent clinical resistance to intravenous amphotericin B, intra-articular injections of amphotericin B were instituted. The rapid response and complete resolution of symptoms following intra-articular amphotericin B was dramatic, suggesting that this route of administration should be considered as an adjunct to intravenous amphotericin B in the management of Candida arthritis.

Infection with Candida is an increasingly frequent cause of morbidity and mortality in patients with malignancy. The unusual presentation of Candida infection in the form of arthritis underscores its protean nature.

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REFERENCES