

Septic Arthritis as the First Sign of *Candida tropicalis* Fungaemia in an Acute Lymphoid Leukemia Patient

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Fungal infections caused by *Candida* species have increased in incidence during the past two decades in England, North America and Europe. Candidal arthritis is rare in patients who are not intravenous drug users or are who not using a prostheses. We report the case of a 24-year-old man with acute lymphoid leukemia, who developed *Candida tropicalis* arthritis during an aplastic period after chemotherapy. This is the eighth case described in the literature of *C. tropicalis* causing arthritis without intra-articular inoculation. We call attention to an unusual first sign of fungal infection: septic arthritis without intra-articular inoculation. However, this case differs from the other seven, since despite therapy a fast and lethal evolution was observed. We reviewed reported cases, incidence, risk factors, mortality and treatment of neutropenic patients with fungal infections.

Key Words: Septic arthritis, *Candida tropicalis*, fungal infections, *Candida tropicalis* arthritis, systemic candidiasis.

During the past two decades, the incidence of fungal infections has substantially increased in England, North America and Europe. Several risk factors have been found to be associated with these infections, including the prolonged use of broad-spectrum antibiotics, chemotherapy, hyperalimentation with fluids containing high glucose concentrations, neutropenia and central venous catheterization [1].

Systemic candidiasis is a common cause of septicemia, but septic arthritis caused by *Candida* species is rare [1,2]. Fungal arthritis has most commonly been caused by *C. albicans*, although *C. tropicalis* has been reported, especially in granulocytopenic patients [2,3,5,6]. We report an uncommon case of acute monoarthritis caused by *C. tropicalis*, leading to systemic

candidiasis and death in a patient with acute lymphoid leukemia during an aplastic period after chemotherapy.

Case Report

A 24-year-old white man with common acute lymphoid leukemia (ALL) (CD_{10}^+ , CD_{19}^+ and Igs), was scheduled for systemic chemotherapy following the GMALL protocol for ALL [3]. The chemotherapy was administered via "port-a-cath" catheter, and during treatment he developed Diabetes secondary to corticosteroid therapy. Complete remission in the bone marrow was achieved on the 28th day of the protocol. On the 44th day, he had 0.9×10^9 leucocytes/L, and G-CSF treatment was initiated. At the same time he presented a painful left knee erythema, without fever. Blood cultures were positive for methicillin-resistant *Staphylococcus aureus*, and he was treated with intravenous vancomycin. After 5 days, despite G-CSF use, the leucocyte count was 0.1×10^9 /L, he developed fever and his knee became more painful and swollen. Joint fluid aspiration showed yeast with optical microscopy. Several blood and synovial fluid cultures

Received on 10 March 2003; revised 01 September 2003.

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The Brazilian Journal of Infectious Diseases 2003;7(6):426-428
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Table 1. Review of reported cases of *Candida tropicalis* without intra-articular inoculation

Author/Date	Age/Sex	Underlying disease	Risk factors	Affected joint	Treatment	Follow up
Murray et al. 1976 [6]	77/M	Bladder carcinoma	Leucopenia, central catheter, BSA	Shoulder	AMB	Arthritis cured
Bayer et al. 1978 [6]	12/ M	ALL	Chemotherapy, corticosteroid, trauma	Knee	5-flucytosine AMB	Disseminated candidiasis and death (21 st day of AMB therapy)
Fainstein et al. 1982 [6]	59/M	AML	Leucopenia, chemotherapy, corticosteroid, BSA	Knee	AMB miconazole	Arthritis cured
Fainstein et al. 1984 [6]	67/M	CML	Chemotherapy leucopenia, BSA	Knee	Ketoconazole	Arthritis cured
Mandel et al. 1984 [3]	66/ W	LL	BSA, chemotherapy	Knee	AMB miconazole	Arthritis cured
Weisse et al. 1993 [6]	1 month/ M	Prematurity	BSA, hyperalimentation fluids	Knee	AMB, 5-flucytosine	Arthritis cured
Pothoff et al. 1997 [6]	77/W	AML	Leucopenia, chemotherapy, central catheter	Knee	Fluconazole	Arthritis cured
Present case	24/M	ALL	Leucopenia, Diabetes, central catheter, BSA, chemotherapy, corticosteroid	Knee	AMB	Disseminated candidiasis and death (9 th day of AMB therapy)

ALL= acute lymphocytic leukaemia; AML= acute myeloid leukaemia; CML= chronic myelocytic leukaemia; LL= lymphocytic lymphoma; AMB= amphotericin B; BSA= broad-spectrum antibiotics.

were positive for *C. tropicalis*. Treatment with intravenous amphotericin B at a dosage of 1 mg/Kg daily was started, and six hours later he developed skin lesions, identified as candidal embolic skin lesions by biopsy. The patient evolved to hypotension and signs of septic shock. Nine days after the monoarthritis began, he died due to septic shock, secondary to fungaemia.

Discussion

Systemic candidiasis is a common cause of septicemia, but septic arthritis caused by *Candida* species is rare [1,2]. Dissemination to the joint is most frequently provoked by intra-articular inoculation, including injection, surgery and prosthesis; or by hematogenous dissemination, usually in intravenous drug abusers [4,5]. Most of the cases of candidiasis described in the literature caused by *C. albicans* (60%) and *C. tropicalis* (18%) have been reported secondarily, especially in granulocytopenic patients [5].

We report the eighth known case of the arthritis caused by *C. tropicalis* without intra-articular inoculation (Table 1) [4,6]. The mortality associated with candidemia in hospitalized patients with cancer is 60%, and without cancer it is 38% [5]. A multivariate analysis for mortality rates associated with candidemia etiology indicated a significantly better survival rate for *C. albicans*. Furthermore, in animal and human studies *C. tropicalis* has also been found to be intrinsically more virulent than *C. albicans* [5]. The increasing use of potent antibiotics, immunosuppressives, parenteral nutrition, and corticosteroids, as well as the presence of neutropenia, central venous catheters, traumatized skin, diabetes, and joint prosthesis are predisposing factors for fungal infection [1,2]. Fungaemia in patients on chemotherapy may be attributable to the absence of fluconazole prophylaxis.⁽¹⁾ However, this type of prophylaxis has resulted in a rise in the proportion of hematogenous candidiasis caused by *C. glabrata* and *C. krusei* [5].

Our patient presented several of the clinical pathological features identified by Leung et al., including neutropenia, central venous catheter use, and treatment with broad-spectrum antibiotics, as well as diabetes

secondary to corticosteroid therapy, which is a known predisposing factor for fungal infection [1].

The standard recommendation for patients with candidemia or deep candidal infection is administration of amphotericin B. Generally 800 mg daily of fluconazole or > 0.7 mg/kg daily of amphotericin B is given. However, fluconazole has been associated with a 15% failure rate. The treatment should be continued for more than two weeks after the last positive blood culture results, and resolution of all clinical manifestations of candidal infection [5].

Conclusion

We call attention to an unusual first sign of fungal infection, septic arthritis without intra-articular inoculation. However, this case differs from the seven other known cases, since despite therapy a fast and lethal evolution was observed. We emphasize that the most important factors for the successful treatment of fungal arthritis are early diagnosis and prompt therapy.

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