Disseminated soft tissue infection and sepsis with *Stenotrophomonas maltophilia* in a bone marrow transplant patient

JEFFREY HL LIPTON PhD MD FRCPC, KELLY SMACDONALD MD FRCPC

Infectious complications following bone marrow transplantation are a major side effect causing significant morbidity and mortality (1,2). Developments in the management of fever and infection have resulted in major improvements in the therapy of immunosuppressed and neutropenic patients (3-5), but changes in antimicrobial selection for prophylaxis and therapy and increasing and more prolonged immunosuppression have resulted in different infectious profiles and complications. One organism being found more frequently in the immunocompromized host is *Stenotrophomonas maltophilia*, previously called *Xanthomonas maltophilia*. Recently a series of mucocutaneous and soft tissue infections with this organism have been described. A 32-year-old female presented with aplastic anemia and subsequently underwent a one-antigen mismatched bone marrow transplant from her brother. She failed to engraft and a second graft was attempted. Protracted neutropenia of three months' duration despite the use of broad spectrum antibiotics occurred. *Stenotrophomonas (Xanthomonas) maltophilia* metastatic cellulitis developed that did not respond to appropriate antibiotics.

Key Words: Bone marrow transplantation, Metastatic cellulitis, Soft tissue infection, Stenotrophomonas, Xanthomonas

Infection disséminée des tissus mous et septicémie à *Stenotrophomonas maltophilia* chez une patiente ayant subi une transplantation de moelle osseuse

RÉSUMÉ : Une patiente de 32 ans, souffrant d’anémie aplasique et ayant par la suite reçu une transplantation de moelle osseuse de son frère malséparée à l’égard d’un antigène. La première greffe a échoué et une a été tentée. Une neutropénie prolongée d’une durée de trois mois s’est installée malgré l’emploi d’antibiotiques à large spectre. Une cellulite métastatique à *Stenotrophomonas maltophilia* (xanthomonas) est apparue et n’a pas répondu aux antibiotiques appropriés.
one blood culture completed after a repeat temperature spike. The patient responded to amphotericin B. She remained neutropenic, and a bone marrow aspirate done on day 30 revealed a failure of engraftment. Routine surveillance cultures were not done. Computed tomography scan of the abdomen on day 45 revealed ascites only.

After repeat conditioning with antithymocyte globulin (ATGAM, Upjohn, Michigan) 40 mg/kg/day for four days, she underwent repeat transplantation from the same donor on December 1, 1994. Graft-versus-host prophylaxis was with cyclosporine and methylprednisolone, and granulocyte colony-stimulating factor was administered from day +1. On day +4 after being febrile for eight days without positive cultures, antibiotics were switched to oral ciprofloxacin. However, on day +6, she again became febrile and developed right upper quadrant pain and hepatomegaly (but no peritoneal signs), and ceftazidime, tobramycin, metronidazole and amphotericin B were started in view of concern about both intrabdominal sepsis and a recurrent candidal infection. Continuing jaundice and ascites were noted. On day +7 a cellulitis was noted, and antibiotics were switched to clindamycin, ceftriaxone and intravenous ciprofloxacin. Subsequently two red fir nodular lesions with necrosis which enlarged rapidly developed on her buttock. Intravenous ciprofloxacin was continued, and imipenem was added to her regimen for a Gram-negative organism on Gram stain of a blood culture. Ultimately, a skin biopsy from day +8 and four of six blood cultures taken both peripherally and through a central venous catheter grew S maltophilia. Antibiotics were subsequently switched to high dose cotrimoxazole, intravenous ciprofloxacin and ticarcillin/clavulanic acid. Amphotericin B was continued. On testing, the organism was sensitive to cotrimoxazole with a minimum inhibitory concentration (MIC) of less than 0.5 µg/mL, and resistant to ceftazidime with an MIC of greater than 128 µg/mL using microbroth dilution. The skin lesions progressed to cover her buttocks and left thigh (Figure 1). She developed hypotension, pneumonia and progressive renal failure. She died on day +13.

**DISCUSSION**

*S maltophilia* colonization and infection have been shown to be strongly associated with prolonged broad spectrum antibiotic use, particularly imipenem, but also third-generation cephalosporins (6,7). Pulmonary infections have predominated in most series but increasingly septicemia and line infections have been observed (8).

A recent review of skin and mucous membrane infections in cancer patients showed that different mechanisms involving direct inoculation or hematogenous dissemination accounted for distinct clinical syndromes (6). Vartivarian et al (6) reported five patients with a previously undescribed syndrome metastatic cellulitis characterized by multiple tender hard nodules associated with bacteremia in neutropenic patients on broad spectrum antimicrobial therapy. This differs from ecthyma gangrenosum in that the central nodules are not well demarcated, there is no central necrosis and the nodules spread rapidly to generalized necrosis.
Stenotrophomonas metastatic cellulitis in a BMT patient

Prolonged neutropenia and antimicrobial use in this patient and the clinical presentation are consistent with this newly described syndrome. Of interest, imipenem was not employed in this patient initially; however, ceftazidime and ciprofloxacin both were used, and other recent reports suggest that they are risk factors for subsequent stenotrophomonas infection (6,9). This patient initially received cotrimoxazole as prophylaxis, the drug of choice for the treatment of S maltophilia infections, but for the four weeks before the stenotrophomonas bacteremia she had not been on cotrimoxazole.

The increasing use of fluoroquinolone prophylaxis (10) and prolonged use of broad spectrum antimicrobials in the face of prolonged neutropenia almost certainly sets the stage for colonization of patients with this ubiquitous and somewhat opportunistic pathogen. In this setting, it has been shown to be highly virulent and fatal when disseminated infection develops. This report confirms the clinical syndrome of this characteristic metastatic cellulitis and underscores the need to consider S maltophilia as well as other organisms including fungal pathogens in neutropenic patients presenting with rapidly progressive soft tissue infections.

ACKNOWLEDGEMENTS: Thanks to Debra Pelissero and Cindy Walker for typing this manuscript.

REFERENCES