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Bloodstream infections in organ transplant recipients receiving alemtuzumab: No evidence of occurrence of organisms typically associated with profound T cell depletion

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Summary *Background:* Alemtuzumab is a humanized monoclonal antibody directed against CD52, a cell surface antigen expressed on B and T lymphocytes, monocytes and NK cells. Its use results in a profound decrease in CD4 positive T lymphocytes. Alemtuzumab is used as induction immunosuppression and therapy for rejection in organ transplant recipients in some centers. We followed a cohort of 449 consecutive transplant recipients who received alemtuzumab to determine the occurrence of bloodstream infections, particularly those previously associated with decrease in CD4 positive T lymphocytes.
Patients and methods: Fifteen percent (69/449) patients had at least one episode of bloodstream infection. However, no patient had bacteremia with *Streptococcus pneumoniae*, *Listeria monocytogenes*, non-typhoidal *Salmonella* or *Mycobacterium avium* complex. Fungaemia was rare, occurring in 1.5% of patients. The most common organisms isolated from the blood were *Staphylococcus aureus* (21 episodes), coagulase negative *Staphylococcus* (14 episodes), *Klebsiella pneumoniae* (12 episodes), *Enterococcus faecium* (11 episodes), *Pseudomonas aeruginosa* (10 episodes), *Enterococcus faecalis* (9 episodes) and *Escherichia coli* (7 episodes).

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Discussion: We conclude that although alemtuzumab use is associated with profound CD4 positive T lymphocyte depletion, alemtuzumab does not seem to be associated with an increased risk of bloodstream infection with pathogens typically seen in other disorders of CD4 cell depletion, such as acquired immunodeficiency syndrome.

Background

In an increasing number of transplant centers alemtuzumab is used as preconditioning or induction immunosuppression for organ transplantation and for the treatment of acute rejection.[1–7] Alemtuzumab is a humanized monoclonal antibody directed against CD52, a cell surface antigen expressed on B and T lymphocytes, monocytes and NK cells. The administration of alemtuzumab causes profound depletion of peripheral blood lymphocytes.[8] This lymphoid depletion prior to exposure to donor alloantigens decreases global immune reactivity, leading to a lower anti-donor response. The desirable effects are a lower incidence of rejection episodes and reduced dependence on maintenance immunosuppression.[4,9–12]

Use of anti-lymphocyte antibodies has been previously reported to be a risk factor for bacteraemia in solid organ transplant recipients.[13,14] Bacteraemia is a significant event post-transplantation; it is associated with up to a 3-fold increase in the mortality of transplant recipients.[13,15] The lymphocyte depletion in alemtuzumab treated patients is significant, with CD4 counts usually lower than 100, for as long as 18–24 months.[16–22] Such a degree of iatrogenic lymphopaenia could increase the prevalence of certain bloodstream infections typically seen in patients with profound CD4 depletion, such as patients with acquired immunodeficiency syndrome (AIDS). Bacteria and fungi known to produce bloodstream infection more frequently in patients with AIDS include *Mycobacterium avium complex*,[23] *Cryptococcus neoformans*,[24,25] *Streptococcus pneumoniae*,[26–28] non-typhoidal *Salmonella*[29] and *Listeria monocytogenes*.[30]

Therefore, we evaluated consecutive organ transplant recipients who received alemtuzumab for preconditioning or induction immunosuppression or for the treatment of acute rejection at the University of Pittsburgh Medical Center, with the aim of describing the pathogens causing bloodstream infections in the first 12 months following alemtuzumab therapy.

Patients and methods

Consecutive organ transplant patients at the University of Pittsburgh Medical Center who received alemtuzumab from January 2002 to February 2004 were evaluated. Alemtuzumab was given as preconditioning/induction immunosuppression or as therapy for acute rejection to kidney, kidney/pancreas, lung, heart/lung, liver, intestinal and multivisceral transplant recipients. The two indications for alemtuzumab use, induction therapy or rejection, were assessed separately. The patients who initially received alemtuzumab for preconditioning/induction and who later were also treated with this drug for acute rejection were analyzed in the same group as the patients who received it for induction only.

All episodes of BSI occurring in the first year after receipt of alemtuzumab were reviewed in detail. Bacteraemia was defined as the isolation of bacteria other than common skin contaminants, from at least one set of blood cultures. Bacteraemia caused by common skin contaminants, e.g. coagulase negative staphylococci, was considered significant only if the organism was isolated from at least two sets of blood cultures. Additional cultures for the same organism within a 14-day period were considered to represent the same episode. Fungaemia was defined as the isolation of a fungus from at least one set of blood cultures. Blood cultures were obtained at the discretion of attending physicians. Collection of blood in isolator blood tubes for the enhanced isolation of fungi and mycobacteria was typically performed in patients with fever for more than four days, and in whom conventional blood cultures were negative.

Peri-operative prophylaxis was ampicillin/sulbactam or vancomycin and cefotaxime in liver transplant recipients or cefazolin or levofloxacin in renal transplant recipients. Prophylaxis was usually discontinued within 24–48 h of transplantation. Prophylactic regimens for lung transplant and intestinal transplant recipients were patient specific depending on prior colonization of the patient.