Management of Patients Receiving Antithymocyte Globulin for Aplastic Anemia and Myelodysplastic Syndrome

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Antithymocyte globulin (ATG) is used commonly in patients with severe aplastic anemia and those undergoing renal transplant. Its utility also is being explored in the treatment of myelodysplastic syndrome, conditioning regimens for hematopoietic stem cell transplant, and prophylaxis of graft-versus-host disease. As indications for ATG expand, knowledge regarding its administration and management of associated toxicities is needed. These toxicities range from life-threatening anaphylaxis associated with the infusion to flu-like symptoms that occur one to two weeks after the infusion. Adverse effects are classified according to the severity and system impacted. Mild toxicities respond to comfort measures and include fever, chills, urticarial rash, and vomiting. Moderate toxicities require acute interventions and include fluid-responsive hypotension, nonischemic chest pain, and reversible oxygen desaturation. Severe toxicities require intensive support and include those refractory to earlier intervention. Management of these toxicities usually is limited to fluid resuscitation and noninvasive monitoring. Occurrence of infusion-related toxicities may require premature discontinuation of therapy. Therefore, an educated healthcare team and interdisciplinary clinical management guidelines are important to ensure the safe administration and complete course of ATG.

Key Words: aplastic anemia, antilymphocyte serum, myelodysplastic syndrome

Antithymocyte globulin (ATG) is a polyclonal antibody preparation with well-described efficacy in the treatment of severe aplastic anemia (AA) and in the treatment and prevention of acute rejection of renal transplantation. In addition, the benefit of ATG in the treatment of graft-versus-host disease in hematopoietic stem cell transplant (HSCT) and myelodysplastic syndrome (MDS) continues to be explored. Two preparations of ATG currently exist: Atgam® (Pfizer Inc., New York, NY) and Thymoglobulin® (Genzyme Corporation, Cambridge, MA). Atgam is a purified gamma globulin solution obtained by the immunization of horses with human thymocytes. Thymoglobulin is a purified immunoglobulin prepared from hyperimmune serum of rabbits immunized with human thymic lymphocytes (Gorantla et al., 2000). The result is a product rich in antihuman T cell antibodies. These antibodies bind to the surface of circulating T cells and T cells within lymphoid organs, reducing the number of functional T lymphocytes and creating an immunosuppressive effect (Gaber et al., 1998; Gorantla et al.). Antibodies to other hematopoietic cells have been reported (Pfizer Inc., 2002). These additional antibodies react against platelets, neutrophils, and red blood cells (RBCs) and may cause a transient decrease in peripheral blood counts during ATG administration. Although the origins of Atgam and Thymoglobulin are different, the administration issues are similar. The focus of this article will be on Atgam (40 mg/kg per day) and Thymoglobulin (3.5 mg/kg per day) in patients with AA and MDS.

Application in AA and MDS

AA is an acquired hematologic disorder characterized by pancytopenia and hypocellular bone marrow. The pathophysiology of AA is hypothesized as an autoimmune attack mediated by T lymphocytes against the bone marrow (Young, 2002; Young & Maciejewski, 1997). In severe AA, patients may require immediate medical and supportive therapy for life-threatening infection or bleeding. To move beyond supportive care into the realm of treatment, factors such as age, degree of neutropenia, and availability of a human leukocyte antigen- (HLA-) matched donor must be considered. Bacigalupo et al. (2000) presented three treatment recommendations based on two important predictors of outcome: age and neutrophil count (see Table 1). Allogeneic HSCT is the recommended...