Acquired Aplastic Anemia and Bone Marrow Transplantation

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By definition aplastic anemia is described as pancytopenia with empty bone marrow in which the marrow is replaced by fat cells. The etiology of acquired aplastic anemia is largely unknown; however in one third of the patients it is associated with either viruses, drugs or chemicals.[1] The way in which these agents produce aplastic anemia is unknown but it has been suggested that both stem cells and micro environmental factors play a part.[2] As far as pathogenesis of the disease is concerned, there is little doubt about the immune mediated destruction of the stem cells. Activated CD8+ lymphocytes may play a role in inducing production of gamma interferon, which lead to nitrous oxide synthesis in stem cells causing apoptosis.[2] It is also confirmed by the response of the disease to immunosuppressive agents. Without treatment, it is invariably a fatal disease with a mortality of 80% at one year.

However, age at presentation and absolute neutrophil count are important prognostic factors.[3,4] They also guide the physician to plan the management amongst the treatment options. Selection of best treatment modality is not straight forward. Response to immunosuppressive therapy has been claimed equivalent to results of bone marrow transplants in some studies.[5,6] However the response rate is inferior in patients with very severe aplastic anemia (absolute neutrophil count less than 200 per cubic millimeter). Other concerns are relapse of the disease and long term sequelae. Relapse rate is around 35% at 10 years.[7] Similarly the long term sequelae such as paroxysmal nocturnal hemoglobinuria occurs in nine percent of the patients, and acute leukemia and myelodysplasia occurs in approximately 16% of the patients after ten years of treatment with immunosuppressive agents.[2]

On the other hand allogenic bone marrow transplantation is the potential curative treatment option, however this is applicable in only 25 to 30 percent of the patients because of the unavailability of the potential HLA matched sibling. This procedure also carries a substantial risk of transplant related mortality and graft versus host disease. Graft versus host disease not only contributes to the increase in mortality rate but also severely affects the quality of life of the patients. However, long term sequelae such as paroxsysmal nocturnal hemoglobinuria, myelodysplasia and acute leukemia are infrequent when compared to immunosuppressive therapy. Taking into consideration the high relapse rate with immunosuppressive therapy, it should be the treatment of choice in young patients with severe aplastic anemia. Similarly, those with very severe aplastic anemia, should be offered bone marrow transplantation because of poor response to immunosuppressive agents in this particular group.

matched donor for allogenic bone marrow transplantation is high. However, an important limitation in the provision of curative treatment for this disorder appears to be the high cost of different modalities, especially allogenic bone marrow transplantation. Efforts from all quarters including the pharmaceutical industry are needed so that the treatment cost becomes affordable for needy patients.

References

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