Severe Fatigue: Could It Be Aplastic Anemia?

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Case Study

Mr. X, a single, 55-year-old administrative assistant, presented to his family practice clinic with a complaint of fatigue. He was previously healthy and enjoyed walking his dog in his free time.

Mr. X reported that he was easily fatigued and often short of breath. He said that it was difficult to walk several blocks. Mr. X also reported a low-grade fever and suspected that he had an upper respiratory infection, but he did not seek medical treatment for those symptoms. He has had some bruising on his extremities, and colleagues have told him that he looks pale. Mr. X, however, denied any headaches, lightheadedness, dizziness, chest pain, or palpitations.

A general examination revealed an obese, afebrile, normotensive white male. No oral lesions, mucosal bleeding, or cervical lymphadenopathy were noted. Respiratory and cardiovascular examinations were unremarkable. Mr. X's liver and spleen were not enlarged and no bruising or petechiae were noted.

A complete blood count (CBC) with differential was ordered. Mr. X's hemoglobin was 6.4 g/dl, white blood cell count was 3.1 k/ul, and platelets were 6,000 x 10⁹/L.

Treatment Plan

Mr. X was admitted to the hospital for evaluation and treatment of severe anemia. A bone marrow biopsy was remarkable for a severely hypoplastic marrow with 5% cellularity. Very few megakaryocytes were present with no definite dysplastic changes. A flow cytometry also was done and did not reveal any evidence of a lymphoproliferative disorder. A cytogenetic study was normal. Mr. X was evaluated by a hematology consultant and given a provisional diagnosis of aplastic anemia (AA). The hematologist ordered red blood cell and platelet transfusions. Mr. X also was started on prednisone. His CBC rose to a hemoglobin level of 11.8 g/dl, white blood cell count to 3.8 k/ul, and platelets to 16,000 x 10⁹/L.

Mr. X was then discharged from the hospital with a referral to a specialty oncology center for further evaluation.

A repeat CBC was obtained at the oncology center and revealed a white blood cell count of 1.93 k/ul, hemoglobin of 9.1 g/dl, platelet count of 3,000 x 10⁹/L, and absolute neutrophils of 0.12 K/ul. Diagnoses of AA or hypoplastic myelodysplastic syndrome were considered. A repeat bone marrow biopsy was done and revealed a paucicellular (5%) bone marrow with panhypoplasia. Flow cytometric analysis reported no evidence of lymphoproliferative disorder. Cytogenetic testing revealed a normal male karyotype. Additional testing favored an AA diagnosis. Mr. X decided to be treated with antithymocyte globulin (ATG) in combination with cyclosporine (CsA). Mr. X was given the combination of rabbit-derived ATG (r-ATG) plus CsA and received steroid prophylaxis for seum sickness. Mr. X was supported with platelet and blood transfusions during the first week after treatment and started to have hematologic improvement eight weeks after ATG treatment. About 60% of patients respond at three or six months after initiation of ATG, so Mr. X was ahead of the curve (Rosenfeld, Follman, Nunex, & Young, 2003). His siblings were human leucocyte antigen-typed, but no match was found. Mr. X's options, in the event of relapse, included more ATG treatment, which would be with the horse form based on high response rates after first relapse (60%–70%), or a matched-unrelated donor allogeneic bone marrow transplantation if a suitable donor is found.

Discussion

AA is a bone marrow failure disorder characterized by pancytopenia (a significant decrease in blood cells and platelets) and a hypoplastic (appearance of fat cells and very few hematopoietic cells) bone marrow. Although rare, AA can be life threatening and, if untreated, is associated with a high mortality rate (Young, Scheinberg, & Calado, 2008). The curative approach for patients with severe and very severe forms of AA is bone marrow transplantation. However, this option is only available to about 30% of patients (Maciejewski & Risitano, 2005). Factors that limit this option include comorbidities such as diabetes mellitus, hypertension, advanced age, and limited human leucocyte antigen-matched donors.

Epidemiology

Acquired AA is a rare disease. In the Western world, the incidence is about two cases per million per year but is actually about two- to three-fold higher in Asia (Young et al., 2008). The Thai National Heart Lung and Blood Institute’s...