LETTERS AND CORRESPONDENCE

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Allopurinol-Induced Pure Red Cell Aplasia

To the Editor: Acquired pure red cell aplasia (PRCA) is a rare condition characterized by a profound anemia associated with reticulocytopenia and bone marrow remarkable for the absence of erythroid precursors while other cell lineages are preserved (see [1] for review). Although PRCA is most often idiopathic in the adult, associations with several conditions have been clearly established, including systemic lupus erythematosus, thymomas, lymphomas, ABO-incompatible blood transfusion, and viral infections, most notably parvovirus B19 and viral hepatitis. Some drugs have also been implicated in the development of PRCA, most notably phenytoin, azathioprine, and isoniazid [2]. Allopurinol has been associated with nine cases of aplastic anemia but with only two cases of PRCA in the medical literature [3,4]. We report a third case linking allopurinol to the development of PRCA.

T.M. is a 79-year-old man with coronary artery disease and hypertension who was admitted to the hospital with the chief complaint of shortness of breath of 1-week duration. Physical examination was remarkable for extreme pallor without icterus, lymphadenopathy, or splenomegaly, and stool guaiac test was negative. His CBC revealed a hemoglobin of 7.9 g/dL, a hematocrit of 22.4%, an MCV of 109 fL, a RDW of 17.1%, a white blood cell count of 6.1×10^3 c/μl, a platelet count of 367,000 c/μl, and a normal leucocyte differential count. The peripheral blood smear showed anisocytosis with macrocytosis. Initial assessment revealed that the patient had suffered a myocardial infarction. CBC performed 3 months prior to his admission was normal with a hematocrit of 44%. Initial workup excluded vitamin B_{12}, folate, and iron deficiencies as well as bleeding and hemolysis. Bone marrow biopsy showed moderate hypocellularity, with maturing granulocytic and megakaryocytic lineage. Most interestingly, the virtual absence of erythroid precursors was conspicuous. Flow cytometry revealed a small monoclonal population of mature lymphocytes with kappa light chain restriction expressing CD19, CD20, and CD22 surface antigens. Serum titers for parvovirus B19 and viral hepatitis antibodies were negative. A lupus screen was unremarkable. Because the patient had been started on allopurinol 8 weeks earlier and in view of the association between PRCA and allopurinol in two reports, this medication was discontinued. The patient was transfused to a hematocrit of 31% and discharged from the hospital. Without any further therapeutic intervention or transfusion, his hematocrit rose to 36% eight weeks later. A bone marrow biopsy performed then revealed a normal cellularity with maturing trilineage hematopoiesis and adequate erythroid precursors. Although the patient has an underlying low-grade lymphoproliferative disorder, the prompt resolution of the PRCA after discontinuation of allopurinol, along with the exclusion of any other therapeutic intervention, strongly argues in favor of a toxic drug effect. This is the third report linking the intake of allopurinol to the development of PRCA and strengthens this association. The mechanism of this drug toxicity is uncertain. Physicians should be alerted to the possibility of this rare but serious side effect of this widely used medication.

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