

Letter to the Editor: Fatal Aplastic Anemia Associated With Allopurinol Therapy

Allopurinol (Zyloprim) is a drug widely used for the treatment of hyperuricemia. Although fatal agranulocytosis has been reported, significant hematologic toxicity is uncommon and has been reported previously only in patients receiving other drugs with a known myelosuppressive potential [1-5]. We have observed a patient with severe myelosuppression on two separate occasions following the administration of allopurinol who died with aplastic anemia.

A 63-year-old white grocer was hospitalized for a grand mal seizure. His blood pressure was 230/120 mmHg. Laboratory studies revealed a serum creatinine of 4 mg/dl, blood urea nitrogen of 50 mg/dl, and uric acid of 10 mg/dl. A complete blood count was normal. Cranial computerized axial tomography showed changes compatible with intracerebral hemorrhage. His hypertension was initially controlled with sodium nitroprusside, and he subsequently was treated with dilantin, allopurinol, and methyldopa (Aldomet®). In addition, he received brief courses of therapy with hydralazine (Apresoline®) and propranolol (Inderal®). Two months later, he developed weakness and fatigue and was found to have a hematocrit of 17% with normocytic and normochromic red blood cells. The white blood count was 4,000 cells mm³ with 68% neutrophils, and the platelet count was 130,000 cells mm³. A bone marrow aspirate showed hypocellular spicules with a virtual absence of erythroid precursors. An acid hemolysis test and sucrose hemolysis test were negative. An antiglobulin test (direct) was weakly positive on admission but not thereafter. Medications were stopped, and he was treated with nandrolone decanoate (Deca-Durabolin), prednisone, and metolazone (Zaroxolyn). Steroid therapy was stopped after a 2-month trial, but the antihypertensive medication was continued. He required transfusion with three units of packed red blood cells monthly for 3 months. Then he developed reticulocytosis and his hematocrit rose from 23% to 36%. A bone marrow biopsy specimen was mildly hypocellular (25% nucleated cells) with adequate numbers of erythroid precursors. Blood studies showed hematocrit 36%, white blood count 3,800 cells mm³ with 70% neutrophils, platelets 135,000 cells mm³, serum creatinine 3.8 mg/dl, and uric acid 13 mg/dl. The patient developed tender, swollen joints, and fluid aspirated from the knee contained uric acid crystals. Allopurinol therapy was reinstated. Three weeks later, he became severely anemic and thrombocytopenic, and a bone marrow biopsy specimen showed aplasia (5% nucleated cells). Marked granulocytopenia developed 10 days later. The antiglobulin test (direct) was again transiently positive. Recovery of the bone marrow did not occur despite cessation of therapy with allopurinol and treatment with oxymethalone and prednisone. Death occurred 1 month later from septicemia.

The occurrence of marked anemia and bone marrow hypoplasia on one occasion and severe pancytopenia and aplasia after a second exposure to allopurinol suggests that this drug is capable of producing aplastic anemia. This is the first description, to

our knowledge, of aplastic anemia resulting from allopurinol in which other potential myelosuppressive agents can be excluded. This must be a rare event because of the widespread use of this drug. However, physicians utilizing allopurinol should be aware of its potential for occurrence.

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REFERENCES

1. Greenberg MS, Zambrano SS: Aplastic agranulocytosis after allopurinol therapy. *Arthritis Rheum* 15:413-415, 1972.
2. Wilkinson DG: Allopurinol and agranulocytosis. *Lancet* 2:1282-1283, 1977.
3. Hawson GA, Bain BJ: Allopurinol and agranulocytosis. *Med J Aust* 1:283, 1980.
4. Scobie IN, MacCuish AC, Keson CM, McNeil IR: Neutropenia during allopurinol treatment in total therapeutic starvation. *Br Med J* 280:1163, 1980.
5. Lee EJ, Kueh YK: Allopurinol induced skin reactions and agranulocytosis. *Singapore Med J* 23:178, 1982.