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Letter to the Editor: Aplastic Anemia Caused by Allopurinol in Renal Insufficiency

Allopurinol is increasingly used for hyperuricemia of various causes, and also in combination with chemotherapy for hematological malignancies. Recently, a few cases aplastic anemia caused by administration of allopurinol were reported [1,2]. We observed two cases of aplastic anemia probably caused by the administration of allopurinol in patients with renal insufficiency.

The first patient was a 48-year-old female who was administered allopurinol (200 mg/day) for hyperuricemia (8.6 mg/dl) associated with renal insufficiency (BUN 67 mg/dl, creatinine 3.8 mg/dl, creatinine clearance 15 ml/min) due to chronic urolithiasis. Severe pancytopenia (Hb 4.5 g/dl, WBC 1.1×10^9/L, N. Segmented 22%, Plt 10×10^9/L) and hypocellular marrow developed 4 months after administration of allopurinol, and she died 3 weeks later of gastrointestinal bleeding and sepsis.

The second patient was a 72-year-old male who was administered allopurinol for hyperuricemia (10.4 mg/dl) associated with renal insufficiency (BUN 92 mg/dl, creatinine 3.9 mg/dl, creatinine clearance 9.4 ml/min) due to macroglobulinemia. Melphalan (12 mg/day) and prednisolone (60 mg/day) were administered for 4 days just before administration of allopurinol. Severe pancytopenia (Hb 6.3 g/dl, WBC 1×10^9/L, N. Segmented 0%, Plt 19×10^9/L) developed 11 days after administration of allopurinol, and bone marrow aspiration was dry tap. A bone marrow biopsy specimen revealed medium-sized immature lymphocytes typical of macroglobulinemia and a marked decrease of normal hematopoietic cells. The cause of pancytopenia in this patient was thought to be due to allopurinol rather than melphalan because the dose of melphalan was small and the duration was too short to cause severe bone marrow suppression.

The mechanism by which allopurinol suppresses hematopoiesis is unknown. The suppression of the de novo purine synthesis has been demonstrated [3]. Severe allopurinol toxicity including suppression of hematopoiesis was associated with the use of a standard dose of allopurinol in renal insufficiency [1,2,4].

The accumulation of oxipurinol, a metabolite of allopurinol, in the blood of the patients with renal insufficiency has been reported [4,5]. In our study, incubation of bone marrow cells with oxipurinol revealed no inhibition of CFU-GM hematopoietic stem cell growth (Fig. 1), and this suggests oxipurinol does not suppress hematopoiesis. These two cases were encountered within a year in our department, and it may not be a rare occurrence. These observations suggest careful monitoring of the hematological status in patients with renal insufficiency who are receiving allopurinol.

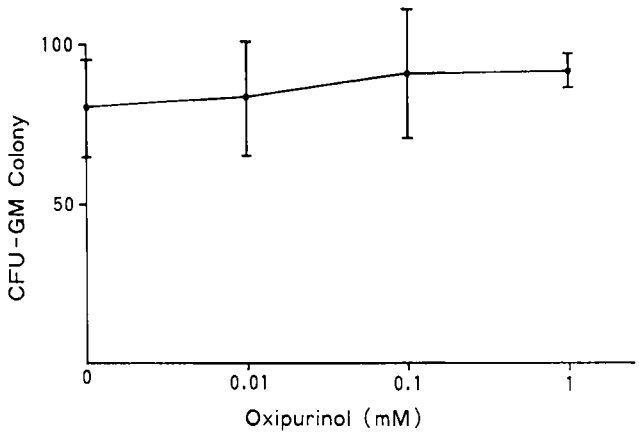

Fig. 1. Effect of oxipurinol on CFU-GM colonies in in vitro culture. Numbers of colonies formed per 2×10^5 bone marrow cells (mean ± SD) are expressed, with continuous exposure of oxipurinol at various concentrations.

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