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An Atypical Case of Hemolytic Anemia

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Introduction

Tumor lysis syndrome (TLS) is a well-known oncologic emergency that can cause significant morbidity and mortality in highly proliferative tumors such as Lymphomas or Leukemias. Rasburicase is a recombinant urate oxidase enzyme that converts uric acid to allantoin, which is 5 to 10 times more soluble in urine than uric acid (1) It is recommended by the 2008 American Society of Clinical Oncology (ASCO) Guidelines for the Management of Pediatric and Adult Tumor Lysis Syndrome as the initial management of patients with high risk of developing TLS and in patients with intermediate risk if hyperuricemia occurs despite allopurinol prophylaxis(2). G6PD-deficient patients are unable to break down hydrogen peroxide that results from the oxidation of uric acid to allantoin therefore increasing their likelihood of developing hemolytic anemia with rasburicase.

Case Presentation

A 68-year-old male with PMH of progressive relapsed CLL/SLL presented to the inpatient Oncology unit for initiation of chemotherapy (Venetoclax- selective, small molecule inhibitor of BCL2). The patient had no acute complaints save mild tension headache. He was initiated on Venetoclax and given prophylactic 3mg Rasburicase as well as IV fluids the same day. The following day the patient had fatigue, shortness of breath and an increase in oxygen requirements requiring nasal cannula which escalated to HFNC. CXR showed evidence of mild pulmonary which was relieved with Lasix. He had a subsequent episode of mild oxygen desaturation the following day with severe shortness of breath and fatigue. Work-up was significant for an ABG with mild decrease in PO2 and normal oxygen saturations. CBC revealed a 2g/dl hemoglobin drop which initially was not adequately responsive to 2 units of packed red blood cell transfusion. Hemolysis workup subsequently revealed an increased LDH of 1151 U/L and decreased haptoglobin (<30 mg/dL).. There was evidence of hemolysis on the pretransfusion specimen and the patient's G6PD screen was positive thereafter. The hemolytic anemia was deemed likely due to Rasburicase. Rasburicase was substituted with allopurinol and the patient was supported with serial monitoring of complete blood count and chemistry profile, supplemental oxygen therapy, transfusion of packed red blood cells, and vigorous hydration with no further episodes of hemolysis. Recommendations were made to screen for G6PD deficiency in all patients with anticipated need for rasburicase.

Images

G6PD phenotype	Implications for phenotypic measures	Dosing recommendations for rasburicase	Classification of recommendations ^a
Normal ^b	Low or reduced risk of hemolytic anemia	No reason to withhold rasburicase based on G6PD status ^b	Strong
Deficient or deficient with CNSHA	At risk of acute hemolytic anemia	Rasburicase is contraindicated; alternatives include allopurinol ^c	Strong
Variable ^b	Unknown risk of hemolytic anemia	To ascertain that G6PD status is normal, enzyme activity must be measured; alternatives include allopurinol ^c	Moderate

CNSHA, chronic nonspherocytic hemolytic anemia.

^aRating scheme described in **Supplementary Material** online (see Strength of Recommendations). ^bA negative or inconclusive genetic test cannot be assumed to indicate normal G6PD phenotype; an enzyme activity test is needed to assign G6PD phenotype in such cases. ^cAllopurinol is associated with severe cutaneous reactions in the rare carriers of the HLA-B*58:01 allele.³⁷

Fig. 1. 2014 Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Rasburicase Therapy in the Context of G6PD Deficiency Genotype

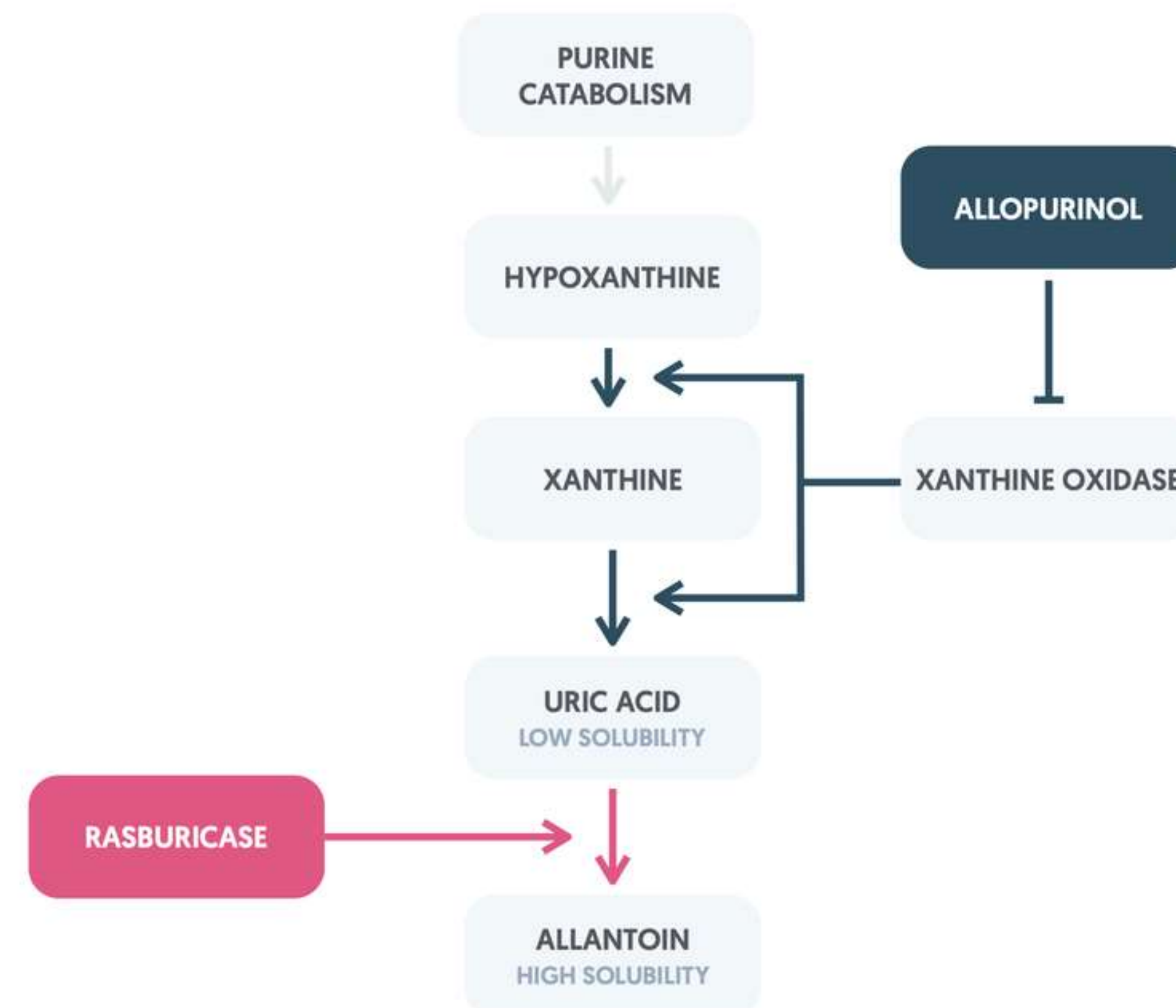


Fig. 2. Rasburicase mechanism of action in the catabolic pathway of purines

Discussion

It is common practice to prophylactically initiate patients that are at high risk for TLS on Rasburicase. As TLS is a significant outcome of chemotherapy causing end-organ damage, it is often not feasible to await test results to initiate prophylaxis. The reported prevalence of rasburicase-induced hemolytic anemia is less than 1%.(3-4) Few cases reports are noted, and hemolysis has been observed during clinical trials. There are 17 reported cases of acute hemolytic anemia or methemoglobinemia after the administration of rasburicase. 12 of those patients were G6PD deficient, 2 patients had normal G6PD activity, and 3 patients had unknown G6PD status or suspected G6PD deficiency(5). Given the lack of significant clinical studies in addition to most studies not including ethnic groups that are at high risk for G6PD deficiency, the representation of morbidity and mortality remains slim. It remains a standard of care to give Rasburicase in anticipation of TLS syndrome even in institutions with a high prevalence of G6PD deficiency within their community. Currently, the use of rasburicase in patients with G6PD deficiency is contraindicated with a black box warning from the FDA(6). Recommendations should be made to review the standard of care and possibly implement testing with a faster turnaround in communities that have a higher representation of G6PD deficiency.

References

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