An Unexpected Emergency Request for Glucose-6-Phosphate Dehydrogenase Testing in a 9-Year-Old African American Boy

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CLINICAL HISTORY

Patient: 9-year-old African American male.

Chief Complaint: Recently diagnosed with acute lymphoblastic leukemia (ALL) after investigation into a large anterior mediastinal mass causing airway compression.

History of Present Illness: The day before the unexpected urgent glucose-6-phosphate dehydrogenase (G6PD) request, the patient was diagnosed with an aggressive form of leukemia and a significant tumor mass causing airway compression. A computed tomography (CT) scan indicated potential renal involvement. Based on this information and the size of the mass, the patient was referred for immediate chemotherapy. However, there was a concern that he could develop tumor lysis syndrome (TLS) during treatment. To avoid this condition, the pediatric intensive care unit (ICU) sought to pretreat the child with rasburicase, which led to the emergency G6PD request.

Previous Medical History: Unknown.

Family History: Largely unknown, but no apparent chronic diseases.

Physical Examination Findings: Three weeks of progressively worsening lymphadenopathy, coughing, night sweats, mild hepatosplenomegaly, and breathing difficulty when supine. The patient arrived at the medical center for airway management and had a temperature of 36.1°C; blood pressure, 120/87 mmHg; pulse, 115 bpm; respiratory rate, 22 breaths per minute, with labored breathing but normal O2 saturation while upright and awake, in room air.

Principle Laboratory Findings: Table 1.

Keywords: deficiency, glucose-6-phosphate dehydrogenase, leukemia, rasburicase, tumor lysis syndrome, uric acid

Abbreviations:
ALL, acute lymphoblastic leukemia; G6PD, glucose-6-phosphate dehydrogenase; CT, computed tomography; TLS, tumor lysis syndrome; ICU, intensive-care unit; UA, uric acid; FDA, United States Food and Drug Administration; RBC, red blood cells; NADPH, nicotinamide adenine dinucleotide phosphate; NA, not applicable; BUN, blood urea nitrogen.

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Questions

1. What are the most striking clinical and laboratory findings for this patient?

2. Is there a legitimate concern that this patient could develop tumor lysis syndrome (TLS)?

3. What are some treatment options for TLS?

4. What could occur if this patient were deficient in glucose-6-phosphate dehydrogenase (G6PD) after receiving rasburicase?

5. Is it likely this patient has a G6PD deficiency?

6. What types of laboratory tests are helpful in confirming a diagnosis of G6PD deficiency?
Possible Answers

1. On admission, the patient exhibited several mildly abnormal laboratory findings, among which were significantly elevated lactate dehydrogenase, uric acid (UA), and white blood cell count (Table 1). The hyperuricemia of the patient prompted the health care providers to administer chemotherapy immediately, to address the aggressive leukemia and to restore normal pulmonary function.

2. This patient is at high risk to develop potentially life-threatening TLS, a rare condition that often occurs after chemotherapeutic treatment if various malignant neoplasms, especially high-grade lymphomas and ALL. As its name implies, rapid tumor cell lysis often results in elevated levels of UA and significant electrolyte imbalances (ie, potassium, phosphate, and calcium) that can result in crystal deposition in renal tubules and culminate in acute renal failure. Once chemotherapy began, we observed shifts in plasma calcium, phosphorus, and UA levels, consistent with cellular lysis.

3. An effective clinical management strategy is to preclude TLS by concurrently administering intravenous fluids and hypouriciemic drugs, which increase glomerular flow and reduce the risk of crystal formation. Historically, the drug of choice was allopurinol, a competitive inhibitor of xanthine oxidase. In 2002, the United States Food and Drug Administration (FDA) approved the use of rasburicase, a recombinant urate oxidase that compensates for the inability of the human body to express this enzyme. Use of rasburicase in patients yields significantly faster reduction in uricemia and more efficient kidney function than use of allopurinol in comparable patients. In our patient, judicious use of rasburicase resulted in the rapid reduction of UA levels and the avoidance of TLS.

4. Rasburicase is contraindicated in patients with G6PD deficiency because administration of this drug could cause death. G6PD catalyzes the first step in the pentose-phosphate pathway and is critical for red blood cells (RBCs) to generate the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH). Individuals with G6PD deficiency are unable to produce sufficient NADPH to maintain normal levels of reduced glutathione, making their RBCs highly susceptible to oxidative damage from certain drugs, ketoacidosis, infections, and ingestion of fava beans. Rasburicase reduces UA to the much more water-soluble product allantoin but also produces hydrogen peroxide, which can cause severe hemolysis and methemoglobinemia in patients with G6PD deficiency.

5. G6PD deficiency is the most common type of enzyme deficiency in humans, with an estimated 400 million people affected worldwide. G6PD deficiency is an X-linked inherited disorder most commonly affecting persons of African, Southeast Asian, and Mediterranean ethnicity. The disease is usually more severe in individuals who are homozygous for the deficiency. In the United States, African American males are most commonly affected, with a prevalence of approximately 10% in that population. Because our patient is male and African American, he had an increased likelihood of G6PD deficiency.

6. Appropriate tests to screen for G6PD deficiency involve assessing the endogenous RBC activity of the patient; qualitative and quantitative laboratory tests are available for this purpose. The former test type is much more commonly used; it is based on an ultraviolet fluorescence spot test. However, colloquially, these qualitative tests have been shown to lack sufficient sensitivity to identify many of the moderate G6PD deficiencies in males or heterozygotic females. Recently, a 62-year-old African American man with leukemia was misdiagnosed as not having G6PD deficiency due to the results of a spot test; after being administered

<table>
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<tr>
<th>Test</th>
<th>Resulting Value</th>
<th>Reference Interval</th>
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<tr>
<td>Albumin</td>
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<td>Anion gap</td>
<td>21‡</td>
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<tr>
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<td>Creatinine</td>
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</table>

NA, not applicable; BUN, blood urea nitrogen; G6PD, glucose-6-phosphate dehydrogenase.

‡Abnormal result.
rasburicase, he developed fatal methemoglobinemia. In our patient, a quantitative assay unequivocally showed that he did not display G6PD deficiency.

Dedication

We are grateful to have worked with Joseph Andris, BS. To all who knew him he was a divine inspiration and gallantly remained an optimist until recently succumbing to the scourge of cancer.

LM

References


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