Scrub typhus infection precipitating hemolysis in a patient with G6PD deficiency: A case report

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Key Clinical Message

Glucose 6 phosphate dehydrogenase (G6PD) deficiency is a well-known red blood cell enzymopathy and a cause of intravascular hemolysis. The patient may present with a chronic or acute episode of hemolysis. This case report presents a child with underlying G6PD deficiency who presented with an episode of extensive intravascular hemolysis, induced by a scrub typhus infection. The essence of this report is a scrub typhus infection without a typical eschar and a covert G6PD enzyme activity found normal during the acute phase of hemolysis, later found to be mild enzyme deficient. Later in the report is how, after systematically ruling out other potential causes, the diagnosis of scrub typhus was eventually confirmed using a reliable serology kit and a false negative covert G6PD enzyme deficiency got uncovered in follow-up reports.

INTRODUCTION

The average life span of red blood cells is 120 days, and hemolysis is a state of premature destruction of red blood cells. When bone marrow cannot compensate for the ongoing loss of red blood cells, anemia develops. Hemolysis can be intravascular or extravascular. Among numerous causes of intravascular hemolytic anemia, commoner ones are malaria, autoimmune hemolysis, G6PD deficiency, and RBC membrane defects. Glucose-6-phosphate dehydrogenase is a housekeeping enzyme that plays a vital role in the prevention of cellular damage from reactive oxygen species.[1] G6PD deficiency is an X-linked disorder, and its estimated global prevalence is 4.9%.[2] Usually the enzyme deficient is asymptomatic until presenting with an acute episode of intravascular hemolysis after being triggered by an oxidant stress. An oxidant stress could be due to an infection, consumption of certain group of drugs, or fava beans.[3]

Scrub typhus is a tropical disease, caused by *Orientia tsutsugamushi* , a gram-negative bacillus and an obligate intracellular parasite belonging to the family Rickettsiaceae. It is transmitted due to bites of infected chiggers (larva form of trombiculid mites). Mostly scrub typhus infection presents with flu-like symptoms (fever, headache, myalgia, etc.), and sometimes severe infection can lead to pneumonia, acute respiratory failure, shock, meningoencephalitis, and DIC.[4] During an episode of hemolysis, identifying the underlying cause is crucial, as controlling the precipitating factor is essential for effective management of the current episode and to consider prophylaxis for the future episodes. Also, understanding potential triggers may shorten hospital stays and reduce healthcare costs. Here, we report a case of scrub typhus infection presenting with extensive intravascular hemolytic anemia, which was later diagnosed as mild G6PD deficiency.

Case History/Examination

A 5-year-old male resident of Kathmandu, Nepal presented to our center with a history of fever and dark-colored urine. According to his mother, the child had been apparently well and actively playful until the previous day when he developed a sudden fever. The fever was intermittent, maximum noted 101°F, and was not accompanied by chills or rigors. The child had a headache, body ache, and passed dark colored urine three times in the last 12 hours (Figure 1). The child denied having any abdominal or back pain, or any urinary or gastrointestinal symptoms. There was no history suggestive of upper respiratory tract infection, mechanical trauma, porphyria, or bleeding diathesis. The mother denied any recent consumption of beetroot, colored candies by her child, or the introduction of new foods into his diet. There was no significant travel or drug history. The child had no previous similar episodes, and there was no significant family history.

At presentation, the child appeared lethargic with tachycardia (pulse 114 bpm, normal volume). He was afebrile, with a normal respiratory rate, blood pressure of 90/50 mmHg (normal for his age, height and gender), and oxygen saturation of 95% in room air. His Glasgow Coma Scale (GCS) score was 15/ 15. Pallor and icterus were present, but there was no limb or facial edema, signs of dehydration, or lymphadenopathy. A thorough head-to-toe examination, including assessments of the central nervous system, chest, and abdomen, showed no significant abnormalities.

Methods

Blood and urine investigations revealed anemia (Hb: 6.1 g/dL), leukocytosis (WBC count: 25.4x10^9 cells/L) with a differential count of [N65, L32, M2, E1], and elevated C-reactive protein (64.8 mg/L). Serum bilirubin was elevated (total: 5.28 mg/dL, indirect: 4.53 mg/dL), while renal function tests and electrolyte parameters were within normal limits. Peripheral blood smear showed anisopoikilocytosis and a reticulocyte count of 1.1% (corrected for anemia). Reports showed a negative direct Coombs test, significantly elevated lactate dehydrogenase (LDH: 1784 U/L), low haptoglobin levels (13 mg/dL). Urinalysis revealed a dipstick positive for heme protein, with no RBCs or pus cells. The urine test for myoglobin was negative.

The clinical findings and investigation results indicated ongoing intravascular hemolysis with a likely infectious etiology. Empirical treatment with intravenous cefotaxime was initiated. However, the patient's pallor worsened, and urine continued to be dark throughout the day, accompanied by several episodes of fever. The patient was transferred to the pediatric intensive care unit (PICU) for unstable vital signs (tachycardia and hypotension). In the PICU, additional blood investigations, including a tropical panel, were conducted, and 2 pints of packed red blood cells were transfused to address a hemoglobin level of 3.1 g/dL. The child was found to be positive for anti-Scrub typhus IgM antibody. The G6PD spectrophotometry revealed an enzyme level of 7.46 U/gm Hb, which is within normal limits. Abiding to the seropositive status and clinical symptoms suggestive of scrub typhus, oral azithromycin was added to the treatment.

Authorship List

Ravi Shukla: Conceptualization; investigation; methodology; writing – original draft.

Mandira Shrestha: Formal analysis; supervision.

Chaitanya Darshan Bhattarai: Methodology; resources.

Kiran Lamichhane : Visualization; Investigation

Paras Yadav: Methodology; resources

Debendra Tamatta: Writing – review and editing.

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