

RSV-associated methemoglobinemia and hemolytic anemia: first reported case

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Introduction: Viral infections are increasingly recognized as triggers of oxidative stress-mediated hematologic complications, including methemoglobinemia and non-immune hemolytic anemia, most commonly in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Such associations have been reported with cytomegalovirus (CMV) and COVID-19 infection. Respiratory syncytial virus (RSV) is a well-established cause of respiratory illness in older adults; however, RSV-associated methemoglobinemia with intravascular hemolysis has not been reported. We describe a case of concurrent methemoglobinemia and intravascular hemolysis precipitated by RSV infection in an immunocompetent adult.

Case Presentation: A 68-year-old man presented with worsening hypoxia, central cyanosis, and dark urine following a viral prodrome. He was febrile, pale, and icteric, with severe hypoxemia. Arterial blood gas analysis demonstrated methemoglobinemia with type I respiratory failure. Laboratory evaluation revealed anemia, elevated lactate dehydrogenase, reticulocytosis, indirect hyperbilirubinemia, and a negative direct antiglobulin test, consistent with non-immune intravascular hemolysis. RSV was detected on multiplex polymerase chain reaction testing, and inflammatory markers were markedly elevated. G6PD activity was normal but considered unreliable during active hemolysis. The patient was treated with high-flow oxygen, intravenous antibiotics, blood transfusions, and high-dose ascorbic acid. Over 1 week, hemolysis resolved, oxygenation improved, and hemoglobin stabilized. He was discharged in stable condition; repeat G6PD testing after recovery was negative.

Discussion: Methemoglobinemia results from oxidation of hemoglobin iron, impairing oxygen delivery despite preserved arterial oxygen tension. When combined with non-immune intravascular hemolysis, this presentation is classically associated with G6PD deficiency or exposure to potent oxidant stressors. Viral infections may generate excessive reactive oxygen species, overwhelming antioxidant defenses, and leading to simultaneous hemoglobin oxidation and erythrocyte destruction. Similar mechanisms have been proposed in CMV- and COVID-19-associated cases. In this patient, negative follow-up G6PD testing suggests that RSV-induced oxidative stress alone was sufficient to precipitate these complications. Experimental data demonstrating RSV-associated oxidative stress support this proposed mechanism. Ascorbic acid was selected, given uncertainty regarding G6PD status and the risk of hemolysis with methylene blue.

Conclusion: This case represents the first reported instance of RSV-associated methemoglobinemia with non-immune intravascular hemolysis in an adult, expanding the recognized systemic complications of RSV infection.

Keywords: Respiratory syncytial virus (RSV), methemoglobinemia, non-immune hemolytic anemia, oxidative stress, reactive oxygen species, ascorbic acid, viral-induced hemolysis, immunocompetent adult.

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Conflict of interest

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