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A case of sulfhemoglobinemia in a child with chronic constipation

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ABSTRACT

Sulfhemoglobinemia is a rare condition in which a sulfur atom oxidizes the heme moiety in hemoglobin, making the hemoglobin incapable of carrying oxygen and leading to hypoxia and cyanosis.

This condition has been described in patients taking sulfur medications or who have cultured hydrogen sulfide producing intestinal bacteria such as *Morganella morganii*. This case describes a pediatric patient who was found to have cyanosis on two occasions of urinary tract infection in the setting of chronic constipation, with confirmed sulfhemoglobinemia during the second admission. Sulfhemoglobinemia due to increases in sulfur producing intestinal bacteria led to cyanosis and low oxygen saturations. The patient had an incidental finding of a pulmonary arteriovenous malformation (AVM) but had a normal PAO2 so was not hypoxemic though she was cyanotic. Low oxygen saturations by pulse oximetry may be explained by dyshemoglobinemia as opposed to true arterial hypoxemia; the importance of measuring an arterial blood gas in cases of cyanosis is paramount.

1. Introduction

Sulfhemoglobinemia is a hemoglobinopathy caused by the oxidation of hemoglobin with compounds containing a sulfur atom [1,2]. It involves the incorporation of a sulfur atom into the porphyrin ring of hemoglobin; the heme moiety is oxidized from the normal divalent to a trivalent state, resulting in reduced oxygen affinity and cyanosis. Normally, sulfhemoglobin is not present in the blood (levels <2%), and levels of greater than 60% can lead to death due to tissue hypoxia. Unlike methemoglobinemia and carboxyhemoglobinemia, there is no antidote for sulfhemoglobinemia [3]. Resolution of the sulfhemoglobin occurs with the end of the red blood cell life-cycle. Sulfhemoglobinemia has most often been associated with the use of drugs such as phenacetin, metoclopramide, dapsone, phenzopyridine, and trimethoprim-sulfamethoxazole [2]. Other causes of sulfhemoglobinemia include hydrogen-sulfide-producing intestinal bacteria, such as *Morganella morganii* [4]. Sulfhemoglobinemia is a recognized cause of cyanosis in patients without respiratory symptoms. This case report describes a pediatric patient with sulfhemoglobinemia associated with urinary tract infection and chronic constipation, and an incidental finding of pulmonary AVM.

2. Case

The patient was a seven-year-old female with chronic constipation and history of hemorrhagic cystitis associated with urinary tract infection (UTI). She presented with dysuria without fever. She complained of mild rhinorrhea, but no cough, wheeze or chest pain. The patient took only polyethylene glycol for chronic constipation; there were no accidental or intentional ingestions of chemicals or medications. She had one prior hospitalization for UTI three months prior with hemorrhagic cystitis, during which time she was also noted to have low oxygen saturation for three days while hospitalized. She did not have other respiratory symptoms or exam findings at that time; chest radiograph was normal. She was treated with supplemental oxygen and ceftriaxone while hospitalized and sent home to complete eight days of cefdinir. The patient lived in a rural setting near dairy farms, and had outdoor exposure to cigarette smoke. The patient did not have any known family history of cardiopulmonary diseases, and immunizations were up-to-date.

In the patient's community emergency department, her oxygen saturation by pulse oximetry was 82% on room air. Pulse was 130 beats per minute and respirations 24 per minute. Patient was not in respiratory distress and cardiopulmonary exam was benign.

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Complete blood count (CBC) showed a hemoglobin and hematocrit of 12.7 g/dL and 37.6% respectively. Urinalysis demonstrated hemoglobin 3+, with >100 red blood cells (RBCs), moderate leukocyte esterase but negative nitrites. Chest radiograph was normal. Ceftriaxone was given for treatment of UTI. During transfer to the Women and Children's Hospital of Buffalo oxygen saturation was 93% on 3L/min via nasal cannula (NC), pulse was 110 beats per minute, and respiratory rate 18 per minute. She was pale with perioral cyanosis. Chest exam was clear. Electrocardiogram was within normal limits. Capillary blood gas while on 3L NC oxygen showed pH 7.44, pCO2 32 mmHg and pO2 170 mmHg. CBC showed hemoglobin and hematocrit at 9.9g/dL and 30.4% respectively, with normal mean corpuscular volume and reticulocyte count. Methemoglobin levels were indeterminate on co-oximetry due to interference from sulfhemoglobin. Per the manufacturer's reference manual, the levels of sulfhemoglobin had to be between 2 and 10% since sulfhemoglobin was detected but able to be corrected. A venous blood gas the day after admission showed pH 7.35/CO2 47/HCO3 24 and continued elevation of sulfhemoglobin. Hemoglobin electrophoresis was normal; blood and urine cultures showed no growth. A CT angiogram of the chest revealed a tiny (<3mm) right lower lobe AVM, thought to be clinically insignificant (Fig. 1). MRI with and without contrast of the brain was negative for any AVMs. A 2D echocardiogram did not reveal any anatomical or physiological abnormalities.

The patient continued with paleness and perioral cyanosis. Arterial blood gas showed pH 7.42, PCO2 38 mmHg, PAO2 104 mmHg, HCO3 25 mEq/L, base excess 0.2. Carboxyhemoglobin levels were within normal limits. Given the normal PAO2 and the presence of an unknown level of sulfhemoglobin on the co-oximeter, a sulfhemoglobin level was sent to an outside laboratory four days after admission. The result was at 3.4% (normal levels less than 2.0%). Stool cultures showed normal intestinal flora.

The patient's oxygen saturations and dysuria improved; she was discharged on amoxicillin for her UTI. The patient saw hematology nine days later; she had no respiratory distress or cyanosis and pulse oximetry was 98% on room air. Repeat sulfhemoglobin level was normal (<2%).

3. Discussion

This case illustrates sulfhemoglobinemia as a cause of cyanosis in a child with UTI in the setting of chronic constipation. Sulfhemoglobin is a stable green-pigmented molecule that lasts the lifespan of an erythrocyte (approximately 120 days) [1]. The presence of this molecule is rare, and has been associated with the use of drugs such as phenacetin, dapsone, metoclopramide, nitrates, and acetanilide [1,2], none of which our patient ingested. In this case, since there were no exogenous causes identified, we postulate that the sulfhemoglobinemia was most likely due to the transmigration of intestinal bacteria during acute illness of UTI with underlying constipation, leading to hydrogen sulfide production. Constipation has been reported in the literature with cases of sulfhemoglobinemia as early as 1948 [3]. Cases of neonatal sulfhemoglobinemia have been caused by intestinal *Morganella morganii* [4]. In our patient, stool cultures showed normal intestinal growth; blood and urine cultures were negative. However, since the patient has had recurrent UTIs, likely secondary to the constipation, and has been treated with multiple courses of antibiotics, it is likely that the intestinal flora had undergone transformation and could

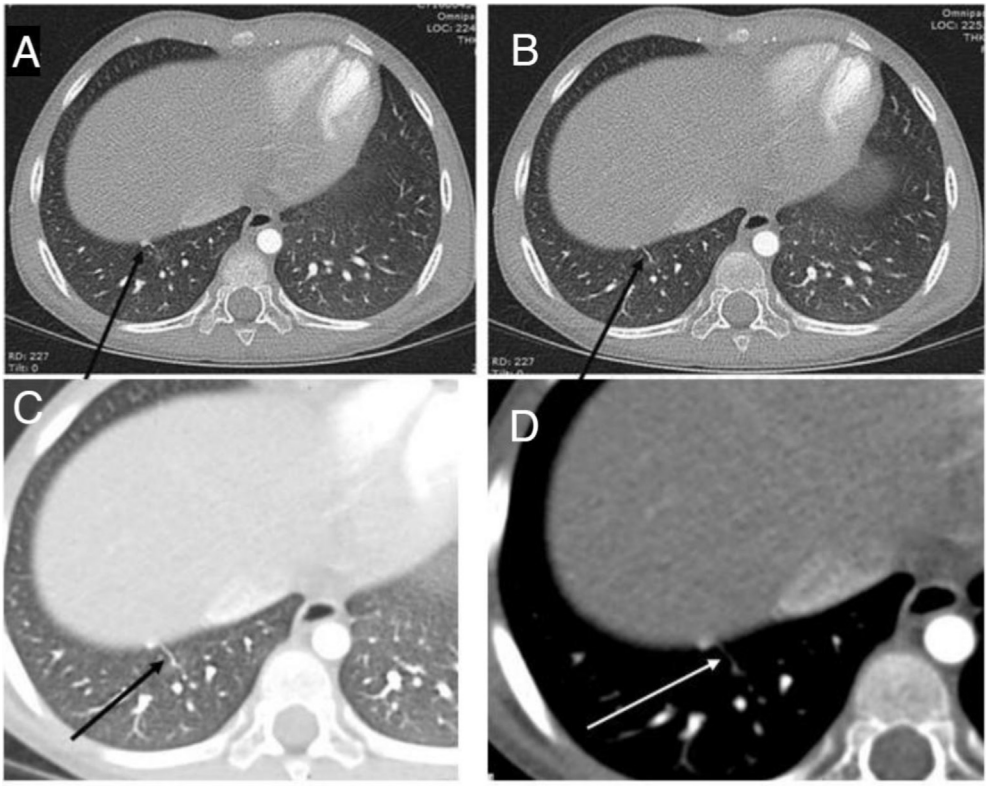

Fig. 1. Right lower lobe arteriovenous malformation.