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Hemoglobin Aalborg Causing Low Oxygen Saturation in a Child

Benjamin Acheampong[1], Melanie Chihak[1,2], Vilmarie Rodriguez[1,2]
[1]Department of Pediatrics and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota; [2]Division of Pediatric Hematology and Oncology, Mayo Clinic, Rochester, Minnesota 55904, USA.

Abstract:

Patients with inherited low oxygen affinity hemoglobin variants such as hemoglobin Aalborg could have low oxygen saturations despite normal oxygen delivery to tissues. Timely and correct diagnosis could help clinicians to avoid unnecessary investigations and spare patients unnecessary cost and anxiety.

Key words: Abnormal Hemoglobins, Hemoglobinopathies, Hemoglobin Aalborg, Humans, Oxygen.

Introduction

Patients with unexpectedly low oxygen saturations may undergo extensive and expensive evaluation to ascertain the cause of their hypoxemia. While cardiopulmonary causes are the main concern in these evaluations, in a subset of patients a hemoglobin variant with low oxygen affinity is the cause and there are several of such variants [1,2]. Hemoglobin Aalborg is one such variant, and was originally reported in some adult patients in Denmark. It is rare, relatively unstable hemoglobin with low oxygen affinity and no significant clinical or hematological complications under normal physiological conditions have been described [3]. Patients who have inherited low affinity oxygen hemoglobin such as hemoglobin Aalborg could have low peripheral oxygen saturations despite normal oxygen delivery to tissues. Timely and correct diagnosis could lead clinicians to avoid unnecessary investigations and spare patients of anxiety.

Case Report

A 8-year-old previously healthy male was seen in our institution for a second opinion regarding low unexplained peripheral blood oxygen saturations. He had presented to an outside facility with cough and was found to have low unexpected peripheral blood saturation on pulse oximetry by his primary care provider. Chest X-ray evaluation was normal. Four days later he presented to the local hospital with a temperature of 104F. His oxygen saturation at room air was 74%, physical examination was normal with no evidence of respiratory distress and a repeat chest X-ray showed a lingular infiltrate suggesting pneumonia. He was admitted to the intensive care unit (ICU) with a presumed diagnosis of acute respiratory failure.

Laboratory evaluation showed hemoglobin of 10.4 g/dL, MCV 76.4 fl, (reference ranges: 11.5-14.5 g/dL; 76-90 fl respectively), normal

Corresponding Author: Dr. Vilmarie Rodriguez
Email: rodriguez.vilmarie@mayo.edu
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reticulocyte count, normal peripheral blood smear and ferritin level. Polymerase chain reaction testing on a throat swab was positive for *Metapneumovirus* and *Mycoplasma pneumonia*. Echocardiography with a bubble study showed a patent foramen ovale with normal left to right shunt. Blood arterial gas analysis revealed a pH 7.42, PO_2 93, and $PaCO_2$ 37 with arterial saturation of 98% and a peripheral blood saturation of 87%. Lactate was normal. He received a 5 day course of azithromycin, and given the persistent low peripheral blood oxygen saturations, a 10 day course of ciprofloxacin for what was thought to be a macrolide resistant mycoplasma infection. A therapeutic trial with steroids was administered for 5 days with no improvement in his saturations. A chest CT was normal except the resolving lingular infiltrate seen on chest X-ray. His pulmonary function tests (PFTs) and diffusing capacity of the lungs for carbon monoxide (DLCO) was normal. Alpha-1-antitrypsin level was checked due to a family history of deficiency, and was found to be normal. Hemoglobin electrophoresis analysis results became available during his third week of hospital stay as hemoglobin Belfast, a high affinity oxygen hemoglobin variant which was inconsistent with his clinical picture. While in the ICU he required 8L of oxygen to maintain his saturations above 90%. His oxygen was gradually weaned and he was discharged home on 1L of oxygen by nasal cannula at night. During an outpatient follow up a sleep study was normal except for low peripheral blood saturations ranging from 74%-84% at room air. A second hemoglobin electrophoresis was sent to another outside laboratory which showed A=72.8%, A2=3.2, Variant=24%, F=0%. Further characterization with genetic analysis showed the variant to be hemoglobin Aalborg. His oxygen was weaned and subsequently discontinued. Patient continued to do well. The patient's family was screened and all had normal peripheral blood oxygen saturations.

Discussion

Mutations in the primary sequence of the hemoglobin molecule lead to alteration in the tertiary or quaternary structure of the hemoglobin tetramer. Such mutations render the molecule unstable resulting in variable clinical and subclinical presentations [4-6]. Hemoglobin Aalborg is one such rare variant resulting from a point mutation involving a CGG to CCG with arginine residue replacing glycine at position 78 of the beta globin chain [4,7]. Hemoglobin Aalborg is considered moderately unstable hemoglobin and is not associated with severe hematological sequelae, although patients can have mild normocytic anemia. Some reports of cyanosis have been described.

Hemoglobin Aalborg has a reduced oxygen affinity due to the altered state of the hemoglobin molecule in the tense and relaxed state [3,6]. This change shifts the oxygen dissociation curve to the right with an increase in the P50. The P50 is the partial pressure of oxygen when half of the hemoglobin molecule is saturated. Measurement of whole blood P50 can be very useful to distinguish between high and low affinity hemoglobin variants. Patients with high affinity variants have low P50 and erythrocytosis without abnormalities of the white cell count or the platelets. In contrast, patients with low affinity hemoglobin variants have a high P50 and in some cases anemia and cyanosis with low peripheral oxygen saturation. Our patient had a calculated P50 of 40.3 (normal 24-28) and low peripheral oxygen saturation. The unexpectedly low saturation results from the different absorption spectrum of the abnormal hemoglobin variant as the conventional dual wavelength pulse oximetry is capable of measuring only oxy-hemoglobin and deoxy-hemoglobin wavelengths. Despite the low peripheral oxygen saturation, oxygen unloading to the tissue is considered normal with no negative effects such as tissue hypoxia [6]. One study looking at six adult family members with hemoglobin

Aalborg reported a concordant low peripheral and arterial oxygen saturation as well as low diffusion capacity for carbon monoxide [3]. Our patient had a high arterial and a low peripheral oxygen saturation on blood gas analysis, as well as a normal DLCO. Whether this represents a developmental variation or it is an inconsistent finding remains to be seen. To our knowledge this is the first reported case of hemoglobin Aalborg variant in a pediatric patient.

The utility of dual wavelength pulse oximetry in monitoring these patients during anesthesia is limited, and thus other monitoring modalities such co-oximetric analysis may have to be employed under such circumstances [1,8,9]. However, in a patient with low oxygen affinity hemoglobin variant, knowledge of the pulse oximetry limitation and attention to the vital signs and end tidal carbon dioxide monitoring may ensure the safety of the patient during brief procedures requiring deeper sedation or anesthesia.

While this hemoglobin variant is asymptomatic, under oxidative stress conditions, significant hemolysis can occur and patients should be counseled appropriately [3,6,7]. Our patient had no symptoms and was incidentally found to have low peripheral oxygen saturation during the evaluation of mild respiratory symptoms. Patients with low oxygen affinity hemoglobin variants may not require any treatment, but knowledge of their condition will help prevent unnecessary therapeutic interventions and expensive investigations. When a low oxygen affinity hemoglobin variant is suspected, it is important to measure a whole blood P50, and if elevated, a high performance liquid chromatography (HPLC) hemoglobin separation should be done. If a variant is identified, genetic analysis should be done to identify the exact mutation [3].

Conclusion

Low oxygen affinity hemoglobin variants such as hemoglobin Aalborg, Kansas, Beth Israel and others should be considered in the rare differential diagnosis of unexplained low oxygen saturations in otherwise healthy individuals once common cardiopulmonary causes have been excluded.

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