A 14-Year-Old Boy with Chronic Cyanosis, Mild Anemia, and Limited Physical Resistance to Stress

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CASE

In April 1997, a then 4-year-old boy suddenly fell ill with fever, cough, fatigue, and poor physical resistance to stress. Marked cyanosis of the lips and the nail beds was noted. During his 3-week hospital stay, mycoplasmosis of the lung and a respiratory syncytial virus infection were diagnosed by the detection of high-titer *Mycoplasma* agglutinins in serum samples and positive test results for the presence of respiratory syncytial virus in nasopharyngeal secretions. In addition, incipient exogenous allergic alveolitis was suspected because of the presence of budgerigars and cockatiels in the boy's home and the finding of serum positivity for IgG precipitin. The boy's condition gradually improved with cefuroxime and clarythromycin treatment and oxygen therapy. α_1-Antitrypsin deficiency and cystic fibrosis were excluded. Because the patient's oxygen saturation failed to improve during sleep and at times dropped to well below 90%, a cardiology examination was performed, and a cardiac defect was ruled out. The reticulocyte count and the curve of the absorption spectrum of oxyhemoglobin and deoxyhemoglobin were within the reference interval. Hemogram results were as follows: leukocytes, 5500/μL (reference interval, 5100–12 900/μL); hemoglobin, 11 g/dL (reference interval, 10.7–13.9 g/dL); thrombocytes, 319 000/μL (reference interval, 200 000–445 000/μL); mean corpuscular volume, 78 fL (reference interval, 74–89 fL); mean corpuscular hemoglobin, 26 pg (reference interval, 24.5–31 pg). At the same time, hemoglobin electrophoresis excluded hemoglobinopathy. One year later, the boy was electively readmitted to the pediatric clinic for assessment of continuous intermittent low oxygen saturation. Exogenous allergic alveolitis was excluded after bronchoalveolar lavage; sarcoidosis was also ruled out. Slight cyanosis of the lips was once again noted, however. Pulse oximetry showed normal oxygen saturation >93% during the day, but oxygen saturation repeatedly dropped to as low as 85% during sleep. Oxygen administration improved saturation immediately to >95%. These fluctuations in oxygen saturation were confirmed by capillary blood gas analysis. When, the mother happened to try out the finger clip of the pulse oximeter on her own finger during the boy's hospital stay, low oxygen saturation was noted in her as well. Apart from hypertension, she had no preexisting conditions. A physical examination revealed neither cardiac nor bronchopulmonary disease. Hemoglobin electrophoresis revealed no abnormal hemoglobin. The mother reported poor physical resistance to stress with dyspnea and intermittent cyanosis of the lips after minor physical activity, which had been present since childhood. Owing to the still unexplained cause of the low oxygen saturation, the

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mother was admitted to a pneumology unit to test her once again for a cardiac defect as well as sleep apnea syndrome. None of the tentative diagnoses could be confirmed. She showed a continuously low oxygen saturation of <90%, and pulse oximetry measurements documented >140 desaturations (as low as 71%) during sleep. This finding was eventually interpreted as a faulty pulse oximetry measurement, however, due to poor acral circulation. Psychiatric treatment was recommended despite the fact that a capillary blood gas analysis also had revealed low oxygen saturation. Because physical resistance to stress continued to be very poor in both the mother and son, the family's general practitioner contacted us after conducting intensive research, because we had previously described a new hemoglobin variant, hemoglobin Bonn, which produces falsely low oxygen saturation measurements *(1)*.

References

1. Zur B, Hornung A, Breuer B, Doll U, Bernhardt C, Ludwig M, Stoffel-Wagner B. A novel hemoglobin, Bonn, causes falsely decreased oxygen saturation measurements in pulse oximetry. *Clin Chem* 2008;54:594–6.

Questions to Consider
• What possible causes for peripheral cyanosis exist once pulmonary and cardiac reasons have been excluded?
• What examinations must be carried out if a hemoglobin anomaly is suspected?
• What limitations exist for identifying hemoglobin variants?

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the February 2012 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol58/issue2 and follow the link to the Clinical Case Study and Commentaries.

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