



Clinical case report based study

A patient with rheumatic heart disease presented with central cyanosis due to acquired methemoglobinemia during late pregnancy – A rare association

Soumya Patra^{a,*}, Jayashree Kharge^b, Ashalatha Bharatha^c, Ramegowda T. Raghu^c, Cholenahally N. Manjunath^d^a Post Doctoral Trainee, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences & Research, Bannerghatta Road, Bangalore, Karnataka 560069, India^b Asst. Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences & Research, Bannerghatta Road, Bangalore, Karnataka 560069, India^c Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences & Research, Bannerghatta Road, Bangalore, Karnataka 560069, India^d Professor & Head, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences & Research, Bannerghatta Road, Bangalore, Karnataka 560069, India

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ABSTRACT

A 21-year-old pregnant female of known rheumatic heart disease presented to us for evaluation of central cyanosis during her late pregnancy. Though she was investigated for any associated congenital heart disease or pulmonary arteriovenous fistula, but incidentally she was diagnosed of having acquired methemoglobinemia. Her serum methemoglobin level was 33% which was far above the normal range. Ultimately, she was managed conservatively and delivered through elective caesarean section. Though the delivered baby was lethargic after birth, but later he was improved and discharged. This was the first case reported so far that a pregnant patient of rheumatic heart disease developed cyanosis due to methemoglobinemia.

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1. Introduction

Pulmonary disorder could be associated as a complication of rheumatic heart disease and especially mitral stenosis.¹ Central cyanosis is usually not seen in all these cases, except during acute pulmonary edema.¹ Methemoglobinemia is characterized by high levels of MetHb in the blood. It occurs by oxidation of the iron moiety of hemoglobin from the ferrous state (Fe^{2+}) to the ferric state (Fe^{3+}), forming MetHb. The MetHb is incapable of transporting oxygen and shifts the oxygen dissociation curve leftward.² This reduces oxygen delivery, thereby increasing the risk of tissue hypoxia.² Methemoglobinemia should be considered in the differential diagnosis of patients who present with central cyanosis and decreased peripheral oxygen saturation.³ In our case, the patient in her third trimester of pregnancy presented to us with central cyanosis. This is the first case we are reporting, where a pregnant patient of rheumatic heart disease presented with cyanosis due to methemoglobinemia and was managed conservatively with elective caesarean section.

2. Case report

A 21-year-old primigravida was referred to our hospital for cardiac evaluation. She was a known case of rheumatic valvular

heart disease and was in regular follow-up in our hospital. This time, in her 36th week of gestation, she was referred by her obstetricians for the evaluation of her bluish discoloration of whole body. She did not have dyspnea, fever, cough, or swelling of leg but had excessive fatigability. She did not give any specific history of ingestion of any drug or substances which can cause bluish discoloration of whole body. But she gave the history of drinking tube-well water. Past history was also uneventful. On general physical examination, she was found to have central cyanosis, mild tachypnea (respiratory rate: 22/min), tachycardia (pulse rate: 96/min), and no clubbing. Pulse oximeter showed the saturation of oxygen of 86%. On cardiovascular examination, soft first heart sound and a grade 3 pan systolic murmur were auscultated. Other system examinations were found to be normal.

On investigation, her hemoglobin was 10.7 g/dl and the electrocardiogram showed only sinus tachycardia. Arterial blood gas analysis showed pH, 7.44; pCO_2 , 38 mm of Hg; and pO_2 , 112 mm of Hg. Echocardiography report showed rheumatic valvular heart disease with moderate mitral regurgitation and no evidence of congenital heart disease. As this patient presented with acute onset cyanosis and echocardiography did not reveal any congenital heart disease, so we are suspecting that she might have pulmonary arteriovenous (AV) fistula. So contrast echocardiography was done to rule out pulmonary AV fistula and it was found to be a suspected case. As she had normal pO_2 in blood with low oxygen saturation and no clubbing, serum methemoglobin level was sent and found

* Corresponding author. Tel.: +91 9686480971.

E-mail address: dr_soumyapatra@rediffmail.com (S. Patra).

to be 33% (normal: <2%). Due to her cyanosis, excessive fatigability with mild tachypnea and tachycardia, obstetricians planned elective caesarean section as soon as after 37th completed weeks of gestation. The color of the blood was found as chocolate brown during operation. She was not treated with methylene blue injection as it was not available. A male baby of 2 kg was born. As she was given narcotics during general anesthesia, baby was lethargic after delivery and was intubated and ventilated. Baby was treated with naloxone injection after birth as an antidote of narcotic analgesic used intraoperatively. Later, baby was survived, accepted breast feeding, and discharged after 5 days of birth. Her serum methemoglobin level estimated on 4th day after delivery was reduced to 12% and cyanosis was also improved. Oxygen saturation was also increased to 92% during discharge. As she had doubtful contrast echocardiography of pulmonary AV fistula, she had undergone computed tomography pulmonary angiography 6 weeks after delivery and it was completely within normal limit. Later for further confirmation to rule out pulmonary AV fistula, she had undergone pulmonary angiogram which was also found to be normal. Now both the mother and baby are doing well in follow-up.

So, this pregnant lady with rheumatic mitral regurgitation had presumed to have acquired methemoglobinemia as she was not cyanosed since birth and had history of drinking of tube-well water. Though confirmatory test for diagnosis of variety of methemoglobinemia is genetic analysis, due to her financial constrain, this test could not be done.

3. Discussion

Peripheral cyanosis is common among patients with severe rheumatic valvular disease especially those who have low cardiac output.¹ The occurrence of central cyanosis in these patients is, however, rarely seen in the absence of overt pulmonary edema or hypertension. Congenital pulmonary AV fistulas usually present in adult life as incidental chest radiographic findings or recurrent bleeding from mucosal telangiectasias. Dyspnea, cyanosis, and clubbing are found only among patients with large shunts.¹ In our case, we have ruled out the presence of pulmonary AV fistula or other associated congenital heart disease.

Methemoglobinemia may be congenital or acquired.⁴ In the congenital homozygote's variety, the defect in methemoglobin reductase lacks the ability to convert methemoglobin to hemoglobin and they are cyanosed from birth. But in heterozygote's variety, as they have a partial defect in methemoglobin reductase, they may develop methemoglobinemia when challenged with oxidative drugs.⁴ Acquired methemoglobinemia may result from oxidant drugs including nitrites, nitrates (from contaminated well water), aniline dyes, antimalarial drugs, and phenacetin.⁵ But in our case, no specific drug or substance was used except for drinking tube-well water in home. There are some literatures which have demonstrated that methemoglobinemia can be associated with drinking of tube-well water.⁶ As she is not having methemoglobin in normal range even after delivery, so it is also supporting that due

to drinking contaminated water, her baseline value is on higher side. Though heterozygote's variety of methemoglobinemia can present as same pattern and for this genetic study is needed. In our case, she developed cyanosis acutely during her third trimester and she was acyanotic during her previous follow-up for rheumatic heart disease, so we can presume that her cyanosis was due to acquired methemoglobinemia. As the presence of methemoglobin shifts the oxygen dissociation curve to the left, resulting in decreased unloading of oxygen to the tissues, so symptoms depend on the quantity of methemoglobin.² Normal adults can have methemoglobin up to 2% in the blood and its production by auto-oxidation is balanced via methemoglobin reductase. Clinically detectable cyanosis usually develops at levels of over 10%, whereas at 30%, hypoxia appears and levels of 60–70% are often fatal.⁴ Treatment of methemoglobinemia with ascorbic acid or methylene blue is effective.⁷ Our patient had excessive fatigability with mild tachypnea and tachycardia. As there are evidences which suggest that epidural anesthesia may further cause neonatal methemoglobinemia⁶ and she was deeply cyanosed and fatigued so obstetricians have decided to go for elective caesarean section at 37th completed gestational weeks. In our case, the baby was affected due to the effect of general anesthesia but not due to methemoglobinemia. Methemoglobin level was reduced after delivery with improvement in cyanosis. As pregnancy is a stressful event, methemoglobin level can be increased during pregnancy especially during delivery and it may be normalized after delivery.⁸

This is the first case of acquired methemoglobinemia in pregnancy in a patient with rheumatic mitral regurgitation. So, any patient of rheumatic heart disease, if they developed cyanosis, along with congenital malformation like pulmonary AV fistula, methemoglobinemia also has to be ruled out.

Conflict of interest

All authors have none to declare.

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