AN INTERESTING CASE OF FEVER WITH CENTRAL CYANOSIS

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Abstract:
A 13 years old female presented with fever for 10 days with central cyanosis, which did not improve with supplemental oxygen, with no clinical evidence of respiratory or cardiac disorder. Pulse oximetry showed spO2 of 82 percent and arterial blood gas analysis showed PaO2 and SaO2 in the normal range. Echocardiography and CT chest were normal. All other tests including tests for hemolysis were within normal limits. As there was saturation gap, blood methemoglobin was tested. Methemoglobin level was 11 percent on the second day of admission, which decreased to normal values in 8 days. G6PD levels within normal limits. Patient had been treated with chloroquine for 3 days before she was referred to us. Fever subsided on the second day with symptomatic treatment. So we report this case, a case of acquired methemoglobinemia due to chloroquine, a rare complication.

Keyword:
Methemoglobinemia, saturation gap, chloroquine.

CASE REPORT:
A 13 year old girl was admitted with a history of fever for 10 days, which was high grade intermittent associated with chills and rigors, with generalised body pain with no other positive history. She had been treated in a private hospital for the same with chloroquine for 3 day, primaquine 15 mg single dose, ceftriaxone 1gm for 3 days with paracetomol 500mg 8th hourly for 5 days. On examination patient was fully conscious and oriented and she had fever of 100 ° F, with central cyanosis, no clubbing, no pallor, not jaundiced, no significant lymphadenopathy. Respiratory rate was 20/min, pulse rate was 130 / min. normovolemic, had normal blood pressure. Oxygen saturation was 82% in room air. Chest was clear, heart sounds were normal, no organomegaly.
PHOTOGRAPH SHOWING CHOCOLATE BROWN COLOUR BLOOD OF PATIENT ALONG WITH THE CONTROL PHOTOGRAPH SHOWING CENTRAL CYANOSIS IN THE PATIENT

She was given inhaled oxygen, IV Ceftriaxone, T.paracetamol and IV fluids. Investigations showed Hb-10g%, WBC - 12,800 (neutrophils- 58%) and platelets -1.79 lacs. Blood urea and creatinine were normal. Urine routine was normal. Peripheral smear showed microcytic hypochromic anemia with reticulocytosis of 2%. G6PD activity was normal. Serum LDH was within normal limits. Blood gas analysis showed partial pressure of oxygen 96 mm Hg with calculated SaO2 94%. Smear for malaria and malaria antigen test were negative. Ultra sonogram of abdomen revealed no significant findings. Blood cultures showed no growth. MSAT for lep-tospirosis and dengue IgM were negative. As patient's cyanosis did not improve with supplemental oxygen, echocardiography and CT chest were done to rule out cardiac and respiratory disorders, which were normal. As patient had saturation gap (difference between calculated SaO2 and pulse oximetry values), we thought of abnormal haemoglobin in blood. Methemoglobin level estimation was sent on 2nd after admission. It was found to be raised to 12%, confirming the diagnosis of methemoglobinemia. We added oral Ascorbic acid to the treatment. She became afebrile on 3rd day of admission and LDH, complete hemogram, RFT and LFT remained normal. Blood methemoglobin levels on 4th and 7th day were 8% and 5% respectively. Patient made steady progress from 3rd day onwards and was discharged on 8th day.

DISCUSSION: CYANOSIS:
Bluish discolouration of skin and mucous membrane due to increased quantity of 1) reduced hemoglobin >4g/dl 2) methemoglobin>1.5g/dl 3) sulfhemoglobin>0.5g/dl 4) abnormal hemoglobin It is the ABSOLUTE, rather than the relative amount of reduced hemoglobin that is important in producing cyanosis Site: Mainly over lips, nail bed, ear and malar eminences. Diagnosed reliably when SaO2 <85%, and in dark skinned individuals when SaO2 < 75% Causes of central cyanosis:
A. Decreased arterial oxygen saturation
B. Hemoglobin abnormalities
c) Decreased arterial oxygen saturation
1) Decreased atmospheric pressure - high altitude
2) Impaired pulmonary function
   i. alveolar hypoventilation
   ii. ventilation-perfusion mismatch
   iii. impaired oxygen diffusion
3) Anatomic shunt
4) Hemoglobin with low affinity for oxygen
B) Hemoglobin abnormalities
   i. methemoglobin
   ii. sulfhemoglobin
Oxidant exposure is generally the cause of acquired methemoglobinemia as seen in exposure to drugs, chemicals or solvents or indirectly as in sepsis. By oxidation the ferrous molecule in the hemoglobin gets oxidized to ferric form, the resultant molecule is methemoglobin, which is incapable of binding oxygen. Usually levels greater than 2% are non physiological or abnormal.
Symptoms generally appear when levels exceed 15% and levels >70 % may cause death. Spectral properties of methemoglobin are different and it interferes with pulse oximetry readings which are characteristically low. Arterial blood gas partial pressures are very high because of high flow oxygen therapy. This case illustrates an uncommon condition i.e. methemoglobinemia precipitated by a very commonly used drug, Chloroquine. Chloroquine is a very widely used drug in India. Chloroquine induced methemoglobinemia has been reported before. One should have a high index of suspicion and low threshold for investigations where cases are complicated. In the periphery, where investigation facilities are limited and even simple monitoring facilities like pulse oximetry are unavailable, early referral to higher centers in the event of complications is recommended.

Management of methemoglobinemia:
Methylene blue is the preferred antidote for treatment of methemoglobinemia. It should be considered for use in symptomatic patients with methemoglobin levels >20%, or asymptomatic patients with methemoglobin>30%. Patients who are symptomatic or have concomitant medical issues that compromise oxygen delivery to tissues (e.g., anemia, carbon monoxide exposure, cardiac disease, lung disease) should be treated with antidote at lower levels of methemoglobinemia if clinically indicated.

- Methylene blue should be diluted to a 1% solution (10 mg/mL) and dosed as 1-2 mg/kg intravenously over 3-5 minutes.

- Clinical improvement is expected within 15 to 60 minutes. If minimal or no improvement is noted at 30 minutes, a repeat dose of 1 mg/kg should be administered intravenously.

The maximum dosage is 7mg/kg in a 24-hour period.

A continuous infusion (0.1 mg/kg/hr) may be considered in cases of agents (such as dapsone) that generate methemoglobin over a long period of time.

Methylene blue causes the skin and mucous membranes to have a dusky-blue appearance. This can make the patient appear more cyanotic and interfere further with pulse oximetry readings.

- Possible causes of methylene blue treatment failure
- Concomitant severe hypoxemia
- Continued drug/toxin absorption due to inadequate decontamination
- Discoloration of skin due to large dose of methylene blue
- Overwhelming and profound oxidative stress from toxin or ingestion
- Sulfhemoglobinemia

Unrecognized hereditary disorders: Glucose-6-phosphate dehydrogenase (G6PD) deficiency, NADPH methemoglobin reductase deficiency, presence of Hemoglobin M Vitamin C can be used in the treatment of familial idiopathic methemoglobinemia.
CONCLUSION:
Central cyanosis, needs prompt attention management. Respiratory and cardiovascular causes are to be sought in emergency department. A careful drug history and a high index of suspicion are required for diagnosis of abnormal hemoglobins, so that early appropriate therapy can be instituted, especially for toxin induced methemoglobinemia.

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