Ind J Clin Biochem (Apr-June 2017) 32(2):248–250
DOI 10.1007/s12291-016-0586-5

CASE REPORT

Methemoglobinemia: Living with Dormant Devil

Dhiraj J. Trivedi[1] · **Bandi Joshiraj**[2] · **Vijay Bidkar**[3] · **Raghavendra Rao**[2]

Received: 7 April 2016 / Accepted: 1 June 2016 / Published online: 13 June 2016

Abstract Methemoglobin is an oxidized form of hemoglobin. NADH methemoglobin reductase deficiency or inactivity is the cause of methemoglobin. Excessive production, resulting in accumulation, causes methemoglobinemia. It can be congenital or acquired. We present a case of dormant congenital methemoglobinemia detected accidentally on preoperative assessment, due to low oxygen saturation even at $F1O_2$-1.0 associated with central cyanosis. The patient had 27.7 % methemoglobin, living his life without any complications. The patient was operated upon successfully for tympanoplasty and mastoidectomy under local anesthesia by taking proper precautions.

Keywords Methemoglobin · Hemoglobin derivative · NADH methemoglobin reductase · Cyanosis

Introduction

Hemoglobin is a conjugated protein having four iron porphyrin prosthetic groups. Ferrous ion (Fe^{+2}) present in normal hemoglobin binds with oxygen and facilitate its transport to tissue. Fe^{+2} of heme molecule when oxidized to ferric (Fe^{+3}) ionic state, an abnormal form, Methemoglobin results. Oxygen does not bind with methemoglobin, but the presence of methemoglobin increases affinity for oxygen in oxyhemoglobin and shift oxygen dissociation curve to left [1] Normally, 1–2 % of body's total hemoglobin gets oxidized to methemoglobin [2, 3]. Intracellular enzyme of red blood cells, NADH methemoglobin reductase, NADPH methemoglobin reductase, Glutathione reductase and ascorbic acid take care of 95–99 % of methemoglobin produced under normal circumstances and keep the level below 1 % [4].

Methemoglobinemia is rare but, life threatening condition. Increased level of methemoglobin can be congenital or acquired and results in hypoxia, weakness, headache, nausea or dizziness at low concentrations, whereas, metabolic acidosis, Cardiac arrhythmia, seizures, coma or even death can occur at higher concentrations [5]. Due to lack of systematic epidemiological studies and unawareness of disease, very few cases of methemoglobinemia are reported from India. There are reports of acquired methemoglobinemia from industrialized patches of Gujarat, Maharashtra, Karnataka and Punjab states of India.

In the present report, we highlight ignored, hidden and a clinically dormant case of methemoglobinemia detected accidentally during the preoperative anesthesia visit.

✉ Dhiraj J. Trivedi
dhiraj99trivedi@gmail.com

Bandi Joshiraj
josh755pm@gmail.com

Vijay Bidkar
dr.vijaybidkar@gmail.com

Raghavendra Rao
rupprao@gmail.com

[1] Department of Biochemistry, SDM College of Medical Sciences and Hospital, Dharwad, Karnataka, India

[2] Department of Anesthesia, SDM College of Medical Sciences and Hospital, Dharwad, Karnataka, India

[3] Department of ENT, SDM College of Medical Sciences and Hospital, Dharwad, Karnataka, India

Case Report

A 33 years male patient was admitted to Unit I under ENT department and posted for tympanoplasty and mastoidectomy under GA at SDM College of Medical Sciences, Dharwad. In the preoperative period, it was noticed that the patient had blue tongue, dark lips (Fig. 1) and bluish nail beds. Before starting GA SpO_2 was 82–85 % (normal 97 %) and 87 % on $F1O_2$-1.0, SpO_2 did not improve even with oxygen therapy.

The patient had no history of any food or drug intake which could cause cyanosis, but on asking, the patient informed that he has blue skin (cyanosis) since childhood. Since many years patient is working as a heavy automobile driver.

On clinical examination, clear signs of central cyanosis were noted, No Icterus was present. The patient had normal height and weight. Pulse rate, BP and respiratory rate were normal. Oxygen saturation was 82–85 % on ambient air, no improvement was observed even with 100 % oxygenation. CVS, CNS, respiratory examination remained non significant.

Considering above findings, administering GA was suspended due to suspected methemoglobinemia. After obtaining informed consent, arterial blood sample was sent to the Department of Biochemistry and Hematology for further investigations and confirmation.

Lab Reports

Hemogram: Hemoglobin 18.2 g/dl (past report shows consistent high hemoglobin level); PCV:53.2; RBC count: 6.1 lakhs/cmm, Platelet: 1.86 lakhs/cmm, White cell: 7150 cell/cmm, differential count: shows few reactive lymphocytes. PS shows mild polycythemia. Blood group: B Positive.

Biochemical Parameters

Random Blood glucose: 92 mg/dl,
Liver function Test: AST: 34 IU/l, ALT: 51 IU/l, ALP: 71 IU/l, GGTP: 24 IU/l, Total protein: 8.0 g/dl, Albumin: 4.0 g/dl, Globulin: 4.0 g/dl, A/G ratio: 1.0
G6PD test decolorisation time: 38 min (Normal)
Renal Profile: Urea: 14 mg/dl, Creatinine: 1.3 mg/dl,
Electrolyte: Na^+-135 mmol/l; K^+-4.59 mmol/l; Cl^--101 mmol/l
ABG: pH-7.385; pCO_2-24.5 mmHg; pO_2-151.7 mmHg on room air;
O_2Sat 99.2 %; CtO_2 21.2; HCO_3^- 14.3; BE −8.6; Osm 169.1

Hemoglobin Electrophoresis

Chocolate brown colour blood (Fig. 2), Unstable hemoglobin Positive; HbA 95.03 %; HbA2-4.27 %; HbF-0.7 %; HbS-0; HbD-0; HbC-0.

Spectroscopic examination on 2 % RBC lysate displayed the characteristic band in red–orange spectra above 40 % dilution. Indicative of methemoglobinemia [6]. Plasma did not show such band.

Colour comparition test [7] Performed on patients blood matches between 20 and 30 % concentration.

Due to lack of enzyme study at our center and looking at the economical status of the patient, enzyme study was not

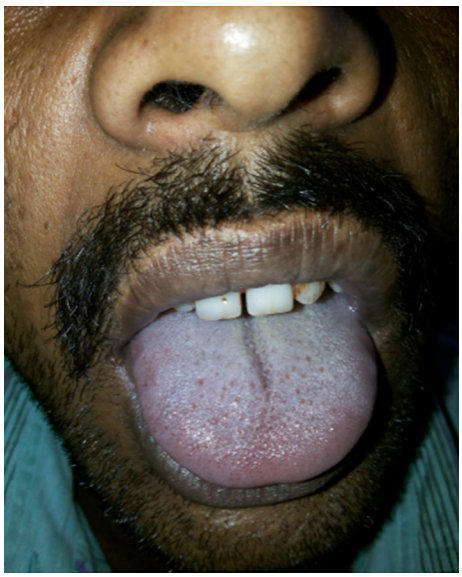

Fig. 1 Central cyanosis (*blue toungue* and *dark lips*)

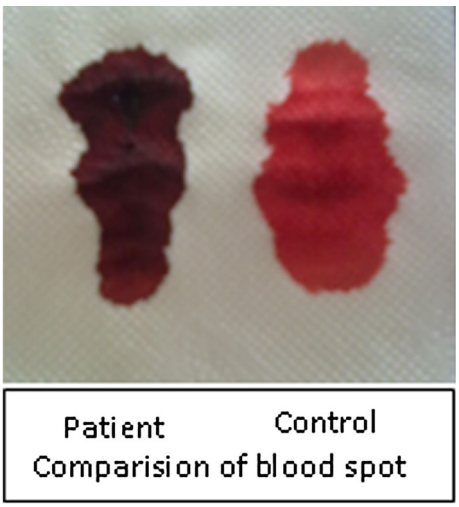

Fig. 2 Blood spot on *white* paper

performed. Patient's family members were examined for any chance of genetic inheritance but results were negative.

The surgery was deferred for 2 days, for investigating the cause of cyanosis and for the proper planning and management of anesthesia. After assessing the complete clinical history and laboratory reports, patient was diagnosed as a case of congenital methemoglobinemia. Two days later, surgery was done under local anaesthesia, using bupivacaine 0.25 % with adrenaline (20 ml of bupivacaine containing adrenaline 1:200,000 concentration), supplemented by low dose propofol infusion for sedation. There were no major problems on table during 2 h of surgery. SpO_2 varied between 87 and 92 %, bolstered by O_2 using a face mask ($F1O_2 = 0.42$). The Patient remained stable in the recovery room and discharged on the 2nd postoperative day with instructions for follow up.

Discussion

We report a clinically dormant case of congenital methemoglobinemia having typical chocolate brown colour arterial blood (Fig. 3), showing symptoms of consistent central cyanosis due to methemoglobin level between 25 and 30 % of total hemoglobin.

Usually methemoglobinemia <5 % is non-complicating, a good history and clinical suspicion help early diagnosis. Genetic or familial methemoglobinemia was first reported in 1948, drug induced cyanosis are known since 1890 [8]. Normally NADH methemoglobin reductase (NADH diaphorase) repairs damage caused due to oxidation of iron atom in hemoglobin. Deficiency or absence of this enzyme leads to congenital methemoglobinemia. Congenital methemoglobinemia are classified as type I to type IV based on the absence or defect in NADH methemoglobin reductase enzyme in various tissues. In congenital methemoglobinemia persistent diffuse slate gray cyanosis is often present from birth and patient remains asymptomatic. Acquired methemoglobinemia is due to oxidant drugs or poor sanitation and water or organic dyes. In the present case, patient suffered from congenital methemoglobinemia which remained silent, But additional nitric oxide fumes of diesel from heavy vehicle driving may have contributed to persistent high levels, to which the body has adapted in the long run. Normally intravenous injection of 1–2 mg/kg methylene blue, or intravenous dextrose is a recommended treatment [5] but it was not administered for this case.

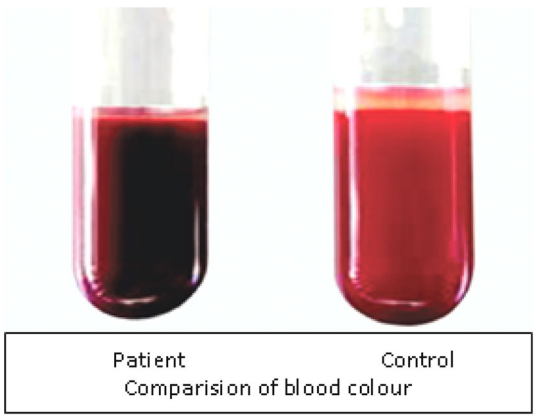

Fig. 3 Comaprision of arterial *blood colour*

Conclusion

With reference to clinical examinations, symptoms and laboratory reports we conclude that the patient is a case of congenital methemoglobinemia. The asymptomatic dormant disease required a closer look.

Acknowledgments We owe thanks and due acknowledgments to Dr. Pryanka for her help in collection of sample and photographs and Mr. Guruswami P, for his technical help in Biochemistry.

Compliance with Ethical Standards

Conflict of interest The authors of this case report have declared that they have no conflict of interest.

Ethical committee This study is purely a self funded study, approved by the institutional ethical committee.

Informed Consent The sample used for the study was blood, which was collected from patient after explaining and taking consent.

References

1. Ramanamurthy SV. Methemoglobinemia: a reappraisal with an indian perspective. www.apiindia.org/medicine_update_2013/chap77.pdf.
2. Guyton AC, Hall JE, editors. Text book of medical physiology. 11th ed. Philadelphia: Elsevier Saunders Publ; 2011.
3. Nelson L, Lewin N, Howland MR, Hoffman R, Goldfrank L, Flomenbaum N, editors. Goldfrank's toxicology emergencies. 9th ed. New York: Mc Graw Hill Professional; 2010. p. 1698–710.
4. Ashurst J, Wasson M. Methemoglobinemia: a systemic review of the pathophysiology, detection and treatment. Del Med J. 2011;83:203–8.
5. Rehman HU. Methemoglobinemia. West J Med. 2001;175:193–6.
6. do Nascimento TS, Lami Pereira RO, Dias de Mello HL, Costa J. Methemoglobinemia: from diagnosis to treatment. Rev. Bras. Anestesiol. 2008; 58.6 (Online ISSN 1806-907x).
7. Barnard RD. The reactions of nitrite with hemoglobin derivatives. J Biol Chem. 1937;120:177–91.
8. Shaihana F, Dhammika MD, Nicholas AB, Andrew HD. A simple quantitative bedside test to determine methemoglobin. Ann Emerg Med. 2010;55–2:184–9.