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DAPSONE INDUCED METHEMOGLOBINEMIA

General Medicine

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ABSTRACT

Methemoglobinemia, a potentially life-threatening condition in which the oxygen-carrying capacity of blood in body tissues is reduced, is a known adverse effect of dapsone. Clinical suspicion of methemoglobinemia can be made when there is cyanosis, saturation gap and chocolate brown color of arterial blood. Here we report a case with classical saturation gap a high index of suspicion for acquired Methemoglobinemia in a patient who is a known case of idiopathic thrombocytic purpura on treatment with Dapsone. Case emphasizes the importance of good history taking and knowledge of drugs likely to cause Methemoglobinemia. Although our patient did not have any signs of peripheral or central cyanosis, Saturation gap on Arterial blood gas analysis suggested the diagnosis of Dapsone induced Methemoglobinemia.

KEYWORDS

INTRODUCTION :

Dapsone is a synthetic sulfone first introduced in 1943 as an effective chemotherapeutic agent for – Leprosy, Malaria, immunosuppression induced infection caused by P.Carinii and T. Gondii, and variety of blistering skin diseases (dermatitis herpetiformis).(1-3) Long-term administration of dapsone at standard doses(100 mg/day) results in methemoglobinemia in about 15% of patients.(3) Methemoglobinemia, a potentially life-threatening condition in which the oxygen-carrying capacity of blood in body tissues is reduced, is a known adverse effect of dapsone. Clinical suspicion of methemoglobinemia can be made when there is cyanosis, saturation gap and chocolate brown color of arterial blood(4). Here we report a case with classical saturation gap a high index of suspicion for acquired Methemoglobinemia in a patient who is a known case of idiopathic thrombocytic purpura on treatment with Dapsone.

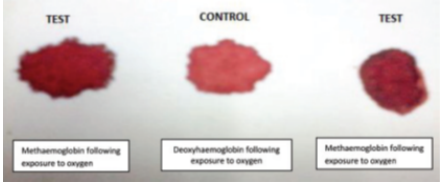
Case report :

38 year old female patient a known case of Idiopathic Thrombocytic Purpura since 5 years, on treatment with oral steroids and Dapsone since 2 years, was received in casualty with complain of headache, dyspnea at rest, arthralgia & fatigue. Now a days Dapsone is used as a 2nd line drug, its immunosuppressive effect have shown increase in platelet count in patient of steroid dependent ITP. On examination patient was afebrile but had tachycardia. Her pulse rate was 122/minute, regular, normal in volume and force. She had a blood pressure of 160/92 mmHg in left arm in supine position. Patient is tachepnoeic with a respiratory rate of 22/min. Oxygen saturation was 86% at room air and 92% at 3L/min O2. She was conscious and anxious. On auscultation lungs were clear with decreased breath sounds bilaterally No abnormality was detected on other systemic examination. Patient was admitted in ICU for evaluation of acute onset dyspnea to rule out Acute Pulmonary Embolism, Infective Etiology (Viral/Dengue/Atypical Pneumonia), Acute Coronary Syndrome.

Her blood investigations on admission revealed haemoglobin of 11.6 mg/dl, total leucocyte count 19000/cu.mm, platelets – 0.70 lakhs/cu.mm. Urine routine microscopy, renal parameters, liver function tests were within normal limits. ECG showed T inversions in II,III,V2-V5. ABG analysis at 3L/min O2 suggestive of Respiratory Alkalosis (pH - 7.46, pCO2 - 33%, pO2 - 110%, HCO3--22.9, sO2 - 99.6%).

Patient was kept on ongoing medication for ITP Omnacortil and Dapsone. Continuous oxygen supply given to patient @ 3-4 lit/min. On further evaluation, patient's Chest X Ray, 2D Echocardiography, Ultrasonography were within normal limit. SOB Profile (Cardiac Profile – Negative, D Dimer – 105, pro BNP Level – 9.5) was done which is normal. Her PCT and G6PD levels were in normal range.

Patient showed no improvement of symptoms such as Dyspnea, Headache and Arthralgia. On repeated ABG analysis, the saturation gap persisted. Methemoglobinemia was suspected due to the persistent saturation gap and deteriorating condition of patient especially dysnea. Filter paper test was done which showed that the patient's blood remained dark even after exposure to atmospheric oxygen suggesting Methemoglobinemia.



Deoxyhemoglobin can be distinguished from methemoglobin by this simple bedside test. By placing 1 or 2 drops of the patient's blood on a white filter paper, deoxyhemoglobin brightens after exposure to atmospheric oxygen, but methemoglobin does not change color.(4)

After reviewing literature, it is found that Dapsone may be a cause of Methemoglobinemia. Dapsone was withdrawn from the treatment and shifted to high dependency unit after 2 days stay in ICU, on continuous nasal O2 supply at 3L/min. Patient's saturation improved with gradual symptomatic improvement of the patient.

DISCUSSION:

According to recent research at several tertiary centers(5), Dapsone has been shown to be the major cause of drug-induced methemoglobinemia. Dapsone (4,4'-diaminodiphenyl sulfone) is the parent compound of many sulfone medications.(1,2,3,6) It is absorbed through the gut and is metabolized by the liver through the oxidation reactions of N-acetylation and N-hydroxylation.(1,2,6,7) Hydroxylated amine metabolites produced in the oxidation reactions are potent oxidants that have been hypothesized to cause Dapsone's hematologic adverse effects, including hemolytic anemia and methemoglobinemia.(1,6) Typically, Dapsone is excreted by the kidneys. However, Dapsone has been known to circulate in the enterohepatic system sometimes, resulting in a relatively long half-life of the drug in the body (i.e. 24-30 hours).(1)

Methemoglobinemia occurs either as a congenital process in which there is a deficiency of nicotinamide adenine dinucleotide plus hydrogen (NADH-cytochrome b5 reductase) or as an acquired disease in which there is an increase in therate of oxidation of hemoglobin to methemoglobin.(2,8,9,10) The newly formed methemoglobin is an aberrant form of hemoglobin in which the original ferrous (Fe2+) atom

is oxidized to a ferric (Fe3+) atom. The ferric atom then causes an allosteric change in the heme portion of the oxidized hemoglobin molecule, resulting in an increase in its oxygen affinity but a decrease in its oxygen binding capacity.(7,8,10)

The symptoms and signs are proportional to the level of methemoglobin. Asymptomatic, if less than 15%. Cyanosis in levels above 15%, Headache, Dyspnoea, Nausea, Tachycardia,and Weakness in levels above 20%; Coma sets in above 45% and a high mortality rate is associated with levelsabove 70%.(11)

Peripheral and central cyanosis is almost always present when there is a minimum methemoglobin level of 15% in the blood (2, 8, 9, 12) but our patient had no cyanosis. Arterial blood gas analysis paired with oxygen saturation analysis by pulse oximetry is now considered the definitive measures for making a correct diagnosis of methemoglobinemia. Blood gas analyses in patients with methemoglobinemia reveal normal to elevated levels of PaO2 with low oxyhemoglobin saturation.(2,7,8,9) A pulse oximeter is now available that uses eight wavelengths of light and can accurately measure both methemoglobin and carboxyhemoglobin (the Rainbow-SET Rad-57 Pulse COOximeter,Masimo, Inc., Irvine, CA). It is capable of giving continuous readings of methemoglobin level at the bedside.13

Initial management consist of removing the offending agent and high dose oxygen. Research has shown that a patient who has symptoms of dyspnoea or a methemoglobin level of at least 30% should receive methylene blue intravenously at 1 to 2 mg per kilogram of body weight over a 5-minute period.2,7,9 . Exchange transfusion and hyperbaric oxygen may also be considered for severe or refractory cases14

Conclusion:

Case emphasizes the importance of good history taking and knowledge of drugs likely to cause Methemoglobinemia. Although our patient did not have any signs of peripheral or central cyanosis, Saturation gap on Arterial blood gas analysis suggested the diagnosis of Dapsone induced Methemoglobinemia.

REFERENCES:

1. Sener O, Doganci L, Safali M, Besirbellioglu B, Bulucu F, Pahsa A. Severe dapsonehypersensitivity syndrome. J Investig Allergol Clin Immunol.2006;16(4):268-270. http://www.jiaci.org/issues/vol16issue04/10.pdf. Accessed November 28, 2009.
2. Turner MD, Karlis V, Glickman RS. The recognition, physiology, and treatment of medication-induced methemoglobinemia: a case report. AnesthProg. 2007;54(3):115-117. .Accessed November 28, 2009.
3. Coleman MD, Rhodes LE, Scott AK, Verbov JL, Friedman PS, Breckenridge AM, et al. The use of cimetidine to reduce dapsone-dependentmethaemoglobinaemia in dermatitis herpetiformis patients. Br J Clin Pharmacol. 1992; 34(3):244-249. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1381395/?tool=pubmed. Accessed November 28, 2009.
4. Steiner IP, Nichols DN. A case of dapsone-induced cyanosis in theemergency department. Isr J Emerg Med 2006;6:10-3.
5. Ash-Bernal R, Wise R, Wright SM. Acquired methemoglobinemia: a retrospective series of 138 cases at 2 teaching hospitals. Medicine. 2004;83(5):265-273.
6. Tingle MD, Coleman MD, Park BK. An investigation of the role of metabolism in dapsone-induced methaemoglobinaemia using a two compartment in vitro test system. Br J Clin Pharmacol. 1990;30(6):829-838. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1368303/?tool=pubmed. Accessed November 28,2009.
7. Falkenhahn M, Kannan S, O'Kane M. Unexplained acute severe methaemoglobinaemia in a young adult. Br J Anaesth. 2001;86(2):278-280.
8. Rehman HU. Methemoglobinemia. West J Med. 2001;175(3):193-196. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1071541/?tool=pubmed. Accessed November 28, 2009.
9. Bayard M, Farrow J, Tudiver F. Acute methemoglobinemia after endoscopy. J Am Board Fam Pract. 2004;17(3):227-229. http://www.jabfm.org/cgi/content/ full/17/3/227. Accessed November 28, 2009.
10. Birchem SK. Benzocaine-induced methemoglobinemia during transesophageal echocardiography. J Am Osteopath Assoc. 2005;105(8):381-384 . http://www.jaoa.org/cgi/content/full/105/8/381. Accessed November 28, 2009.
11. Curry S. Methemoglobinemia. Ann Emerg Med 1982;11:214-21.
12. Mayo W, Leighton K, Robertson B, Ruedy J. Intraoperative cyanosis: a case of dapsone-induced methaemoglobinaemia. Can J Anaesth. 1987;34(1):79-82.
13. Annabi EH, Barker SJ. Severe methemoglobinemia detected by pulse oximetry. Anesth Analg 2009;108:898-9.
14. Mycyk MB. Poisoning and drug overdosage. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, Eds. Harrison's Online. 18th ed. New York: McGraw-Hill; 2012.