Green hands: a rare manifestation of nicorandil-induced methaemoglobinemia

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DESCRIPTION

An 85-year-old woman, known case of diabetes mellitus and essential hypertension, presented with rest angina for 8 days. She was hemodynamically stable, and her ECG showed T-wave inversions in inferior and lateral leads, with poor R-wave progression. An echocardiogram showed regional wall motion abnormality in the right coronary artery and left anterior descending artery territories, with an ejection fraction of 45%. Since the cardiac biomarkers were within normal range, she was diagnosed with unstable angina. She was given dual antiplatelet therapy, statin and nicorandil infusion because of occasional chest pain. A few hours after starting the infusion, the patient developed bluish-green discoloration of hands and feet ([figure 1A](#)). Her oxygen saturation by pulse oximetry was 94% and by blood gas analysis was 97%. Spectrophotometry revealed elevated methaemoglobin levels (3.9%). Routine haematological and biochemical parameters were normal. She did not receive any nitrates nor had any previous exposure to dyes or chemicals. Nicorandil infusion was stopped, and other drugs continued. The discoloration disappeared 2 days after discontinuation of nicorandil and her methaemoglobin level dropped to 0.1% ([figure 1B](#)). The patient subsequently underwent percutaneous coronary intervention and improved symptomatically.

The new-onset bluish discoloration is an alarming sign and may open a portal for numerous investigations to identify the cause of cyanosis. Therefore, distinguishing true cyanosis due to deoxygenation from that caused by methaemoglobinemia is essential. Methaemoglobin is the oxidised ferric form of haemoglobin, with poor oxygen binding and poor tissue delivery. Most cases of methaemoglobinemia are due to

haemoglobin oxidation by drugs or poisoning. Common drugs implicated are dapsone, topical anaesthetic agents, nitroglycerine, nitroprusside and sulpha drugs.¹ Nicorandil contains a nitrate moiety which causes dilatation of veins and epicardial coronary arteries.² This moiety may be a potential cause of methaemoglobinemia at therapeutic doses. In an exhaustive literature review, we found only one other case report demonstrating the same.³ In the report, a 75-year-old man, on treatment for chronic stable angina, presented with bluish discoloration of hands with no other symptoms. He was found to have methaemoglobin levels of 8.7%. His medications included both isosorbide mononitrate (ISMN) and nicorandil. Stopping ISMN did not lower methaemoglobin levels even after 1 month, but subsequent cessation of nicorandil did. Thus, the methaemoglobinemia was attributed to nicorandil.³ Normal methemoglobin levels range from 0% to 2%, and symptoms often occur at levels more than 20%.⁴ Absolute levels of more than 1.5 g/dL usually cause cyanosis.⁵ The discoloration precedes the development of symptoms and should alert the clinician to stop the inciting drug early. Disparity in the oxygen saturation levels between pulse oximetry and blood gas analysis usually clinches the diagnosis, and co-oximetry is confirmatory. No specific treatment is warranted in patients who are asymptomatic and have lower levels of methaemoglobin. Individuals with a methaemoglobin fraction of more than 30% or those with symptoms when the levels are more than 20% require prompt treatment with methylene blue, exchange transfusion and hyperbaric oxygen. Withdrawing the offending agent is the critical step in any severity of this condition.

Figure 1 (A) Greenish discoloration of palms noted few hours after beginning nicorandil infusion. (B) Resolution of greenish discoloration 2 days after stopping nicorandil.

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Learning points

- ▶ Methaemoglobinemia should be considered in the differential diagnosis of new-onset cyanosis, and aetiological evaluation should be done accordingly.
- ▶ Nicorandil can also lead to methaemoglobinemia in therapeutic doses, possibly owing to its nitrate component.
- ▶ Pseudocyanosis of methaemoglobinemia precedes its clinical symptoms; therefore, early detection may help prevent toxicity.

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REFERENCES

- 1 Ash-Bernal R, Wise R, Wright SM. Acquired methemoglobinemia: a retrospective series of 138 cases at 2 teaching hospitals. *Medicine* 2004;83:265–73.
- 2 Ferguson C, McKay G, Fisher M, Nicorandil FM. Nicorandil. *Practical Diabetes International* 2009;26:78–9.
- 3 Ekanayaka RAI. A case of pseudocyanosis. *British Medical Journal Case Reports* 2014.bcr2013201915.
- 4 Rehman HU. Evidence-based case review: methemoglobinemia. *Western Journal of Medicine* 2001;175:193.
- 5 Do Nascimento TS, Pereira RO, De Mello HL, et al. Methemoglobinemia: from diagnosis to treatment. *Revista Brasileira de Anestesiologia* 2008;58:651–64.

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