Rare disease

Smells like a heart attack, but is it?

David R Warriner,¹ Paul Morris,² Vipul Ramjani,² Allison Morton,² Paul Sheridan²¹Medical Physics Department, Sheffield University, Sheffield, UK;²Cardiology Department, Northern General Hospital, Sheffield, South Yorkshire, UK**Correspondence to** Dr David R Warriner, d.r.warriner@sheffield.ac.uk**Summary**

Methaemoglobinemia is rare. Acute myocardial infarction (AMI) is common. The authors present a unique case of methaemoglobinemia masquerading as an AMI. A middle-aged male was urgently referred to a tertiary cardiac centre for primary percutaneous coronary intervention with acute chest pain, cyanosis and tachycardia. However, on arrival, his ECG was felt to be within normal limits. Similarly unremarkable, were his echocardiogram and routine blood tests. Arterial blood gas analysis revealed a methaemoglobinemia of 28.5% which normalised spontaneously. This was thought to be secondary to the use of smelling salts, inhaled earlier that day in the gymnasium. This is the first reported case of smelling salts inducing methaemoglobinemia and of methaemoglobinemia mimicking an AMI.

BACKGROUND

Methaemoglobinemia is a rare cause of breathlessness and chest pain. Although it has been reported as a cause of myocardial ischaemia due to tissue hypoxia caused by the relative anaemia, it has never previously been reported as mimicking an acute myocardial infarction (AMI).^{1 2} Methaemoglobinemia can be easily treated but this depends on accurate and rapid diagnosis. This case illustrates that in an era of increasing specialisation in medicine, one should recognise the importance of a thorough clinical assessment and of always keeping an open mind to alternative diagnoses.

CASE PRESENTATION

A 38-year-old gentleman arrived at work dyspnoeic, cyanosed, clammy and had crushing, severe, retrosternal chest pain. His colleagues were concerned and telephoned for an ambulance. The attending paramedics suspected that he was having an anterior wall ST-elevation MI (STEMI) based on his symptoms and his ECG. He was therefore, transferred to the regional tertiary cardiac centre for primary percutaneous coronary intervention (PPCI). On admission to the cardiac catheter laboratory, it was felt by the admitting team that the ECG (figure 1) actually demonstrated a normal male pattern ST-elevation (early repolarisation pattern) rather than STEMI. A more detailed history revealed a recent prodrome of coryzal symptoms. He gave no medical, drug or family history but was a tobacco smoker and admitted to drinking up to 10 units of alcohol per week.

INVESTIGATIONS

His ECG demonstrated sinus tachycardia and a portable chest radiograph was normal. An echocardiogram revealed a structurally and functionally normal heart with no pericardial fluid collection. Blood tests revealed elevated haemoglobin at 17.1 g/l (13.1–16.6 g/l), white cell count at $12.5 \times 10^9/l$ (3.5 – $9.5 \times 10^9/l$), creatine kinase (CK) 945 u/l (34–306 u/l), CK muscle and brain 29.9% (<3%), lactate

3.5 mmol/l (<2 mmol/l) but normal d-dimer, troponin, liver and renal function (normal ranges in brackets).

DIFFERENTIAL DIAGNOSIS

- ▶ MI
- ▶ Pulmonary embolus
- ▶ Viral myocarditis
- ▶ Acute aortic syndrome

TREATMENT

The following morning the hypoxia, dyspnoea and cyanosis had resolved without any therapy other than inspired oxygen. Further investigation revealed an apparent discrepancy between the normal partial pressure of oxygen (PaO₂) on the admission arterial blood gas (ABG) and the low finger pulse oximeter readings taken at the same time. This is characteristic of methaemoglobin (MetHb). The level of MetHb at admission was significantly raised at 28.5% and on rechecking the following morning it was normal at <1%. The patient denied any exposure to dapsone, anti-malarials, nitrates, illicit drugs or any other compounds which can commonly cause MetHb. The patient subsequently admitted to the long-term use of 'natural' creatine, protein supplements and testosterone to aid physical training. Furthermore, he later described having nasally inhaled smelling salts (figure 2) for the first time while at the gym prior to heavy weight training and this had been approximately 30 min before the onset of symptoms. The patient went on to make a full recovery and was discharged the following day after a period of observation.

OUTCOME AND FOLLOW-UP

The patient went on to make a full recovery and was discharged the following day after a period of observation.

DISCUSSION

MetHb arises due to an excess of MetHb in the blood. In MetHb, the iron group within haem is in the ferric (Fe³⁺), rather than the ferrous (Fe²⁺) state. This adulterated form

Figure 1 ECG.

Figure 2 Picture of smelling salts.

of Hb arises due to a process of oxidation within the erythrocyte that is usually limited by the diaphorase enzymes and glutathione. MetHb does not bind oxygen (O_2), resulting in tissue hypoxia. The deoxygenated blood adopts a blue/brown colour rather than the natural red and this can result in clinically detectable cyanosis. MetHb can be an inherited or acquired condition; the former classically arises secondary to pyruvate kinase or glucose-6-

phosphate dehydrogenase (G-6-PD) deficiency and the latter arises due to ingestion or exposure to oxidising drugs or compounds, typically antibiotics, local anaesthetics, environmental toxins or nitrogenous compounds.³⁻⁶ This overwhelms the inherent protective mechanisms, resulting in a pathological accumulation of MetHb, which in health usually accounts for only 1-2% of total Hb. Treatment is with methylene blue, which reduces the ferric Hb back to

its normal ferrous state and thus a resumption in oxygen carriage. Cyanosis arises due to either a lack of oxygenated haemoglobin or due to the presence of too much of the adulterated form.

If a patient presents with chest pain, cyanosis and breathlessness with a normal ECG, troponin, chest x-ray, echo and d-dimer, by deduction this rules out a pulmonary or cardiac cause, leaving other possibilities including MetHb. Classically, patients with MetHb present with dyspnoea and cyanosis with a normal PaO₂ on ABG but low O₂ saturations on pulse oximetry. Pulse oximetry measures oxygenation by measuring the relative proportion of haemoglobin and oxyhaemoglobin, which absorb light at red (660 nm) and infrared (940 nm) wavelengths, respectively. MetHb interferes with the colourimetric analysis on which oximetry depends by falsely absorbing light at both wavelengths which gives an inaccurate measurement of oxygen saturation. PaO₂ measured by ABG is unaffected since this is a chemical rather than an optical analysis.

Smelling salts are often used by weight lifters seeking that 'extra edge' prior to a maximal effort lift. Their active compound is ammonium carbonate which releases ammonia, irritating the mucous membranes of the upper airways causing an 'inhalation reflex' which in turn leads to increased respiratory rates and alertness.⁷ As far as the authors are aware, smelling salts are not known to directly cause myocardial ischaemia or ECG changes suggesting this, via mechanisms such as coronary spasm for example. Thus we postulate that the nitrogenous vapour released by smelling salts leads to accumulation of MetHb and thus acute hypoxia and symptoms relating to this.

The initial raised lactate is consistent with the tissue ischaemia on admission. The raised CK, which did not fall the following day may reflect the patient's high muscle

bulk, recent vigorous exercise and creatine use.⁸ The high Hb and haematocrit may be explained by tobacco use and/or testosterone use.⁹

Learning points

- ▶ Smelling salts can precipitate MetHb.
- ▶ Symptoms of MetHb can mimic those of an AMI.
- ▶ Doctors should be aware of smelling salt usage among fit and athletic individuals.
- ▶ In an era of increasing specialisation, always keep an open mind to alternative diagnoses.

Competing interests None.

Patient consent Obtained.

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