

Dapsone-induced methaemoglobinaemia in relapsing polychondritis

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DESCRIPTION

Dapsone (4,4'-diaminodiphenyl sulfone) is an anti-bacterial and anti-inflammatory drug, sometimes used for rheumatic disease. It is known to cause various side effects.¹ Here, we report a case of methaemoglobinaemia (MetHb), a rare haematological side effect.

The patient was a female in the 40s with relapsing polychondritis (RP) with tracheobronchial chondritis. On examination, swelling of the right lobe of the thyroid gland was present. Her peripheral oxygen saturation (SpO₂) was 94% in room air, and she had dyspnoea. Remission induction therapy (prednisolone 45 mg/day, dapsone 100 mg/day, and methotrexate 8 mg/week) improved her condition. After 1 month, however, dyspnoea and SpO₂ decline reappeared. Her lips were slightly purplish. Suspecting relapse of RP, we administered tocilizumab, but dyspnoea and SpO₂ decline persisted. We assumed that irreversible tracheal cartilage destruction by RP and tracheal compression by the thyroid gland might be the reason. After 9 months, a right lobectomy of the thyroid gland was performed to relieve symptoms.

After intubation, SpO₂ did not surpass 93% with supplemental oxygen. Her lips remained purplish (figure 1A). Her arterial blood gas (ABG) sample was chocolate-brown (figure 1B). ABG analysis showed a PaO₂ of 550 mm Hg, oxygen saturation of 98.4%, haemoglobin levels of 114 g/dL, and MetHb

of 12.0% (normally up to 1.5%). She denied having a history of congenital MetHb or taking medications that could cause MetHb, other than dapsone. She was diagnosed with dapsone-induced methaemoglobinaemia. Dapsone was discontinued, but the MetHb levels remained high. After administering 50 mg of methylene blue, MetHb levels decreased to 2.1% immediately and normalised the next day. Dyspnoea and SpO₂ decline disappeared, and her lip colour returned to normal (figure 1C). We concluded that MetHb was a contributing factor to her condition.

MetHb is one form of haemoglobin without oxygen-binding capacity.² It is usually maintained at low levels, but exposure to certain drugs can increase MetHb production, leading to functional anaemia and tissue hypoxia.² Symptoms are non-specific, such as dyspnoea, headache and dizziness.² The chocolate-brown coloration of arterial blood, lack of improvement in SpO₂ with supplemental oxygen and a saturation gap (a difference between oxygen saturations of ABG and SpO₂) are unique features.² The elimination of the causative drug is important, as well as administration of methylene blue, which promotes MetHb reduction.³

Although dapsone is considered one of the leading causes of acquired MetHb,² the incidence among dapsone users is considered low. To the best of our knowledge, this is the first case in the RP patients. Dapsone-related adverse events are associated with high-dose use, anaemia, cardiopulmonary disease and glucose-6-phosphate dehydrogenase deficiency.⁴ Some drugs, such as prednisolone, may affect the metabolism of dapsone, leading to producing MetHb.⁴ In our case, pulmonary abnormalities and using prednisolone may have increased the risk.

MetHb diagnosis was delayed because we assumed that lung and airway abnormalities were causing the patient's symptoms. Physicians should be familiar with dapsone's side effects. We need to include MetHb in the differential diagnosis of dyspnoea as well as that of respiratory disease, cardiac disease, anaemia and neuromuscular disease.

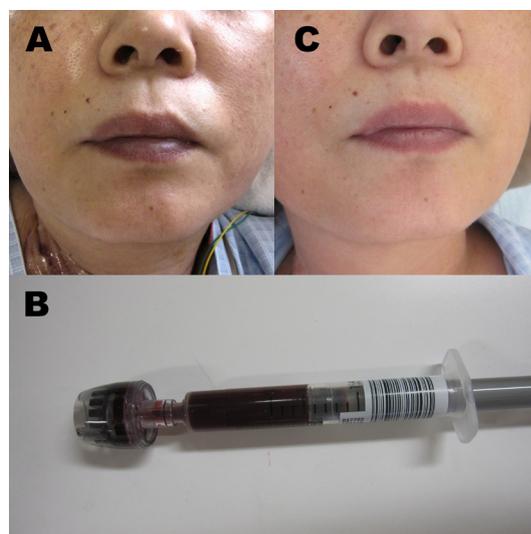


Figure 1 (A): Purple lips (before methylene blue administration). (B): Chocolate-brown coloration of arterial blood (before methylene blue administration). (C): Normal toned lips (after methylene blue administration)

Learning points

- ▶ Dapsone has various haematological side effects, such as methaemoglobinaemia.
- ▶ When we use dapsone in patients with lung and airway abnormalities, methaemoglobinaemia should be listed as a differential diagnosis for dyspnoea.



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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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