Blue and breathless

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CASE REPORT

A 25-year-old HIV-antibody positive female had been admitted to hospital on 12 occasions with respiratory infections over a 3-year period. *Pneumocystis carinii* pneumonia (PCP) had been suspected twice but never proven and sputum culture for tuberculosis was repeatedly negative. Her CD4 count was 6/mm^3. Treatment had been problematic. Antiretroviral therapy was not tolerated, she reported a rash with cotrimoxazole and nebulized pentamidine provoked severe bronchospasm. During her twelfth hospital admission PCP was suspected despite negative induced sputa. She completed treatment with intravenous pentamidine and corticosteroids followed by oral clindamycin with primaquine. Following discharge dapsone 100 mg thrice weekly was started as secondary prophylaxis. Twelve days later she was readmitted with worsening dyspnoea, fever and vomiting. Inadvertently she had taken 300 mg dapsone daily for 4 days. Physical examination revealed a deeply cyanosed patient. Respiratory rate was 50/minute, heart rate 130/minute, temperature 37.6°C and blood pressure 120/70 mmHg. Chest radiograph showed a diffuse bilateral pneumonia and arterial blood gases breathing air revealed a PaO_2 of 8.37 kPa, PCO_2 of 3.92 kPa and a calculated oxygen saturation of 93.3%. Haemoglobin concentration was 9.7 g/dl, blood film demonstrated 6% reticulocytes with Heinz body inclusions and the methaemoglobin level was 30%.

Activated charcoal, high flow oxygen and 2 mg/kg intravenous methylene blue was commenced. Piperacillin-tazobactam and gentamicin were added for presumptive severe hospital-acquired pneumonia and she was transfused one unit of blood. PaO_2 improved to 31.8 kPa on 100% oxygen but she remained deeply cyanosed. The methaemoglobin level 12 hours later was 34% so a further bolus of methylene blue followed by an infusion (0.1 mg/kg/hour) was administered. During the administration of methylene blue pulse oximetry showed a dramatic fall in oxygen 'saturation'. Twenty-four hours later methaemoglobin level was 1.7% and by day three <1% with an oxygen saturation of 88% measured by pulse oximetry. Following discontinuation of methylene blue on day five an arterial blood sample showed PaO_2 was 11 kPa on air with a calculated oxygen saturation of 96%. Repeat chest X-ray showed a right middle-lobe bulla with partial clearing of the infiltrates. She was discharged on day 12 at her own request but died 3 weeks later in hospital following admission with a pneumothorax and severe pneumonia. Autopsy was refused.

DISCUSSION

This case is unusual in that tissue oxygenation was compromised by both serious lung pathology and by dapsone-induced methaemoglobinaemia. The aetiology of this woman's lung disease is uncertain and the differential diagnosis is wide (Miller, 1996).

The case illustrates the problems with compliance and long-term prophylaxis against PCP. Co-trimoxazole remains the agent of choice for the prevention of PCP (Kaplan et al, 1997), although up to 79% of patients cannot tolerate it long term. Dapsone is probably as effective in primary prophylaxis and may be better tolerated (Bozzette et al, 1995).

Many prophylactic regimens using dapsone have been assessed. Current recommendations are for 100 mg dapsone per day or 50 mg daily in combination with weekly pyrimethamine (50 mg) and leucovorin (25 mg) (Hughes, 1998). Asymptomatic dapsone-induced methaemoglobinaemia has been reported in 66% of patients with HIV infection who receive 100 mg per day with trimethoprim for therapy of PCP (Medina et al, 1990).

The prolonged half-life of dapsone and its main metabolite explains the persistence of significant methaemoglobinaemia in our patient with dapsone overdose, despite boluses of methylene blue. Infusions have been used before in patients with methaemoglobinaemia (Dawson and Whyte, 1989), but not to our knowledge in a patient with HIV infection. Pulse-oximetry readings drop during methylene blue infusion because of the absorption characteristics of the drug but once methylene blue is discontinued oxygen 'saturation' improves. Arterial blood gas analysers calculate oxygen saturation of haemoglobin from measurement of pH and PaO_2 and are thus not affected by methylene blue. HM

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