Dapsone-induced Heinz-body haemolytic anaemia

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DESCRIPTION

A man in his 90s with no history of haematological disorder presented with dizziness, general weakness and urine discolouration persisting for 1 week. Four months before the current visit, he developed generalised pruritic erythema and saw a dermatologist. His haemoglobin level at that time was normal (132 g/L). One month before the current visit, he started taking dapsone (50 mg/day) for suspected senile erythroderma. Other medical history included hypertension, insomnia and chronic kidney disease (baseline serum creatinine level 1.12 mg/dL), and the patient was taking levocetirizine, bepotastine, suvorexant, amlodipine and candesartan. On physical examination, the height was 160 cm, and the weight was 52 kg (body mass index 20.3 kg/m^2). His conjunctivae were anaemic and icteric. Laboratory studies showed macrocytic anaemia (haemoglobin level 69 g/L, mean corpuscular volume 116 fL) with reticulocytosis, elevated bilirubin and lactate dehydrogenase levels, and decreased levels of haptoglobin. Urinalysis showed 3+ urobilinogen and 1+ bilirubin without microscopic haematuria. These results suggested haemolytic anaemia. At that time, differential diagnoses were autoimmune haemolytic anaemia, thrombotic thrombocytopenic purpura, malignancy-related thrombotic microangiopathy and drug-induced haemolytic anaemia. A peripheral blood smear showed bite cells (degmacytes) (figure 1A, arrows). Subsequent brilliant cresyl blue staining detected apparent aggregation of Heinz bodies (figure 1B, arrows). Direct and indirect Coombs tests were negative, and ADAMTS13 enzyme activity was within normal range. Upper and lower gastrointestinal endoscopy and chest, abdominal, and pelvic CT revealed no malignancy. Although his glucose-6-phosphate dehydrogenase (G6PD) level was normal, he was diagnosed with dapsone-induced haemolytic anaemia based on his history. After discontinuing dapsone, his haemoglobin level returned to 108 g/L at 3 weeks and 140 g/L at 2 months.

Observing erythrocyte morphology through a blood smear can be critical to rapidly diagnose the cause of haemolytic anaemia.[1 2] Heinz bodies, the denaturing of ferric haemoglobin into multimers, develop under the condition of oxidative damage due to a failure in the reduction of ferric to ferrous iron.[3 4] Macrophages in the spleen remove the damaged portion of the cytoplasm of an erythrocyte, leaving a 'bite' or indentation on the remaining cell membrane.[1 3] Therefore, detecting Heinz bodies and bite cells in peripheral blood smears strongly supports the diagnosis of oxidative haemolysis. Of note, clinicians should be aware that using supravital staining, such as brilliant cresyl blue, is required to look for the presence of Heinz bodies.[2]

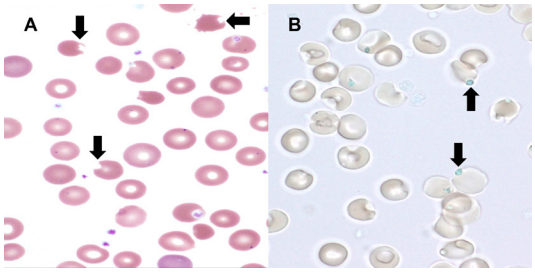

Figure 1 (A) A peripheral blood smear showing erythrocytes with bitten-off margins, so-called 'bite cells' (arrows). (B) Brilliant cresyl blue staining of the peripheral blood smear showing apparent aggregation of Heinz bodies (arrows).

Oxidative haemolytic anaemia can occur in patients exposed to oxidant chemicals, food, or drugs or with Wilson's disease.[1 4] Importantly, although G6PD deficiency is well known as an underlying condition of oxidative haemolysis, some oxidative drugs, such as dapsone, can cause oxidative haemolysis in the absence of G6PD deficiency.[3 5] In patients without G6PD deficiency, dapsone-induced haemolytic anaemia may be related to elevated dapsone levels due to such as renal dysfunction, concurrent use of medications metabolised via the cytochrome P-450 isoenzyme system and low body weight.[5 6] Further, considering older age (90s), reduced clearance of dapsone that led to elevated dapsone level, that seemed to be the cause of haemolytic anaemia in our case. Median days from starting dapsone to haemolysis in these patients were reported to be 13, 23 and 83 in previous studies, as was 1 month in our case.[6] Clinicians should check anaemic symptoms and haemoglobin levels for 2–3 months in patients who have some risks of dapsone-induced haemolytic anaemia.

Learning points

- Observing erythrocyte morphology through a blood smear can be critical to rapidly diagnose the cause of haemolytic anaemia.
- Detecting Heinz bodies and bite cells in peripheral blood smears strongly supports the diagnosis of oxidative haemolysis.
- Some oxidative drugs, such as dapsone, can cause oxidative haemolysis in the absence of glucose-6-phosphate dehydrogenase deficiency.

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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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