Correspondence

A rare case of toxic brain injury with methaemoglobinaemia: Dapsone, the culprit

Methaemoglobinaemia occurs due to oxidation of iron from ferrous to ferric and this form is incapable of binding oxygen and thus leads to tissue hypoxia. Acquired methaemoglobinaemia can be caused due to various exogenous substances such as dapsone, aniline dyes and nitrobenzene. The key to diagnosis is a high clinical suspicion along with presence of cyanosis, saturation gap and chocolate brown blood. Methylene blue is an effective antidote, which reverses the serious effects if given timely. Exchange transfusion can be an option in patients refractory to administration of methylene blue. This is probably the first report where possible direct toxic effects of dapsone on the brain were observed and hence it tells us that involvement of the brain is possible in dapsone poisoning and can cause extensive toxic injury.

A 20-year-old girl presented to the emergency with history of breathing discomfort and bluish discolouration of the tongue and the whole body for 3 days. On examination, she was conscious, alert with marked central and peripheral cyanosis. Digital pulse oximetry showed a saturation of 76% with no tachycardia. She was given oxygen at 15 L/minute but the saturation did not increase. A possibility of drug overdose was kept. Historically, we were able to ascertain that the patient had taken an unknown number of dapsone tablets 2 days back. Methaemoglobinaemia due to dapsone toxicity was suspected. Arterial blood sample showed chocolate brown coloured blood with pH 7.46, pO_2 298, HCO_3 19.9, pCO_2 28 and methaemoglobin level of 41.9%. She was immediately given methylene blue 50 mg i.v. along with vitamin C following which her saturation levels improved from 75% to 92%. The repeat methaemoglobin levels decreased to 13%. Chest X-ray and cardiac evaluation were normal. Blood investigations revealed anaemia (haemoglobin 7.4 g/dl), normal liver function, kidney function and normal anaemia profile.

After a few hours, her saturation again started decreasing. Repeat acid–base gas analysis was done, which showed a rise in methaemoglobin levels and the methylene blue dose was repeated. Due to refractory methaemoglobinaemia and decline in her parameters, an exchange transfusion was done with 7 units of packed red blood cells on day 3 but she kept desaturating and became drowsy. Hence, she was intubated.

Her CT head (Fig. 1) showed bilaterally symmetrical hypodense areas in the thalamus, external capsule, posterior brainstem and superior cerebellar cortex with mild-to-moderate hydrocephalus. Her urine toxicology was negative and electroencephalogram (EEG) showed diffuse slowing suggesting diffuse cortical dysfunction. She remained on the ventilator for 4 days and despite all efforts succumbed to her illness on day 6.

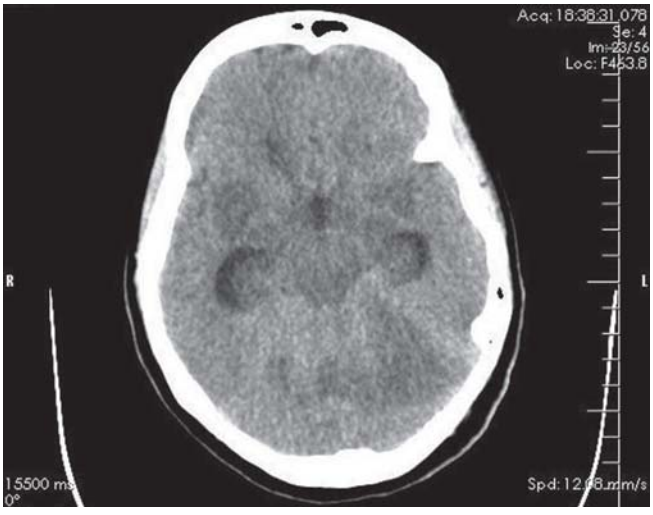

FIG 1. CT scan of the head

Dapsone acts by inhibition of folate synthesis.[1] Methaemoglobin is the oxidized form of haemoglobin not capable of binding oxygen molecules leading to reduced oxygen-carrying capacity, thereby impairing the unloading of oxygen at the tissue.[2] Methaemoglobin levels may rise due to congenital deficiencies or exposure to oxidizing agents such as dapsone. The diagnostic key is the presence of cyanosis, low oxygen saturation and normal pO_2 on acid–base gas analysis referred to as the saturation gap along with chocolate blood colour on sampling. Interestingly, there have been reports of suicidal thoughts in patients taking dapsone.[3] Methylene blue is the antidote and should be given in patients with methaemoglobin levels of >30% in a dose of 1–2 mg/kg body weight over 5 minutes and can be repeated after 30 minutes if the cyanosis does not improve.

The peculiar feature in our patient was the encephalopathy due to bilateral symmetrical involvement of posterior brainstem, superior cerebellar cortex, thalamus and external capsule with hydrocephalus and a small fourth ventricle. Encephalopathy due to toxins is mainly attributed to hypoxia but the CT features were not classical of hypoxia where mainly the cerebral cortex, basal ganglia, hippocampi and cerebellar cortex are involved. Lesions of the posterior circulation are commonly seen in Wernicke encephalopathy, which does not seem to be the possibility in our patient. Since the lesions did not correspond to the hypoxic injury, dapsone can be considered as a direct cause for them.

Similar radiological lesions have also been documented in mice after nitrobenzene poisoning due to energy deprivation syndrome.[4] Methylbromide exposure also has bilateral symmetrical involvement of the fourth ventricle, dorsal medulla, dorsal pons, periaqueductal matter, colliculi, posterior putamen, subthalamic nuclei and cerebellar cortex.[5]

In patients refractory to methylene blue therapy, exchange transfusion and hyperbaric oxygen can be considered.[6]

This case signifies the importance of early suspicion and management of methaemoglobinaemia, which may result in complete recovery and high chances of survival. The neuroradiological involvement as seen in our patient has never been reported with dapsone in the past and suggests the need for high suspicion of extensive brain involvement in such poisonings.

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