

# PostScript

## LETTERS

### Diffuse lesion in the splenium of the corpus callosum in patients with methyl bromide poisoning

Imaging abnormalities of the splenium of the corpus callosum (SCC) are uncommon but have been described in various clinical conditions such as Marchiafava-Bignami disease, trauma, infectious diseases, acute disseminated encephalomyelitis, epilepsy, altitude sickness, hypoglycaemia, electrolyte abnormalities, leukodystrophy, and infarction, and following radiation therapy and chemotherapy.<sup>1,2</sup> We have detected a diffuse lesion in the SCC of two patients with methyl bromide intoxication.

#### Case report 1

The first case involved a previously healthy 31 year old man. He had worked in a

fumigating plant spraying strawberries for 1 month prior to admission. Strawberries were fumigated with methyl bromide for 2 h in an enclosed room. After fumigation, the room was ventilated for 10 min with electric fans. Thereafter, the subject transferred the fumigated fruits to a warehouse. He worked for 3 h every other day. The subject reported experiencing intermittent nausea, dizziness, and ambulatory difficulty. On the day of hospital admission, the patient complained of general weakness, developed paraesthesia in the hands and feet, and was unable to recall daily events. He was admitted to the nearest hospital. The patient exhibited urinary incontinence, talked to himself, and was unable to walk unaided. He was transferred to our hospital 2 days later. Upon examination, all of the patient's vital signs proved normal. However, he attempted to grab phantom objects in the air, sucked his fingers, and had difficulty with speech comprehension. He received antiplatelet

agents, vitamin B complex, and folic acid. The patient began to understand what was said to him 3 days after admission, although his comprehension of language was still defective. After 2 weeks of hospitalisation, he was discharged, and exhibited no further cognitive deterioration.

Laboratory tests of blood and cerebrospinal fluid excluded anaemia, electrolyte abnormalities, diabetes, hepatic and collagen diseases, syphilis, human immunodeficiency virus infection, encephalitis, and multiple sclerosis. Serum folate levels (3.4 nmol/l) were below normal. However, serum vitamin B12 and homocysteine levels were within normal limits.

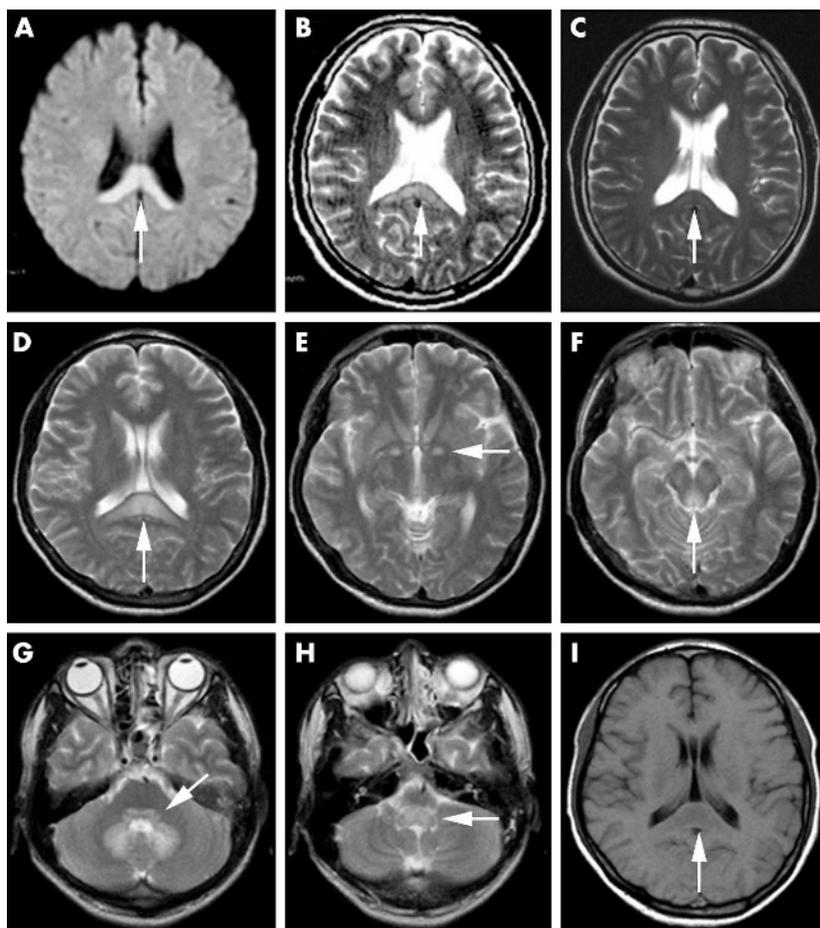
Electroencephalography revealed many mixed slow waves on all leads. Diffusion weighted imaging and T2 weighted magnetic resonance imaging (MRI) taken 1 day prior to transfer to our hospital revealed increased signal intensity of nearly the entire SCC (fig 1A,B). The lesions extended into the lateral portion of the SCC. These lesions were isointense on the T1 weighted images. No parenchymal enhancements were observed following intravenous administration of gadolinium contrast agents. T2 weighted images obtained 1 month after the detection of the lesions demonstrated they had nearly disappeared (fig 1C).

#### Case report 2

Five days before the discharge of the first patient, a 32 year old man was admitted to the same hospital because of sudden dysarthria, headache, dizziness, and confusion. Prior to admission, this second patient had worked for 15 days in the same fumigation company as the previous subject. His job was to carry the fumigated strawberries to the warehouse. He had no history of severe head trauma, febrile convulsions, or encephalitis.

Upon examination, all of the patient's vital signs proved normal. The patient was confused, and both temporally and spatially disoriented. Mild dysarthria was also present. Tendon reflexes were hyperactive. Bilateral extensor plantar responses were present. Nuchal rigidity was absent. The patient became lethargic and 2 h after admission developed a generalised tonic-clonic seizure, which resolved after intravenous administration of lorazepam. The patient was then treated with emergent haemodialysis daily for 3 days. He remained lethargic and irritable, and although he was aroused by speaking, he failed to respond to spoken commands. He attempted to sit up in bed and thrashed his limbs violently. His condition remained unchanged until hospital day 7 when he was transferred to another hospital at his family's request.

The following investigations were normal or negative: blood cell count, serum glucose, creatinine, serum electrolytes, thyroid function test, electrocardiogram, and chest roentgenogram. Serum glutamic oxaloacetic transaminase level was 0.83  $\mu$ kat/l and serum glutamic pyruvic transaminase was 2.08  $\mu$ kat/l. Serum bromide concentration was a remarkable 0.412 mmol/l (normal: 0.028-0.065 mmol/l) on the third hospital day, as determined with ion chromatography.



**Figure 1** Axial diffusion weighted image from case 1 demonstrates an increased signal intensity area in the splenium of the corpus callosum (A). Axial T2 weighted magnetic resonance image demonstrates hyperintense lesions in the same region (B). Another T2 weighted image obtained 1 month later discloses near resolution of the lesions (C). T2 weighted axial image in case 2 shows bilateral symmetric high signal intensities in the splenium of the corpus callosum (D), the globus pallidus (E), the periaqueductal grey matter of the midbrain (F), the pontine tegmentum (G), the dentate nucleus (G), and the medulla oblongata (H). These lesions were hypointense on T1 weighted images (I).

T2 weighted brain MRI revealed bilateral symmetric high signal intensities in the SCC, the globus pallidus, the periaqueductal grey matter of the midbrain, the pontine tegmentum, the dentate nucleus, and the medulla oblongata (fig 1D–H). These lesions were hypointense on T1 weighted images (fig 1I). The shape of the SCC lesions was similar to that of case 1.

## Discussion

Exposure to high concentrations of methyl bromide can result in gastrointestinal, neurological, and respiratory symptoms.<sup>3,4</sup> The neuropathological alterations associated with methyl bromide intoxication include small subarachnoid haemorrhage, capillary proliferation, demyelination, degeneration of neurons, and gliosis. The sites of involvement include the cerebral cortex, quadrigeminal bodies, red nuclei, dentate and olivary nuclei, and the superior cerebellar peduncles.<sup>4</sup> Ichikawa *et al* reported a case of methyl bromide intoxication involving bilateral symmetrical lesions on MRI in the putamen, the subthalamic nuclei, the dorsal medulla oblongata, the inferior colliculi, and the periaqueductal grey matter of the midbrain.<sup>5</sup>

Methyl bromide intoxication can be suspected on the basis of history of exposure, clinical findings, and results of laboratory studies. There are no reliable indicators of exposure to methyl bromide; due to its short half life, it rapidly becomes undetectable in human tissues, and serum bromide concentrations are considered to correlate poorly with clinical symptoms and outcome.<sup>3</sup>

To our knowledge, lesions confined to the SCC have not previously been reported in patients with methyl bromide poisoning. The imaging differential diagnosis of SCC abnormalities includes Marchiafava-Bignami disease, trauma, infectious diseases, acute disseminated encephalomyelitis, epilepsy, altitude sickness, neoplasia, radiation therapy, chemotherapy, hypoglycaemia, electrolyte abnormalities, renal failure, leukodystrophy, infarction, and hypertension.<sup>1,2</sup> In our cases, these diagnoses were excluded by both the clinical setting and the laboratory findings.

In conclusion, diffuse lesions in the SCC can be seen on MRI of patients with methyl bromide poisoning. If a patient with a splenic lesion is encountered, a detailed history regarding to their occupation and substance abuse should be obtained.

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## Wasp sting induced autoimmune neuromyotonia

A 53 year old man was stung behind the knees by five wasps, subsequently identified as belonging to the species *Vespa germanica* (commonly known as “yellow jackets”). Within a few minutes, he became dizzy, began to wheeze, and collapsed. He responded rapidly to intramuscular epinephrine administered by the attending paramedics, but showed a persistent sinus tachycardia during the subsequent hospital admission. Thus, when he was discharged the following day, he was put on sotalol for 1 week.

He had been stung by a wasp 1 year previously, suffering only extensive local swelling. There was no personal or family history of atopic disease or of reactions to ingested or topical allergens.

He remained free of symptoms for the next 5 weeks, but then developed rapid onset, severe, and painful muscular twitching throughout his limbs, profuse generalised sweating, and insomnia. For 3 weeks prior to his second hospital admission, he was treated with a combination of amitriptyline 10 mg nightly and gabapentin 300 mg thrice daily without effect.

On examination, the patient was afebrile but had hyperhidrosis and tachycardia. He appeared emotionally labile. There were continuous coarse fasciculations throughout all limbs, most markedly in the deltoid and quadriceps bilaterally. The limb tone was normal, with preserved power and normal sensation.

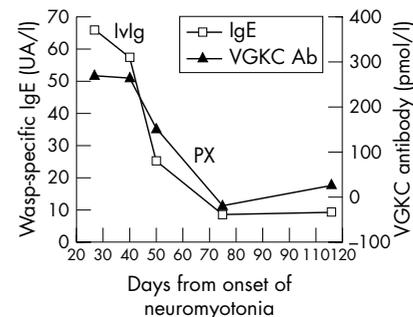
Serum creatine kinase (CK) level on admission was 10 756 IU/l. Serum urea and creatinine levels were normal and no urinary myoglobin was detected in laboratory analysis. The CK level returned to normal following 1 week of bed rest. Electromyography was characterised by spontaneous multiplet

motor unit potential discharges with high intraburst frequency, typical of neuromyotonia. There was no evidence of polyneuropathy on nerve conduction study. Electroencephalography demonstrated poorly sustained 8 Hz alpha rhythm with posterior delta slow wave activity. Cerebrospinal fluid examination demonstrated 2 leucocytes/mm<sup>3</sup>, protein 0.226 g/l and glucose 4.6 mmol/l (serum 6.3 mmol/l). No oligoclonal bands were detected. Magnetic resonance imaging of the brain and spinal cord, computed tomography scan of the chest and abdomen, and bone marrow aspiration were all normal.

Antibodies to the voltage gated potassium channel (VGKC) were raised, with a titre of 340 pmol/l on admission, in conjunction with a wasp venom specific immunoglobulin E (IgE) level of class 5/6 measured by radioallergosorbent test. Acetylcholine receptor and antineuronal antibodies were not detected.

Electrocardiography revealed paroxysmal atrial tachycardia requiring temporary treatment with oral amiodarone and digoxin. In an attempt to treat the neuromyotonia, the patient received oral carbamazepine up to a dose of 400 mg twice daily for the first 2 weeks after admission, without effect. He was then given a 5 day course of intravenous immunoglobulin at a dose of 0.4 g/kg daily, also without effect. Methylprednisolone 1 g was then administered intravenously every day for 5 days, but the neuromyotonia persisted. Oral mexiletine was then commenced at a dose of 200 mg thrice daily for the following 2 weeks, without significant symptomatic relief. Finally, the patient underwent plasma exchange therapy over 5 days, which was coincident with his symptoms beginning to subside. Nearly 4 months after onset, the neuromyotonia, sweating, and insomnia had completely resolved. Amiodarone and digoxin therapy was withdrawn with no recurrence of the cardiac arrhythmia.

Levels of both VGKC antibodies and total IgE fell in parallel with the patient's clinical recovery over the following weeks (fig 1).



**Figure 1** Graph showing the change in VGKC antibody and wasp venom specific IgE levels with time. The first measurements were taken approximately 3 weeks after the onset of fasciculations. There is a close relationship between the two indices, which matched the clinical recovery of the patient. The timing of immunoglobulin therapy and plasma exchange is also shown. VGKC, voltage gated potassium channel titre; IgE, immunoglobulin E titre; Ivlg, intravenous immunoglobulin; PX, plasma exchange.