LESSON OF THE MONTH

Lead poisoning from complementary and alternative medicine in multiple sclerosis

Alex A Fisher, David G Le Couteur

Abstract

A patient with multiple sclerosis is described who was treated for neurological symptoms thought to be a progression of his disease but subsequently found to be caused by lead poisoning secondary to the use of alternative medicine. His clinical signs improved with oral chelation therapy. Neurologists should consider asking about the use of complementary and alternative medicine before simply attributing symptoms and signs to exacerbation of multiple sclerosis.

(*J Neurol Neurosurg Psychiatry* 2000;**69**:687–689)

Keywords: multiple sclerosis; lead; complementary medication; alternative medication

The use of complementary and alternative medicine is widespread among people with chronic illness[1] and between one third and two thirds of patients with multiple sclerosis use alternative medicine, including homeopathic, herbal, chiropractic, and nutritional therapies.[2 3] Multiple sclerosis is characterised by a progressive and relapsing time course and fluctuations in neurological status are easily ascribed to the natural course of the disease. Here we describe a patient with multiple sclerosis who was treated for neurological symptoms thought to be progression of his disease but subsequently found to be caused by lead poisoning secondary to using complementary and alternative medicine.

A 47 year old man was diagnosed with multiple sclerosis 9 years previously by two academic neurologists on the basis of slowly progressive ataxia, blurred vision, dizziness, horizontal nystagmus, positive Babinski's responses, and urge incontinence. The diagnosis was confirmed by MRI. He had been treated with pulse methylprednisolone on six occasions for exacerbation of his symptoms. He also had depression treated with sertraline.

Five months before admission he noted worsening unsteadiness, tremor, impaired memory, irritability, and double vision. This was diagnosed as an exacerbation of multiple sclerosis and he received treatment for 5 days with pulse methylprednisolone. His symptoms continued to progress despite this therapy and he started using a walking stick.

Three months before admission he underwent neuropsychological assessment. This showed impairment of all phases of short term memory, but intact remote and immediate memory. The Wechsler memory scale revised memory quotient was 87, the verbal index was 89, the visual index was 88, delayed recall was 94, and attention/concentration was 127. Apart from attention, these indices were all at the lowest limits of normal and well below expectation. He had a compromised capacity to recognise new ideas. In the Wisconsin card sort trial the number of trials to recognise a shape was 26 (normal range 6–8), the number of trials to recognise numbers was 15 and fail (normal range 4–6), and the number of perserveration errors was 30 (normal range<8). The verbal fluency test was performed very poorly (mean words/letter/minute 5.3, normal 12–15) indicating that he had great difficulty in initiating and maintaining activity to demand. His score on the Rey figure test was below the 10th percentile (32/26 in 171 seconds) which is consistent with poor problem solving capacity. Assessment of mood and affect showed an Institute for Personality and Ability Testing (Champaign, IL, USA) IPAT) depression inventory score of 34 out of 80 consistent with depression. The psychologist concluded that there was evidence of moderate neuropsychological impairment involving mainly the central and frontal regions of the brain that was consistent with subcortical demyelination with no localising cortical signs.

One month before admission he noted further worsening of tremor and ataxia with difficulty in bladder control. He also developed periumbilical colic, constipation, and anorexia. He was treated with ranitidine and omeprazole with no effect. His family noted that he became more confused with outbursts of violent behaviour and was occasionally incoherent. One week before admission a full blood examination showed anaemia with haemoglobin (Hb) of 82 g/l and erythrocyte basophilic stippling. A measurement of blood lead concentration was recommended and was 4.4 μmol/l (92 μg/dl). This was performed by the Central Sydney Laboratory Service by induction coupled mass spectrometry and the recommended range of this laboratory is 0.00–0.48 μmol/l (0–10 μg/dl).

On admission, he was pale and underweight. There were no gingival lead lines. He had mild periumbilical tenderness but the general examination was otherwise normal. He was apa-

Department of Clinical Pharmacology and Toxicology, The Canberra Hospital, Garran ACT 2605 Australia
A A Fisher
D G Le Couteur

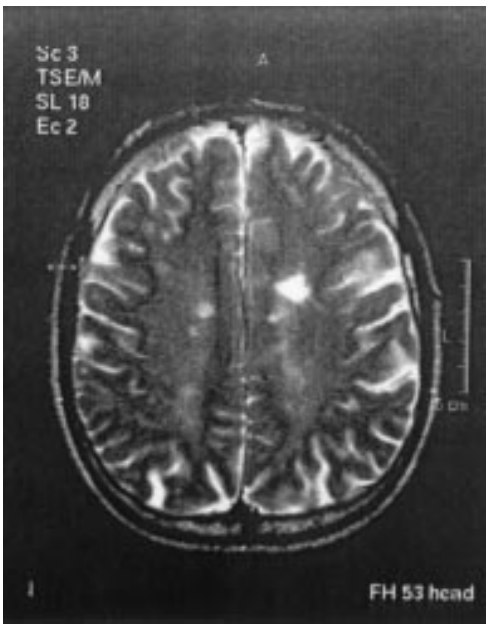
Correspondence to:
David G Le Couteur
david.lecouteur@act.gov.au

Received 31 March 2000 and in revised form 31 May 2000
Accepted 2 June 2000

thetic and oriented in place and person but not in time. He demonstrated marked ataxia, nystagmus, intention tremor, dysarthria with scanning speech, and impaired finger-nose and heel-toe tests. In addition leg weakness was noted but there were no other clinical features of peripheral neuropathy.

Additional laboratory studies showed normal renal and liver function apart from a mildly increased bilirubin (28 μmol/l; normal range 3–20 μmol/l). The 24 hour urine protein was 0.15 g and the creatinine clearance was 133 ml/min. The plasma porphyrin concentration was 112 nmol/l (normal range 0–10 nmol/l). The red blood cell porphyrin was 14.70 μmol/l (normal range 0.40–1.40 μmol/l) and this was mainly zinc protoporphyrin. Sensory and motor nerve conduction studies of the left upper limb (ulnaris and median) and the right lower limb (sural) were within normal limits. Brain MRI showed multiple focal white matter hyperintensities mainly in periventricular locations with marked involvement of the inferior corpus callosum and atrophy involving the cerebellar vermis (figure).

On subsequent questioning it was found that 8 months before admission the patient started a homemade homeopathic remedy called plumbum metallicum for treatment of symptoms of multiple sclerosis. The remedy that he had taken was not available for analysis but was prepared using lead. He continued taking this remedy intermittently until admission. In addition, during this period he started smoking marijuana for treatment of symptoms of multiple sclerosis. He used a metallic silver pipe made in Thailand that had metallic inlays. A metallic lump the size of a match head found inside the cone was tested by the ACT Government Analytical Laboratories. It contained 26%–39% lead and the laboratory considered that this would give off large quantities of lead with smoking. His family members were also tested and not found to have significant lead concentrations. This probably excludes domestic or environmental exposure to lead.



MRI showing multiple focal white matter hypertensities mainly in periventricular locations.

He was treated with oral chelation therapy using 2,3-dimercaptosuccinic acid (DMSA or succimer) in recommended doses (30 mg/kg/day in three divided doses for 5 days and then 20 mg/kg/day in two divided doses for 14 additional days). The medication was tolerated well apart from mild metallic taste and mercaptic odour. He responded with a rapid decrease of lead concentrations from 4.4 to 1.9 μmol/l and improvement in Hb to 135 g/l. This was accompanied by significant improvement in his clinical signs. In particular he noted marked improvement in lower limb power, ataxia, tremor, cognition, and memory. The abdominal colic, nystagmus, and diplopia resolved fully. He was able to walk short distances without a stick and stated that he had never felt so good. He required several courses of succimer because of mild rebound increases in lead concentrations but these were not associated with significant symptoms.

This patient had many typical features of lead toxicity including confusion, colic, anaemia, and basophilic stippling. The increased lead and porphyrin concentrations confirmed the diagnosis. It is of interest that he had marked cerebellar features and some cognitive and behavioural problems. We think that these features were secondary to lead toxicity and not multiple sclerosis because they responded rapidly to chelation therapy and had not responded to previous methylprednisolone therapy. In addition, there has been another recent report of lead encephalopathy that presented with cerebellar ataxia and behavioural disturbance.[4]

Lead is not associated with the pathogenesis of multiple sclerosis[5 6]; however, lead poisoning can mimic many diseases. Our study indicates that lead poisoning is a possible differential diagnosis for exacerbation of the symptoms of multiple sclerosis, in particular the cerebellar and cognitive features. The rapid and dramatic response of many of his symptoms and signs to oral chelation therapy with succimer suggests that this is an important diagnosis to consider.

The most likely sources of lead were a homeopathic remedy and a pipe used to smoke marijuana. He took both of these as alternative medicine for his symptoms of multiple sclerosis but did not disclose this to his medical practitioner. The use of complementary and alternative medicine among patients with multiple sclerosis is extensive[2 3] and this case report indicates that on some occasions they may exacerbate symptoms. Therefore, neurologists should consider asking about such medicines before simply attributing symptoms and signs to exacerbation of multiple sclerosis.

We thank Lyn Cridland and Nora Estrellado for their help in preparation of this manuscript. We acknowledge Lindsay Vowels (neuropsychologist), the ACT Government Analytical Laboratory (analysis of lead content of pipe), and the Central Sydney Laboratory Service (analysis of blood lead concentrations).

1 Zollman C, Vickers A. ABC of complementary medicine. Complementary medicine and the patient. *BMJ* 1999; **319**:1486–9.
2 Winterholler M, Erbguth F, Neundorfer B. The use of alternative medicine by multiple sclerosis patients—patient characteristics and patterns of use. *Fortschr Neurol Psychiatr* 1997;**65**:555–61.
3 Schwartz CE, Laitin E, Brotman S, *et al*. Utilization of unconventional treatments by persons with MS: Is it alter-native or complementary? *Neurology* 1999;**52**:626–629.
4 Mani J, Chaudhary N, Kanjalkar M, *et al*. Cerebellar ataxia due to lead encephalopathy in an adult. *J Neurol Neurosurg Psychiatry* 1998;**65**:797.
5 Westerman MP, Bruetman M, Pfitzer E. Lead poisoning and multiple sclerosis. *Arch Environ Health* 1974;**29**: 355–6.
6 McGrother CW, Dugmore C, Phillips MJ, *et al*. Multiple sclerosis, dental caries and fillings: a case control study. *Br Dent J* 1999;**187**:261–4.