

The spinocerebellar ataxia type 1 expansions were found in three patients and dentatorubral-pallidolusian atrophy expansions were found in five. The remaining six patients showed no expansion in any locus. After exclusion of these three types, three patients from two families having pure cerebellar ataxia with retained deep tendon reflexes and slight to moderate atrophy limited to the cerebellum on MRI, were diagnosed with ADCA type III. The remaining three patients from two families were suspected as having spinocerebellar ataxia type 2 because of decreased deep tendon reflexes, slow eye movement without nystagmus and pronounced atrophy in the pons and cerebellum on MRI.

In the nationwide epidemiological study in Japan without genetical evaluation reported by Hirayama *et al.*,<sup>5</sup> Machado-Joseph disease occupied only 11% of all ADCA and was regarded as a relatively rare disorder. On the other hand, the Menzel type of hereditary cerebellar ataxia was 49% of all ADCA. Our findings, however, showed that Machado-Joseph disease, which accounted for 56%, is a common ADCA using the genetic estimation. Although the sample size of our study was not large enough to obtain good epidemiological reliability, a significant difference was shown by  $z$  test between the results of Hirayama *et al.*<sup>5</sup> and our findings on Machado-Joseph disease ( $P < 0.002$ ) and on Menzel type of hereditary cerebellar ataxia ( $P < 0.002$ ), but not on dentatorubral-pallidolusian atrophy. These differences may be due to the difficulty in clinical diagnosis of Machado-Joseph disease and Menzel type of hereditary cerebellar ataxia. In fact, five patients confirmed as having Machado-Joseph disease in this study were clinically suspected of having a Menzel type of hereditary cerebellar ataxia before the genetic analysis.

In conclusion, Machado-Joseph disease is a common ADCA in the Japanese and epidemiological re-examination of Japanese ADCA is necessary to obtain correct proportions of each genetically diagnosed disorder.

KEN INOUE  
TOKIJI HANIHARA  
YOSHITERU YAMADA  
KENJI KOSAKA  
Department of Psychiatry,  
Yokohama City University,  
School of Medicine,  
3-9 Fukuura,  
Kanazawa-ku,  
Yokohama 236,  
Japan  
TOSHIO KATSURAGI  
KIYOSHI IWABUCHI  
Department of Neurology and Psychiatry,  
Kanagawa Rehabilitation Centre,  
516 Nanasawa,  
Atsugi 243-01,  
Japan

Correspondence to: Dr Ken Inoue, Department of Psychiatry, Yokohama City University, School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236, Japan.

- 1 Kawaguchi Y, Okamoto T, Taniwaki M, *et al.* CAG expansions in a novel gene for Machado-Joseph disease at chromosome 14q32.1. *Nature Genet* 1994;8:221-7.
- 2 Koide R, Ikeuchi T, Onodera O, *et al.* Unstable expansion of CAG repeat in hereditary dentatorubral-pallidolusian atrophy (DRPLA). *Nature Genet* 1994;6:9-13.
- 3 Orr HT, Chung M, Banfi S, *et al.* Expansion of an unstable trinucleotide CAG repeat in spinocerebellar ataxia type 1. *Nature Genet* 1993;4:221-6.
- 4 Harding AE. Clinical features and classification of inherited ataxias. In: Harding AE, Deufel T, eds. *Advances in neurology: inherited ataxias*. New York: Raven Press, 1993: 1-14.

5 Hirayama K, Takayanagi T, Nakamura R, *et al.* Spinocerebellar degenerations in Japan: a nationwide epidemiological and clinical study. *Acta Neurol Scand* 1994;153:1-22.

### Amyotrophic lateral sclerosis after accidental injection of mercury

Mercury has been widely discussed in the pathogenesis of amyotrophic lateral sclerosis.<sup>1,2</sup> We describe a case of amyotrophic lateral sclerosis after accidental injection of mercury.

While shaking a mercury thermometer, a female nurse plunged it into her left hand. Elementary mercury infiltrated into the soft tissues of her palm (figure). The diffusely distributed mercury particles could not be removed completely by surgical means. Two years later, blood mercury concentrations, analysed with atomic absorption spectroscopy, were raised (15  $\mu\text{g/l}$ , reference  $< 5 \mu\text{g/l}$ ), but declined soon afterwards to normal values.

Three and a half years after mercury infiltration, the 38 year old woman was admitted with progressive weakness of the legs which had begun a few weeks before. She had moderate weakness of the musculature—most pronounced in the lower limbs—slight cerebellar ataxia, and fasciculations in the thighs. Deep tendon reflexes were hyperactive at all her limbs. Babinski's sign was positive on the left. Cranial nerves and sensation were normal. Electromyography showed pathological spontaneous activity in muscles of both legs. Gastrocnemius muscle biopsy suggested neurogenic muscle atrophy. Mercury and lead concentrations in blood, urine, and hair were not raised. Medical history was unremarkable.

With a presumptive diagnosis of amyotrophic lateral sclerosis, we performed a chelation treatment with dimercaptosuccinic acid. Urinary mercury excretion increased (peak value 41.6  $\mu\text{g}/24\text{h}$ , reference  $< 10 \mu\text{g}/24\text{h}$ ) without clinical improvement. Muscular atrophy, cramps, and fasciculations become prominent in all limbs. Six months later, a severe bulbar syndrome developed.

Four years after the onset of neurological symptoms, the patient is tetraplegic. Communication is possible via eye movements. There is no respiratory insufficiency, sensory deficits, or dementia.

Mercury accumulates within the CNS, entering either by crossing the blood-brain barrier or via retrograde axonal transport. In our patient, mercury from the deposit in the hand could have slowly accumulated in the CNS over time. This would explain the dissociation between exposure to mercury and onset of clinical symptoms. Initial trauma and repeated surgical interventions may have enabled retrograde axonal transport.

It has been speculated that a pre-existing impairment or a genetically determined dysfunction of motor neuron metabolism could be aggravated by various exogenous factors such as trauma, triggering the manifestation of amyotrophic lateral sclerosis.<sup>3</sup> Thus mercury and trauma could have worked as synergistic factors in our patient.

Chelation treatment, as in this patient, has never been successful in amyotrophic lateral sclerosis. Such treatment—to be of any use—should be initiated shortly after exposure to mercury to prevent an accumulation and irreversible damage within the CNS.

Pure coincidence of a rare disease with an extraordinary preceding event cannot be ruled out, but the unusual appearance of amyotrophic lateral sclerosis in a young woman supports the role of mercury as a causative factor in this case.

In previous reports of motor neuron diseases after mercury incorporation, clinical symptoms developed shortly after the intake of large amounts of mercury and included typical signs of mercury intoxication.<sup>1,2,4,5</sup> Our patient illustrates the possibility that, if present over a longer period of time, relatively small amounts of mercury may cause sporadic amyotrophic lateral sclerosis without other signs of mercury intoxication.

STEFAN SCHWARZ  
Department of Neurology,  
University of Heidelberg,  
400 Im Neuenheimer Feld,  
Heidelberg 69120, Germany  
INGO W HUSTEDT  
Department of Neurology,  
University of Münster,  
33 Albert-Schweitzer-Strasse,  
Münster 48129, Germany  
H P BERTRAM  
Department of Pharmacology and Toxicology,  
University of Witten-Herdecke,  
Herdecke 58313, Germany  
KLAUS KUCHELMEISTER  
Department of Neuropathology,  
University of Münster,  
33 Albert-Schweitzer-Strasse,  
Münster 48129, Germany

Correspondence to: Dr Stefan Schwarz.

- 1 Brown IA. Chronic mercurialism. A cause of the clinical syndrome of amyotrophic lateral sclerosis. *Arch Neurol Psychol* 1954;72: 674-81.
- 2 Kantarjian AD. A syndrome clinically resembling amyotrophic lateral sclerosis following chronic mercurialism. *Neurology* 1961;11: 639-44.
- 3 Kurtzke JF, Beebe GW. Epidemiology of amyotrophic lateral sclerosis: 1. A case-control comparison based on ALS deaths. *Neurology* 1980;30:453-62.
- 4 Adams CA, Ziegler DK, Lin JT. Mercury intoxication simulating amyotrophic lateral sclerosis. *JAMA* 1983;250:642-3.
- 5 Barber TE. Inorganic mercury intoxication reminiscent of amyotrophic lateral sclerosis. *J Occup Med* 1978;20:667-9.



Radiograph of the left hand after injury with a mercury thermometer. Incorporated mercury particles are diffusely distributed in the soft tissues of the palm.