Toxic leukoencephalopathy after inhalation of poisoned heroin: MR findings.

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Toxic Leukoencephalopathy after Inhalation of Poisoned Heroin: MR Findings

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Summary: Retrospective MR studies of four patients with neurologic symptoms after inhalation of contaminated heroin vapor revealed extensive, typically symmetrical lesions in the white matter of the cerebrum, cerebellum, and midbrain. Selective involvement of the corticospinal tract, the solitary tract, and the lemniscus medialis also has been found.

Index terms: Drugs, effects; Brain, effects of toxic substances on; Brain, magnetic resonance; Brain, diseases; Degenerative brain disease

The inhalation of black-market heroin vapors (pyrolysate) can cause specific leukoencephalopathy (1, 2). In 1982, 47 such patients were described after the inhalation of heroin vapors. Later the number of patients rose to about 75, mainly cases in the Netherlands, Italy, and Switzerland.

This leukoencephalopathy is characterized by typical neurologic symptoms with three clinical stages apparently related to the extent of white-matter involvement. In stage 1 the patient will show mainly cerebellar symptoms. In stage 2 there will be cerebellar and (extra) pyramidal symptoms. Finally, in stage 3 the patient will suffer from stretching spasms and akinetic mutism or hypotonic mutism eventually followed by death (1). The exact nature of the poisonous factor has never been elucidated.

In this article a retrospective view is given of four recent cases of this entity with a description of the associated magnetic resonance (MR) findings.

Case reports

Case 1

A 33-year-old man first presented in July 1989 with progressive gait disturbances. The last 3 years he had been using heroin only to the extent of inhaling its vapors. Physical examination disclosed a remarkable cerebellar syndrome comprising ataxia and dysarthria. Further neurologic examination showed no abnormalities.

Computed tomography (CT) revealed extensive symmetric white-matter involvement mainly in the cerebellum and, to a much lesser extent, periventricularly in both cerebral hemispheres. In addition to the lesions seen on CT, MR imaging (Fig 1) showed more clearly pronounced white-matter lesions in both cerebral hemispheres.

During hospital admission no significant improvement of his neurologic defects was seen. The patient was unable to walk unaided and still had severe ataxia of all limbs and dysarthria.

Case 2

A 26-year-old man presented in February 1989 with complaints of progressive gait disturbances and speech disorder and minor problems with swallowing. These symptoms had started 4 weeks before admission.

Shortly before his problems arose he had been assaulted and had sustained a minor head injury and a commotio cerebri. The patient was known to have been using drugs for several years including inhalation of heroin vapor.

Physical examination disclosed a cerebellar syndrome with gait ataxia, limb ataxia, and dysarthria. CT scan revealed large areas of white-matter lesions in the cerebellum, and in the supratentorial region there was pronounced atrophy. There was no enhancement of the lesions after intravenous administration of contrast material.

Compared with CT scan the MR showed more extensive lesions both in the supra- and infratentorial region (Fig 2). The supratentorial lesions were most intense around the thalamus, the internal capsule, the globus pallidum, the white matter of the occipital lobes, and the splenium of the corpus callosum.

Case 3

A 34-year-old man was admitted to the hospital in July 1990 with complaints of progressive speech disorders and problems with coordination in his arms and legs.

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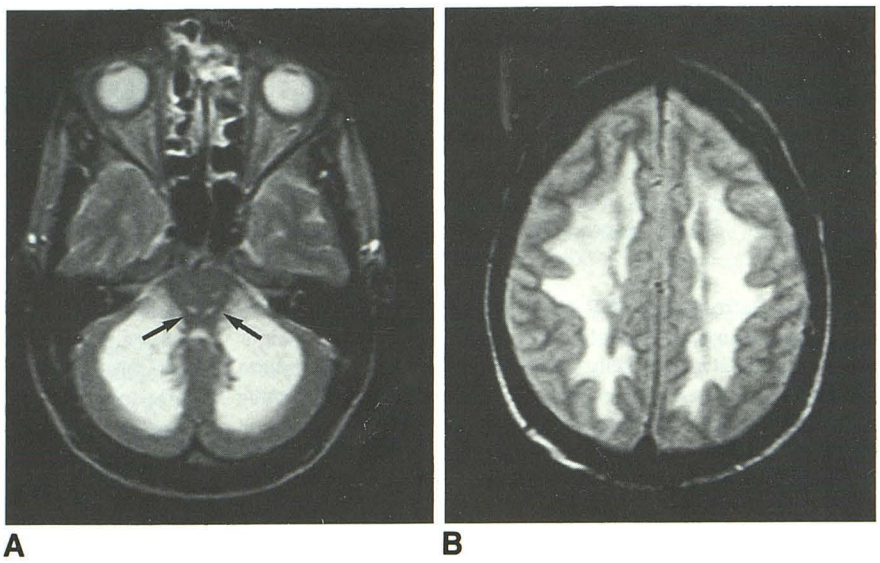

Fig. 1. *A*, Case 1. A 33-year-old man after inhaling heroin vapor. Moderately T2-weighted spin-echo (SE) scan (2000/100/2 [repetition time/echo time/excitations]) depicts symmetric lesions of high signal intensity in both cerebellar hemispheres and subtle lesions of high signal intensity in the brain stem (*arrows*).

B. Case 1. Bilateral, symmetric areas of high signal intensity diffusely in the cerebral white matter.

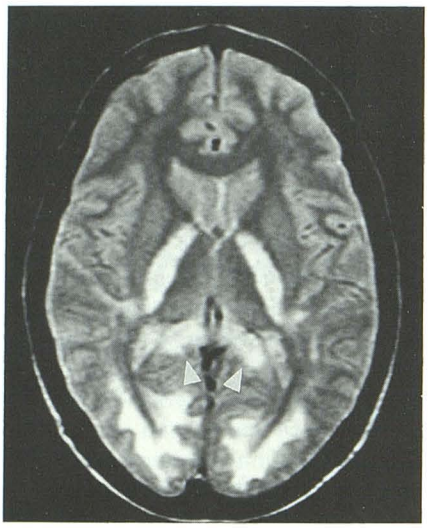

Fig. 2. Case 2. A 26-year-old man after inhaling heroin vapor. T2-weighted SE image shows symmetric bilateral lesions of high signal intensity in the internal capsule, the occipital white matter, and the splenium of the corpus callosum (*arrows*).

The problems started 2 months before admission and progressed very rapidly. The patient stated that he had been inhaling heroin vapor during the last 4 years.

Physical examination revealed a nystagmus when the patient looked to the right and upward, severe dysarthria and tongue apraxia, gait and limb ataxia with slight tetraparesis, and discrete signs of a pyramidal syndrome with high myotatic reflexes. CT scan showed almost symmetrical, extensive hypodensities of the white matter in both cerebral hemispheres.

MR imaging showed, in addition to the lesions noted on CT, clear visible lesions in the crus posterior of the internal capsule and additional parts of the corticospinal tract (Fig 3).

Case 4

A 27-year-old man first presented in March 1985 with complaints of progressive gait disturbances and speech disorders. The problems started a few months before admission. He and other persons in his environment had also noted memory impairments and difficulties with concentration. He had been inhaling heroin almost daily for 6 years.

Physical examination showed a cerebellar syndrome, a slight dysarthria, and a bilateral pyramidal syndrome. MR scan showed symmetric, extensive white-matter lesions both in the cerebellum and periventricularly in the cerebral hemispheres. Lesions also were seen in the region of the brachium pontis and the internal capsule. We concluded that our patient suffered from heroin leukoencephalopathy.

After 2 months of physical therapy, the patient was able to walk unaided. He went to a rehabilitation center, but there was no further improvement in the clinical picture.

Three years later, in 1988, the patient presented again with a cerebral concussion and concussion of the cervical spinal cord from which he made a fast recovery. A CT scan performed during admission showed an almost identical picture compared with CT 3 years before. In the following years the patient recovered very slightly. Follow-up MR scan in 1991 showed less severe white-matter involvement in the cerebral hemispheres but progressive dilatation of the lateral ventricles, suggesting cerebral atrophy (Fig 4).

Discussion

The patients were young men who for several years had been inhaling heroin vapor sold on the black market in Amsterdam before the symptoms of severe progressive cerebellar impairment developed. The cerebellar syndrome was mainly characterized by ataxia, gait disturbances, and dysarthria. In nearly all cases the procedure of

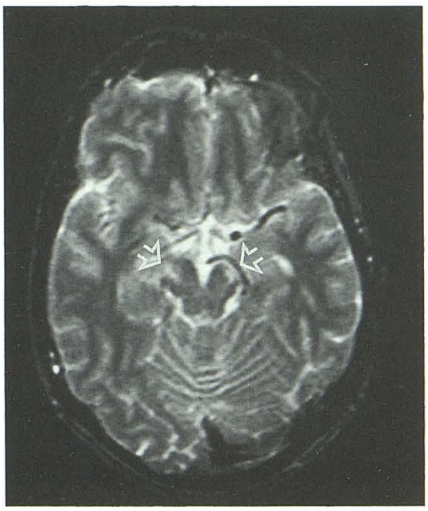

Fig. 3. Case 3. A 34-year-old man. T2-weighted SE image shows bilateral symmetric lesions of high signal intensity in the midbrain (*arrows*).

sniffing the heroin was identical. The heroin was heated on a piece of tin foil as powder, without the addition of other substances. Because no side effects in the same period were recorded with other methods of administration, heating must have activated the toxic substance.

Heroin is known to cause several neurologic disorders such as myelopathy of the thoracic and cervical cord, poly(radiculo)neuropathy, and stroke. (1, 2). Overdose of heroin may result in death within a few minutes; in some patients diffuse cerebral edema is found at necropsy (1).

The administration of pure heroin intravenously is not known to cause leukoencephalopathy; to our knowledge, the clinical symptoms and characteristic changes on CT and MR, as seen in our patients, have not been described after intravenous use of heroin (1). In those patients described in the literature who died after inhaling the toxic heroin vapors, light microscopy revealed spongiform degeneration of the central nervous system white matter (1). This degeneration showed many vacuoles of the oligodendroglia (Figs 5*A* and 5*B*). Electron microscopy revealed that the vacuoles are formed between the myelin lamellae by splitting at the intraperiod lines. The fluid-filled spaces coalesce and the electron microscopic image is then referred to as vacuolating myelinopathy.

This form of myelin disorganization also has been described after hexachlorophene or triethyltin was administered to young rats in an experimental setting (4). Hexachlorophene is known to have caused leukoencephalopathy in preterm neonates treated with hexachlorophene solutions for dermal reasons. This leukoencephalopathy also has been described in adult women who used vaginal tampons containing hexachlorophene and in patients treated with hexachlorophene solutions for extensive burns. Triethyltin and anesthetic gases may also cause a vacuolating myelinopathy.

The involvement of the white matter in all these cases has a common ground. Myelin has a high lipid content and a long half-life, which makes it extremely vulnerable to lipophilic substances and lipid peroxidation. It is highly probable that the toxin in the heroin belongs to this lipophilic category.

In all the heroin cases described in the literature (1) neuropathologic studies revealed that the cerebral and cerebellar white matter and the cerebellar peduncules were involved. Also, the tractus corticospinalis, the lemniscus medialis, and the tractus solitarius were frequently affected. The neuropathologic findings are consistent with our findings by CT and MR imaging.

We consider these findings highly specific. There is selective, symmetrical involvement of white-matter structures and tracts with a characteristic distribution (5). To our knowledge, no other toxic encephalopathy with a similar destruction has been described. Infections and inflammatory disorders may solely affect white matter, but they rarely show a symmetrical distribution and certainly not the patterns of involvement as shown in our cases. Inborn errors of metabolism, especially the leukodystrophies, show symmetrical involvement of the white matter. Adrenoleukodystrophy preferentially involves the occipital white matter at the onset of the disease. The age of onset is usually in the first decade; the MR image shows the typical three areas of involvement (6), which differ from the vacuolating myelinopathy that was found in our patients.

Vacuolating myelinopathy in a symmetrical distribution is found in Canavan disease and idiopathic spongy sclerosis. In these disorders the arcuate fibers are involved throughout the hemispheres and the disease spreads centripetally. In Canavan disease the putamen is often spared in a characteristic way. We conclude that the distribution of the demyelination in the occipital and cerebellar white matter sparing the U fibers, with the pattern of a vacuolating myelinopathy, is highly characteristic for this type of toxic encephalopathy.

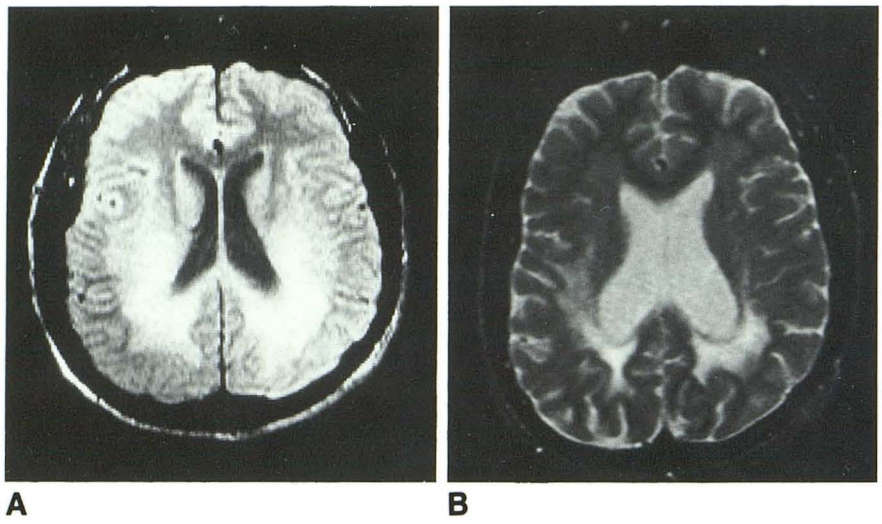

Fig. 4. *A*, Case 4. A 27-year-old man. T1-weighted SE image (2000/50) shows extensive, bilateral symmetric white matter involvement in the parietooccipital region.

B, Case 4. Six years later follow-up T2-weighted SE image (2000/100) shows dilatation of the lateral ventricles suggesting cerebral atrophy.

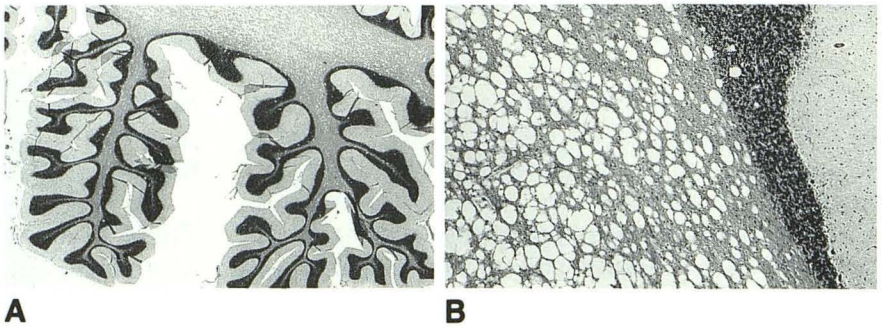

Fig. 5. *A*, Light microscopic image of the brain of a patient who died of toxic encephalopathy after inhalation of poisoned heroin shows extensive, diffuse white matter involvement with sparing of the U fibers.

B, Light microscopic image of the same patient with greater magnification more clearly depicts the vacuolating myelinopathy of the white matter.

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