J Neurol (2003) 250 : 496 – 498
DOI 10.1007/s00415-003-1012-5

Thomas Nyffeler
Anne Stabba
Matthias Sturzenegger

Progressive myelopathy with selective involvement of the lateral and posterior columns after inhalation of heroin vapour

Received: 31 January 2002
Received in revised form: 25 October 2002
Accepted: 30 October 2002

Sirs: Intravenous heroin abuse is associated with a broad spectrum of neuropathological changes [2]. To avoid the risks of parenteral drug administration intranasal application has become increasingly popular. Whereas acute myelopathy has been reported after insufflation of heroin [9], heating the heroin on an aluminium foil and inhaling the vapour through a metallic tube, a procedure called "chasing the dragon" may lead to progressive spongiform leukencephalopathy [2]. It is the purpose of this report to present a new disease entity in the context of inhalation of heroin vapour, namely a progressive myelopathy with selective involvement of the lateral and posterior columns.

A 46 year old man had abused heroin since 1975, initially by intravenous injection and since 1986 exclusively by inhalation of heroin heated on a metallic foil. After a complete abstinence lasting two months in spring 2001 he resumed excessive heroin consumption by the same route. However he then bought the heroin from a different source and complained about its poor quality. During the next few weeks he noticed a slowly progressive gait disorder with paresthesia in the lower limbs. After another few weeks he developped urinary incontinence and impotence and was then admitted to our neurological department in June 2001.

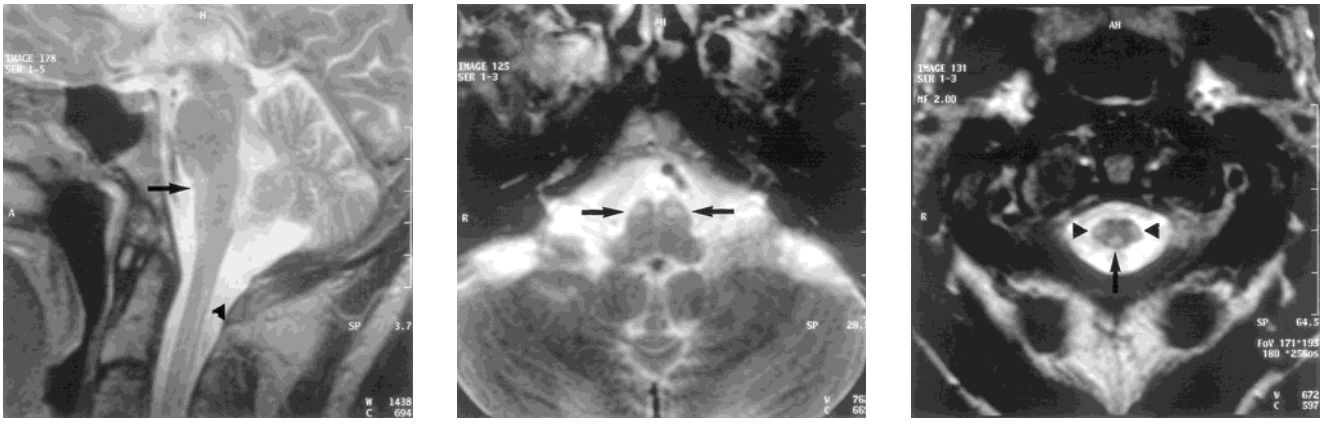
Apart from persistent lumbar pain following a lumbar disc operation L5/S1 in 2000 he had had no prior neurological symptoms. There was no neurological disease in his family; from 1982 laboratory markers for hepatitis B and C had been known.

On examination he was alert and fully oriented. Motor examination revealed a mild left-sided facial weakness. Strength was proximally and distally diminished in the upper and lower extremities, predominantly on the left side and in the legs. There was spasticity in the legs. Tendon reflexes were exaggerated apart from Achilles tendon reflexes which were slightly diminished. The plantar response was extensor on both sides. There was impaired vibration sense and proprioception in the legs. Romberg sign was positive. Gait was slow, ataxic and spastic.

Magnetic resonance imaging of the brain showed bilateral multiple subcortical lesions, hyperintense on T2 weighted and FLAIR images and an additional subacute lesion in the crus posterior of the right capsula interna with the typical pattern (size and location) of lacunar strokes. Magnetic resonance imaging of the neck showed bilateral signal abnormalities in the corticospinal tract and the posterior columns: hypointense on T1 weighted images, hyperintense on T2 weighted images without gadolinium enhancement.

The motor evoked potentials showed a prolonged central motor conduction time. The somatosensory evoked potentials of both tibial nerves had markedly prolonged central sensory conduction times. There was furthermore prolonged F wave latency indicating additional peripheral nerve disease and only slightly delayed lumbar response. Cerebrospinal fluid analysis was normal with normal immunoglobulin G, albumin, IgG/albumin ratio and absence of oligoclonal bands. He had negative serological tests for HIV-1/2, HTLV-1/2, *Borrelia burgdorferi* and *Treponema pallidum*, but suffered from chronic hepatitis B and C. The levels of Vitamin B12 (360 pmol/l), erythrocyte folate (854 nmol/l), homocysteine (12 µmol/l) and niacin (148 nmol/l) were normal. White blood count, sedimentation rate, serum protein analysis, coagulation tests, antinuclear antibodies, antineuronal nuclear antibodies and anti-Purkinje cell cytoplasmic antibodies and rheumafactor were normal. After the hospitalisation in our neurological department the patient was transferred to a regional hospital. Prolonged multivitamin supplementation and later highdose prednisone therapy for ten days did not improve the symptoms.

We present a 46 year old patient with progressive myelopathy affecting only the corticospinal tract and posterior columns following inhalation of heroin vapour. To our knowledge this has not been reported until now. So far all case reports of myelopathy following IV heroin use [2] or following insufflation of heroin [9] presented with acute symptoms. As possible mechanisms embolism of adulterants, hypotension with borderzone infarction, hypersensitivity reaction, vasculitis, hyperextension injury of the neck or a direct toxicity have been discussed [2]. For intranasal use, however, immunpathological or direct neurotoxic mechanisms have to be considered primarily [9]. The fact that they occurred usually after a period of heroin abstinence followed by a single use and the MRI findings which were consistent with an acute inflamma-



a) b) c)

Fig. 1 (**A**) Sagital T2 weighted image of the craniocervical junction showing selective hyperintense signal alterations in the ventral pontomedullary area (pyramidal tract) (arrow) and in the dorsal cervicomedullary area (posterior columns) (arrow heads). (**B**) Axial T2 weighted image of the caudal pons showing bilateral hyperintense signals in the ventral pons (pyramidal tract) (arrows). (**C**) Axial T2 weighted image of the spinal cord at the craniocervical junction. There are symmetric bilateral hyperintense signals in the posterior columns (arrows) and in the anterolateral columns (pyramidal tracts) (arrow heads).

tory process like in transverse myelitis favor the assumption of an immunopathological etiology. In our patient, who showed no acute but a chronic progressive symptom evolution, the following conditions have to be ruled out before connecting the findings with heroin: In younger people multiple sclerosis is the first of these. However, the MRI findings in our patient would be atypical and the cerebrospinal fluid was completely normal with absence of oligoclonal bands. The clinical and radiological findings he presented with resemble the subacute combined degeneration of the spinal cord following deficiency of Vitamin B12 [5], folate [10] or niacin [1] which may involve both the posterior columns and the corticospinal tracts. However, all three vitamins repeatedly showed normal serum levels. Furthermore, there were no laboratory findings indicating malnutrition. Myelopathy caused by infection with HTLV-1-, HIV-, *Borrelia burgdorferi* and *Treponema pallidum* could be excluded with negative serological tests, normal cerebrospinal fluid results and absence of gadolinium enhancement on MRI. An immunopathological mechanism would be a possible cause. Since our patient reported a total drug withdrawal lasting two months, a hypersensitivity reaction to heroin vapour after reexposure to the drug is conceivable. However the normal results of cerebrospinal fluid and the MRI findings with an absence of gadolinium enhancement are not consistent with an inflammatory process. After all, because of the patient's statement about a new source of his heroin with poor quality, because the myelopathy developed at a time of excessive inhalation of heroin vapour, and because of the selective involvement of anatomically defined parts of the spinal cord (Fig. 1c), a toxic effect is most likely.

Because of the unknown amount of adulterants in heroin and the complex chemical reactions when heating heroin, the underlying pathophysiology is far from clear. The fact that two functional systems are involved symmetrically may be interpreted as a regional vulnerability of brain tissue to a toxin or a highly specific toxin. The only well known inhalative toxin that may cause the symptomatology of our patient is nitrous oxide. Nitrous oxide inactivates irreversibly cobalamin by oxidizing the cobalt core from the Cob(I) to the Cob(III) state while the plasma cobalamin levels remain normal [8]. However such a toxicity has been described only in anesthesia [6] and in abuse of whipped cream bulbs [3].

Theoretically nitrous oxide may originate by burning of nitrogenous substances. Since a chemical analysis of the heroin sold on the streets of our town showed a content of 30 % both of paracetamol and coffeine, both substances rich in nitrogen, one might argue that our patient has been exposed to nitrous oxide by inhalation of heroin vapor. However, this explanation is speculative. First, the quantity of nitrous oxide would be very low and as the inactivation of cobalamin leads to an increase of homocysteine which is normally converted to methionine by methyl cobalamin [4], one would not expect a normal plasma level of homocysteine like in our patient.

In autopsy examinations of heroin abusers with a spongiform leukoencephalopathy after inhaling heroin vapour [7], an increase of brain lactate and changes of the mitochondria were found suggesting an inhibition of mitochondrial functions. The toxin responsible

for the leukoencephalopathy, however, could not be found.

In summary: chronic progressive myelopathy should be included in the spectrum of neurological abnormalities resulting from intranasal heroin abuse.

References

1. Adams RD, Victor M, Ropper A (1997) Principles of Neurology. 6th ed. McGraw Hill
2. Büttner A, Mall G, Penning R, Weis S (2000) The neuropathology of heroin. Forensic Science International 113: 435–442
3. Butzkueven H, King JO (2000) Nitrous oxide myelopathy in an abuser of whipped cream bulbs. J Clin Neurosci 7(1):73–75
4. Ermens AA, Refsum H, Rupreht J, Spijkers LJ, Gutormsen AB, Lindemans J, Ueland PM, Abels J (1991) Monitoring cobalamin inactivation during nitrous oxide anesthesia by determination of homocysteine and folate in plasma and urine. Clin Pharmacol Ther 49(4):385–393
5. Green R, Kinsella J (1995) Current concepts in the diagnosis of cobalamin deficiency. Neurology 45:1435–1440
6. Kinsella L, Green R (1995) "Anesthesia paresthetica": nitrous oxide-induced cobalamin deficiency. Neurology 45: 1608–1610
7. Kriegstein AR, Shungu DC, Millar WS, Armitage BA, Brust JC, Chillrud S, Goldman J, Lynch T (1999) Leukoencephalopathy and raised brain lactate from heroin vapor inhalation ("chasing the dragon"). Neurology 53: 1765–1773
8. Masson C (1999) Combined sclerosis of the spinal cord "revisited". Presse Med 28(37):2048–2049
9. McCreary M, Emermann C, Hanna J, Simon J (2000) Acute myelopathy following intranasal insufflation of heroin: a case report. Neurology 55: 316–317
10. Ravakhah K, West BC (1995) Case report: subacute combined degeneration of the spinal cord from folate deficiency. Am J Med Sci 310(5):214–216

T. Nyffeler, MD · A. Stabba, MD · Matthias Sturzenegger, MD (✉)
Department of Neurology
University Hospital
University of Berne
Freiburgstrasse 10
3010 Berne, Switzerland
Tel.: +41-31/632-21 11
Fax: +41-31/632-96 79
E-Mail: matthias.sturzenegger@insel.ch