Heroin Vapor Inhalation-induced Spongiform Leukoencephalopathy

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A 26-year-old man with a 3-year history of heroin vapor inhalation developed spongiform leukoencephalopathy. T2-weighted magnetic resonance imaging showed characteristic high signals over subcortical white matter, including bilateral frontoparietal lobes, posterior limbs of internal capsules, splenium, occipital lobes, cerebellum and brainstem. Signal intensity of diffusion-weighted imaging was high, and apparent diffusion coefficient in corresponding areas was increased. Pathologic features of heroin-induced spongiform leukoencephalopathy were unique, characterized by demyelination and vacuolar formation. 99m-Technetium-ECD SPECT and F18 FDG PET demonstrated decreased radiotracer uptake in the corresponding areas. 99m-Technetium-TRODAT SPECT showed no definite decreased uptake of radiotracer at basal ganglia, which suggests that the dopamine neurons were not affected. [J Formos Med Assoc 2009; 108(6):518–522]

Key Words: F18 FDG PET, heroin vapor inhalation, spongiform leukoencephalopathy, 99m-technetium-ECD SPECT, 99m-technetium-TRODAT SPECT

Cases of heroin-induced spongiform leukoencephalopathy are rare in Taiwan. Only two cases have been reported.1,2 There are unique magnetic resonance imaging (MRI) findings as a result of the severe demyelination and degenerative vacuolar degeneration over subcortical white matter.3,4 We report a patient who developed spongiform leukoencephalopathy caused by heroin vapor inhalation. Findings from 18-fluorine 2-fluoro-2-deoxyglucose positron emission tomography (F18 FDG PET) and single photon emission computed tomography with dopamine (DA) transporter radiotracer (99m-technetium-TRODAT SPECT) are demonstrated. The effects of heroin on cerebral glucose metabolism and dopamine neurons are reviewed.

Case Report

A 26-year-old man had been inhaling heated heroin vapor (0.1–0.4 g/day) for 3 years. He quit when he experienced progressive dysarthria and spastic weakness of the extremities. He became bedridden 1 year after symptom onset. He could speak coherently but he needed to be fed by nasogastric tube. Pupil sizes were 3 mm bilaterally, promptly reactive to light. Deep tendon reflexes
of the four limbs were increased with ankle clonus and extensor plantar responses. Complete blood count and serum biochemistry were normal. Serum cobalamin, lactate, HIV serology, immune profile and cerebrospinal fluid studies were within normal limits.

**Diagnosis**

T2-weighted MRI demonstrated hyperintense signals over the subcortical white matter of bilateral frontal, parietal and occipital lobes. Moreover, high signals were also found at the posterior limbs of internal capsules, splenium, cerebellum and brainstem (Figures 1A to 1D). Diffusion-weighted imaging (Figure 1E) showed high signal intensity in the corresponding areas. The apparent diffusion coefficient (ADC) (Figure 1F), however, was increased. 99m-Technetium-ECD SPECT study revealed decreased perfusion of bilateral parietal and occipital lobes (Figure 2A). F18 FDG PET study demonstrated decreased FDG uptake in bilateral parietal and occipital cerebral cortex (Figure 2B). TRODAT SPECT demonstrated structural changes in dopaminergic neurons and there was no definite decreased radiotracer uptake in basal ganglia (Figure 3).

After obtaining informed consent, we performed brain biopsy to evaluate treatable causes. Stereotactic biopsy was conducted by using Leksell frame, guided by computed tomography and BrainLAB navigation system. Through right Kocher’s point, we obtained two specimens of white matter from the right occipital and outer right basal ganglia. Pathology revealed severe myelin destruction and diffuse vacuolar formation (Figure 4). The final diagnosis was spongiform

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**Figure 1.** Axial spin echo T2-weighted (TR/TE/BW: 4200/95/19.23) magnetic resonance images show hyperintense signals in the areas indicated by the white arrows: (A) white matter of cerebellum; (B) pontine tegmentum and occipital lobe; (C) posterior limbs of internal capsules, splenium and occipital lobes; (D) subcortical white matter of frontal and parietal lobes. (E) Diffusion-weighted imaging (TR/TE/BW: 8000/81.9/62.5) demonstrated high signals in the corresponding areas. (F) However, apparent diffusion coefficient was high.
leukoencephalopathy induced by heroin vapor inhalation.

The patient took coenzyme Q10 1200 mg, vitamin C 2000 mg and vitamin E 1200 mg daily. He recovered 6 months later with neurologic sequela of mild spasticity of all four limbs. Follow-up MRI showed no obvious improvement.

**Discussion**

The histopathology of the brain specimens from our patient was characterized by severe myelin destruction and vacuolar formation, which are identical to the pathologic features of typical cases reported in the literature. The disease mechanism...
of heroin-induced spongiform leukoencephalopathy is still unclear. The MRI features of the second case reported in Taiwan were characterized by high-signal abnormalities on T2-weighted and diffusion-weighted images. However, ADC map of the corresponding areas were decreased. The MRI of our patient demonstrated high ADC. We believe that profound cellular damage is the reasonable explanation.

In heroin abusers, regional hypoperfusion is significantly found in the frontal, occipital, temporal lobes, basal ganglia and cerebellum. The perfusion defects are partially reversible with short-term abstinence. Heroin addicts with spongiform leukoencephalopathy have obviously decreased regional cerebral blood flow in the subcortical white matter of bilateral cerebral and cerebellar hemispheres. The mechanism of regional hyperfusion is unknown.

Martin et al reported the alteration of local cerebral glucose utilization following intravenous administration of heroin in Fischer 344 rats. When low dose heroin was acutely administered through the intravenous route, the glucose utilization rate was higher in the medial olfactory tubercle, anterior nucleus accumbens and dorsolateral caudate. However, glucose utilization rate was lower than in controls in the habenula, dorsal raphe and central gray. Discrete regions with the effects most evident in motor areas and structures related to analgesia were affected in high dose heroin administration. The glucose utilization alteration differs for individual doses of heroin and the mechanism is still unclear. Findings from FDG PET study of our patient were identical to those demonstrated by Wang et al who studied six patients with a history of heroin vapor inhalation. There were significant symmetric decreased uptakes of radiotracer over bilateral posterior limbs internal capsule, white matter of cerebellum and occipital lobe. By concluding results of F18 FDG PET study and using the Cornell Dysthymia Rating Scale, Galynker et al demonstrated that opiate-abstinent subjects had lower regional cerebral glucose metabolism than control subjects in the bilateral perigenual anterior cingulate cortex and left mid-cingulate cortex, which are believed to be aberrant mood processing cortex.

Chronic exposure to heroin is associated with structural changes in dopaminergic neurons and prolonged withdrawal syndrome is relevant to the disorder of corpus striatum DA metabolism. TRODAT scan in these patients demonstrated different levels of abnormality in the corpus striatum, which were much smaller than in normal subjects. Our patient demonstrated normal TRODAT uptake in the corpus striatum. A postmortem study has shown that the striatal level of the vesicular monoamine transporter in heroin users is normal.
Our patient suffered from mild spasticity, probably caused by irreversible damage to subcortical white matter, degeneration of corticospinal tracts and tegmentum in brainstem. He was not in an akinetic-mute state, which is a clinical syndrome liable to be induced by diversely localized lesions, and invariably bilateral involvement of frontal lobes, subcortical white matter, pallidum, thalamus or midbrain. Some patients with presynaptic deficit in the nigrostriatal dopamine pathway may also present with akinetic mutism. FDG PET is significant for detection of regional alteration of glucose metabolism associated with chronic heroin exposure. Perhaps TRODAT SPECT can also be performed routinely on chronic heroin abusers to demonstrate dopamine neuron degeneration and evaluate its validity in predicting prognosis of akinetic mutism.

References