

## Case Report

# Intravenous Heroin-Associated Delayed Spongiform Leukoencephalopathy: Case Report and Reviews of the Literature

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*Heroin-associated spongiform leukoencephalopathy is a rare, and sometimes fatal, condition usually caused by vapor inhalation of heroin. The authors report a 41-year-old man who was diagnosed with delayed spongiform leukoencephalopathy three weeks after injecting heroin intravenously. He had been admitted to another hospital due to acute heroin overdose, which had occurred four hours after intravenous injection of an unknown amount of heroin. His clinical condition showed progressive improvement and he was discharged 12 days after admission. Three weeks after this episode, his cognitive functioning declined. Akinetic mutism, spasticity and hyperreflexia of all extremities were observed. Electroencephalography (EEG) and imaging of the brain showed typical characteristics of spongiform leukoencephalopathy. The three and six-month follow-up of the patient showed clinical improvement and this was corroborated through EEG measures and brain imaging. The discussion summarizes eight previously reported cases of intravenous heroin associated spongiform leukoencephalopathy and compares them to the authors' case.*

**Keywords:** Spongiform leukoencephalopathy, Heroin, Akinetic mutism

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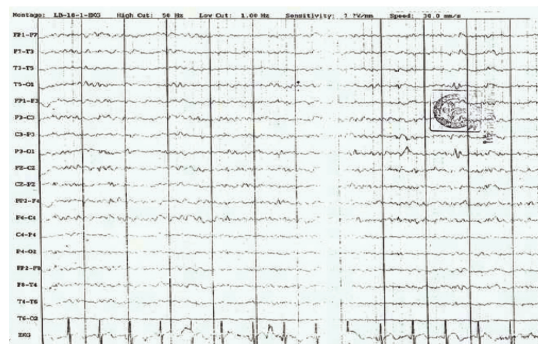
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Heroin abuse, although a serious worldwide problem, is usually underestimated. Many neurological complications, such as acute delirium, delayed post anoxic encephalopathy and coma have been recognized<sup>(1)</sup>. Heroin-associated spongiform leukoencephalopathy is a rare and sometimes fatal condition, with a mortality rate of 23%<sup>(2)</sup>. It is usually caused by vapour inhalation, a practice called "chasing the dragon"<sup>(2)</sup>. A review of the literature revealed a total of 100 cases with toxic leukoencephalopathy following heroin abuse, including both intravenous use and vapor inhalation<sup>(3)</sup>. To the authors' knowledge, there have been only eight case reports of spongiform leukoencephalopathy worldwide caused by intravenous heroin injection<sup>(3-10)</sup>. We report the ninth case and also summarize the previously reported cases and compare those results with the authors'.

### Case Report

A 41-year-old man was transferred to the authors' hospital due to a decline in cognitive functioning over a five-day period. Three weeks

previously, he had been admitted to another hospital due to acute heroin overdose, which had occurred four hours after intravenous injection of an unknown amount of heroin. At that time, he was in a stupor and therefore was intubated and given naloxone intravenously but without showing improvement of consciousness. Computed tomography (CT) imaging of the brain showed diffuse brain swelling and electroencephalography (EEG) showed a mild to moderate degree of diffused slow wave abnormalities. These results were consistent with toxic or metabolic encephalopathy (Fig. 1). Toxicological screening was



**Fig. 1** EEG shows mild to moderate degree of diffused slow wave abnormality consistent with toxic or metabolic encephalopathy.

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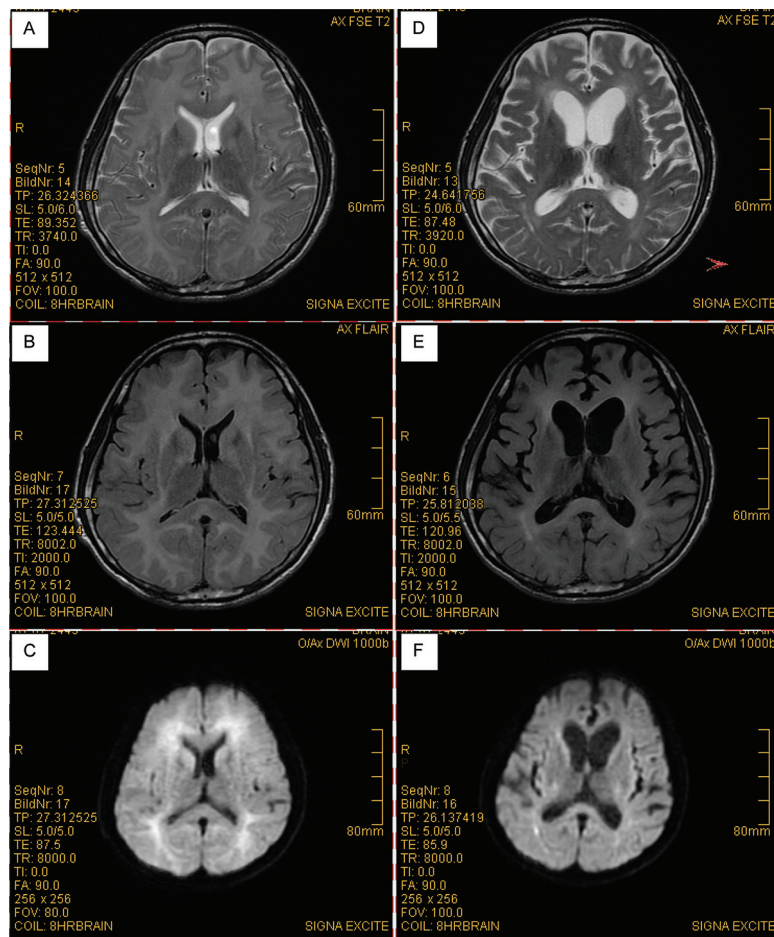
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positive for both heroin and morphine in the urine but negative for amphetamine.

He was treated conservatively and showed gradual clinical improvement and was extubated four days after admission. On the 12-day after admission, he was discharged home showing only mild cognitive impairment but being able to perform the activities of daily living (ADL). Five days after discharge he was confused, could not remember his family members and could not perform ADL. His wife denied illegal drug use while he was at home. One week later, he was sent to the Addiction Treatment Center, Directory of Drugs in Chiang Mai then transferred to the authors' hospital on the same day. On examination he was confused, afebrile and had no neck stiffness. Akinetic mutism, spasticity, and hyperreflexia of all extremities were observed.

Complete blood count, renal function and liver function were in normal limits except for mild elevation of the aminotransferase level (AST 69 U/L [3-35], ALT 97 U/L [7-33]). Serologic screening was positive for anti-HCV and negative for anti-HIV and HBsAg. A lumbar puncture showed a normal CSF profile. CT imaging with contrast media of the brain was normal. Magnetic resonance imaging (MRI) of the brain performed one week after admission showed diffused T2-weighted image and fluid attenuated inversion recovery (FLAIR) hyper-intense lesion symmetrically involving bilateral cerebral white matter with restricted diffusion in diffusion-weighted imaging (DWI) (Fig. 2A-C). No abnormal enhancement was detected in the post contrast study.

The diagnosis of spongiform leuko-encephalopathy was made based on the clinical features



**Fig. 2** (A-C) MRI shows diffused T2 and FLAIR hyper-intense lesion symmetrically involving bilateral cerebral white matter with restriction of DWI. (D-F) MRI at 3-month follow-up shows decreased extent and signal intensity of bilateral symmetrical T2/FLAIR hyper-intensity in white matter of bilateral cerebral white matter with no restriction on DWI. Proportional moderate dilatation of ventricular system, cistern and cortical sulci is seen.

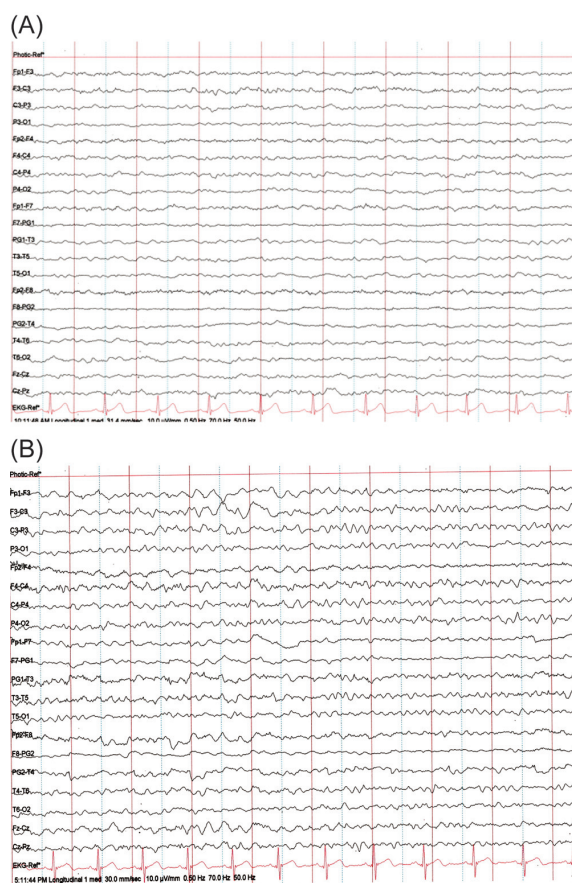
and the imaging findings. The patient was treated conservatively with antioxidants, including co-enzyme Q10 (1,200 mg/day), vitamin C (2,000 mg/day) and vitamin E (2,000 mg/day), as had been done in previously reported cases<sup>(11,12)</sup>. He was discharged showing minimal clinical improvement 19 days after admission. At the three-month follow-up, he could follow a one-step command and spasticity showed improvement. Follow-up MRI of the brain showed regression of bilateral hyper-intense lesion with proportional moderate dilatation of ventricular system, cistern, and cortical sulci (Fig. 2D-F) but the follow-up EEG still showed moderate to severe diffuse slow background activity consistent with severe diffuse encephalopathy (Fig. 3A). At the six-month follow-up, he had only very mild spasticity and mild dysarthria. The EEG showed mild diffuse encephalopathy (Fig. 3B).

## Discussion

Spongiform leukoencephalopathy after inhaling heroin was first described in 1982 by Wolter et al<sup>(2)</sup>. They divided the disease into three stages: initial, intermediate, and terminal, with the last stage including akinetic mutism and stretching spasms. Of the 47 patients studied, all 11 who had progressed to the terminal stage died within 8-12 weeks of initial presentation. To date, the mechanism of the disease is still incompletely understood and four different mechanisms have been proposed. First, direct toxicity from heroin or its additives or impurities in the heroin have been suggested but no specific causative toxin has been identified<sup>(2,4,10)</sup>. Second, pathological study shows abnormal findings of mitochondria and magnetic resonance spectroscopy shows elevation of lactate. These results suggest mitochondrial dysfunction as a mechanism of the disease<sup>(11,13,14)</sup>. Third, profound hypoxia has been suggested as some patients had an interval between the initial coma and the first symptom of encephalopathy. However, delayed post hypoxic encephalopathy usually involves basal ganglion which is not caused by heroin<sup>(4,15)</sup>. This has been confirmed by previous radiologic and pathological reports<sup>(4)</sup>. Finally, genetic predispositions, such as cytochrome P4502D6 gene polymorphism, may increase susceptibility to this disease<sup>(16)</sup>.

Typical MRI findings are usually characterized by bilateral symmetrical hyper-intensity on T2 weighted images and FLAIR of cerebral white matter<sup>(3,12,15,17-19)</sup> with restricted diffusion on DWI<sup>(3,5)</sup>, consistent with the underlying pathological finding which was of severe myelin destruction and diffuse vacuolar formation (spongiform degeneration) of the white matter<sup>(2,12)</sup>. To the authors' knowledge, only eight cases caused by intravenous use of heroin have been reported previously (Table 1).

All nine cases, including the authors', were males with an age-range of 30-46 years (mean 38.5). Seven of the cases (78%) had latency periods between ingestion and onset of around 3 weeks<sup>(3-6,9)</sup>. Akinetic mutism and spastic quadriplegia were found in 5/5 (100%) and 6/8 (75%) respectively. Interestingly, only one of the nine cases died (11%) in contrast with Wolters' report of 100% mortality<sup>(2)</sup>. This improvement in outcome is probably due to early diagnosis and improved supportive care which is the basic standard treatment for this disease. Whether antioxidant use, as was employed in the present case, is actually beneficial is still unknown. A study that evaluated the therapeutic effects of glucocorticoid on heroin-induced spongiform



**Fig. 3** (A) EEG at 3-month follow-up shows diffuse slow background activity, severe diffuse encephalopathy. (B) EEG at 6-month follow-up shows mild diffuse encephalopathy.



**Table 1.** Characteristics of previously reported cases

Country	Italy <sup>(4)</sup>	Taiwan <sup>(5)</sup>	Australia <sup>(6)</sup>	Australia <sup>(7)</sup>	Hong Kong <sup>(8)</sup>	Taiwan <sup>(9)</sup>	Germany <sup>(3)</sup>	Italy <sup>(10)</sup>	Thailand (our case)
Year	1997	2000	2001	2001	2004	2009	2010	2010	2010
Gender	Male	Male	Male	Male	Male	Male	Male	Male	Male
Age	30	46	45	39	41	42	31	32	41
Followed by episode of unconsciousness	✓	✓	✓	x	x	✓	✓	✓	✓
Akinetic mutism	N/A	✓	✓	N/A	✓	✓	N/A	N/A	✓
Spastic quadriplegia	✓	✓	x	N/A	✓	✓	✓	x	✓
Pathological confirmation	✓	x	x	✓	x	x	x	x	x
Treatment	None	Conservative	Conservative	Conservative	Haloperidol, Benzodiazepine	Conservative	N/A	Conservative	Antioxidant
Duration of follow-up	20 days	6 months	9 months	N/A	No	6 months	N/A	2 years	6 months
Result	Died	Complete recovery	Improve	Not improve	N/A	Improve	N/A	Improve	Improve

N/A = not available

leukoencephalopathy showed no obvious therapeutic effects<sup>(20)</sup>.

**Conclusion**

Spongiform leukoencephalopathy should be suspected in middle-age males who have a history of heroin abuse, whether intravenously or through inhalation, who present with a progressive decline in cognitive functioning, or who have an unconscious episode concomitant with akinetic mutism or quadriplegia. The prognosis is good if there is early diagnosis by MRI and best supportive care practices are utilized.

**What is already known on this topic?**

Heroin can cause many neurologic complications such as acute delirium, delayed post anoxic encephalopathy and coma. Heroin-associated spongiform leukoencephalopathy is a rare neurologic complication of heroin but has been described since 1982 after inhaling heated heroin vapors or chasing the dragon. This complication is uncommonly caused by injecting heroin intravenously. There were only eight cases caused by intravenous use of heroin previously reported.

**What this study adds?**

This study adds the information of characteristics of intravenous heroin-associated delayed spongiform leukoencephalopathy. The authors reported the ninth case of this disease caused by intravenous route of heroin and summarized the previously reported cases to give the characteristics of this identity.

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**Potential conflicts of interest**

None.

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ภาวะ *spongiform leukoencephalopathy* แบบล่าช้าที่สัมพันธ์กับการใช้เฮโรอีนทางหลอดเลือดดำ: รายงานผู้ป่วย และบททบทวนบทความ

ภัทริน ภิรมย์พานิช, ศิวาพร จันทร์กระจ่าง

ภาวะ *spongiform leukoencephalopathy* ที่สัมพันธ์กับการใช้เฮโรอีนพบได้น้อยมากและอาจถึงแก่ชีวิตได้ โดยส่วนใหญ่มักมีสาเหตุจากการใช้เฮโรอีนชนิดสูดดมควัน ผู้นิพนธ์รายงานผู้ป่วยชาย อายุ 41 ปี ซึ่งได้รับการวินิจฉัยภาวะ *spongiform leukoencephalopathy* แบบล่าช้า 3 สัปดาห์ หลังการฉีดเฮโรอีนเข้าหลอดเลือดดำ โดยผู้ป่วยได้เข้ารับการรักษาตัวในโรงพยาบาลอื่นเนื่องจากภาวะเฮโรอีนเกินขนาดเฉียบพลัน 4 ชั่วโมง หลังจากฉีดเฮโรอีนไม่ทราบจำนวนเข้าหลอดเลือดดำ หลังจากนั้นผู้ป่วยมีอาการดีขึ้นเรื่อยๆ จนกระทั่งกลับบ้านได้ในวันที่ 12 ของการรับไว้ในโรงพยาบาล 3 สัปดาห์ หลังจากวันที่รับไว้ในโรงพยาบาล ผู้ป่วยมีภาวะการตระหนักรู้ลดลง ไม่พูด ไม่ขยับตัว รยางค์ทั้งสี่มีภาวะแข็งเกร็ง และการตอบสนองของเอ็นกล้ามเนื้อมีความไวมากขึ้น การตรวจคลื่นไฟฟ้าสมอง และการตรวจทางรังสี มีลักษณะตามแบบฉบับของภาวะ *spongiform leukoencephalopathy* การตรวจติดตามที่ 3 และ 6 เดือนต่อมา พบว่าผู้ป่วยมีอาการดีขึ้น ซึ่งได้รับการสนับสนุนจากการตรวจคลื่นไฟฟ้าสมอง และการตรวจทางรังสี ในบทวิจารณ์ได้สรุปรายงานผู้ป่วยภาวะ *spongiform leukoencephalopathy* ที่สัมพันธ์กับการใช้เฮโรอีนทางหลอดเลือดดำที่เคยรายงานทั้งหมด 8 ราย เปรียบเทียบกับรายงานผู้ป่วยรายนี้

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