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Case Report

Cocaine-induced multifocal leukoencephalopathy: A case report and literature review ☆

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ABSTRACT

Cocaine use is associated various complications such as hemorrhagic and ischemic stroke. Another rarely reported complication is cocaine-induced multiple leukoencephalopathy. We report the case of an 18-year-old woman, without any medical history who presented with cocaine-induced multifocal leukoencephalopathy. The patient was treated with intravenous methylprednisolone and showed partial clinical improvement. Initially considered as a consequence of the drug's toxic effects, this condition has more recently been linked to levamisole, a cocaine adulterant known to cause similar cases of multiple leukoencephalopathy.

Introduction

Cocaine use is associated with multiple neurologic complications involving vascular, metabolic and toxic mechanisms, such as ischemic and hemorrhagic stroke, seizures and movement disorders [1]. One very underdiagnosed and sparse condition is cocaine-induced multifocal leukoencephalopathy, a monophasic cerebral demyelinating disease that causes extensive white matter lesions [2]. The clinical manifestations and imaging findings of this condition can be highly variable and nonspecific [2], and the prognosis ranges from complete recovery to fatal outcomes [2,3].

Recently, some reported cases of cocaine-associated leukoencephalopathy were attributed to levamisole, an adulterant identified in cocaine that is also used as an anthelminthic and immunomodulator, and is known to cause severe leukoencephalopathy [3,4].

We present the case of an 18-year-old female who developed toxic leukoencephalopathy induced by cocaine, along with a discussion of the possible involvement of levamisole.

Abbreviations: MRI, magnetic resonance imaging; FLAIR, fluid attenuation inversion recovery; CSF, cerebrospinal fluid.

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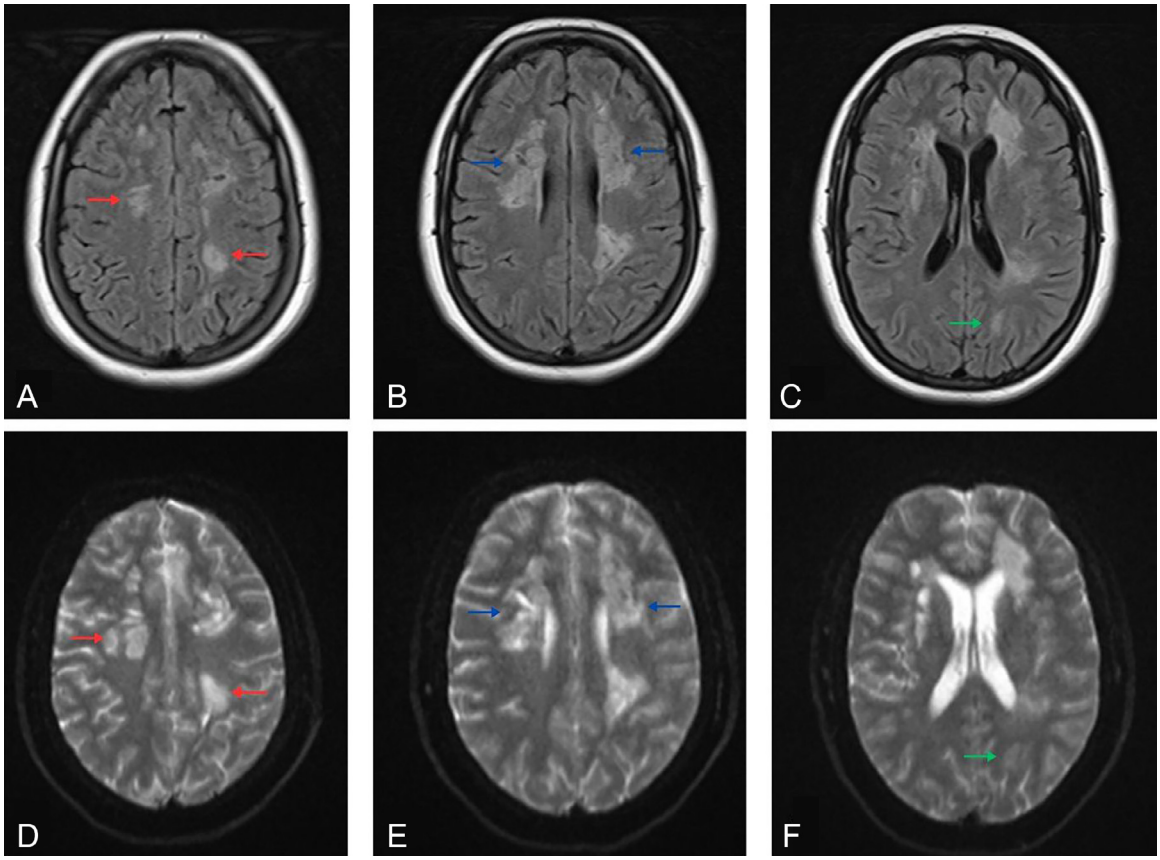

Fig. 1 – Brain magnetic resonance imaging, axial FLAIR images (A-C) and T2 weighted images (D-F) showing bilateral extensive and confluent supratentorial hyperintensities in the centrum semiovale (red arrows), periventricular white matter (blue arrows) and subcortical white matter (green arrows).

Case report

An 18-year-old female without any medical history, presented to the emergency department with mental status alteration and agitation. No hints of prior recent infection or vaccination were noted.

Upon initial examination, the patient was confused and irritable and presented left sided upper and lower limb weakness. The examination of cranial nerves was unremarkable. She was hemodynamically stable, with normal blood pressure of 110/70 mmHg, a pulse rate of 66 beats per minute, and a normal temperature of 37.3°C.

Initial laboratory tests, including a complete blood count and comprehensive metabolic panel, were performed and found to be unremarkable.

Magnetic resonance imaging (MRI) revealed extensive, confluent hyperintensities in the bilateral supratentorial regions on fluid-attenuated inversion recovery (FLAIR) and T2-weighted images, involving the periventricular white matter and the subcortical white including the U fibers (Fig. 1). There was also involvement of the frontal and parietal centrum semiovale (Fig. 1). No enhancement or restricted diffusion was observed (Fig. 2). The imaging features were consistent with multifocal leukoencephalopathy.

Cerebrospinal fluid (CSF) analysis showed normal protein levels, normal glucose, and a normal total cell count. Microbiological tests for HSV-1, HSV-2, JC Virus, and the meningoencephalitis panel, as well as CSF gram staining and culture, were negative.

Urine toxicology was positive for cocaine. Further investigations, including HIV and CMV serology, syphilis screen, vitamin B12 levels, and tests for autoimmune and vasculitis antibodies, were either normal or negative.

After eliminating all other potential causes of the patient's encephalopathy, we concluded that the symptoms were due to cocaine -induced leukoencephalopathy. The patient was treated with intra venous methylprednisolone, 1000 mg daily for 5 days, as recommended in similar case reports. After 2 months of follow up, she showed only partial recovery, with a slight improvement in vigilance, but continued to suffer from spastic left hemiparesis.

Discussion

Cocaine is known to be associated with multiple neurological complications, such as stroke, seizures, and movement

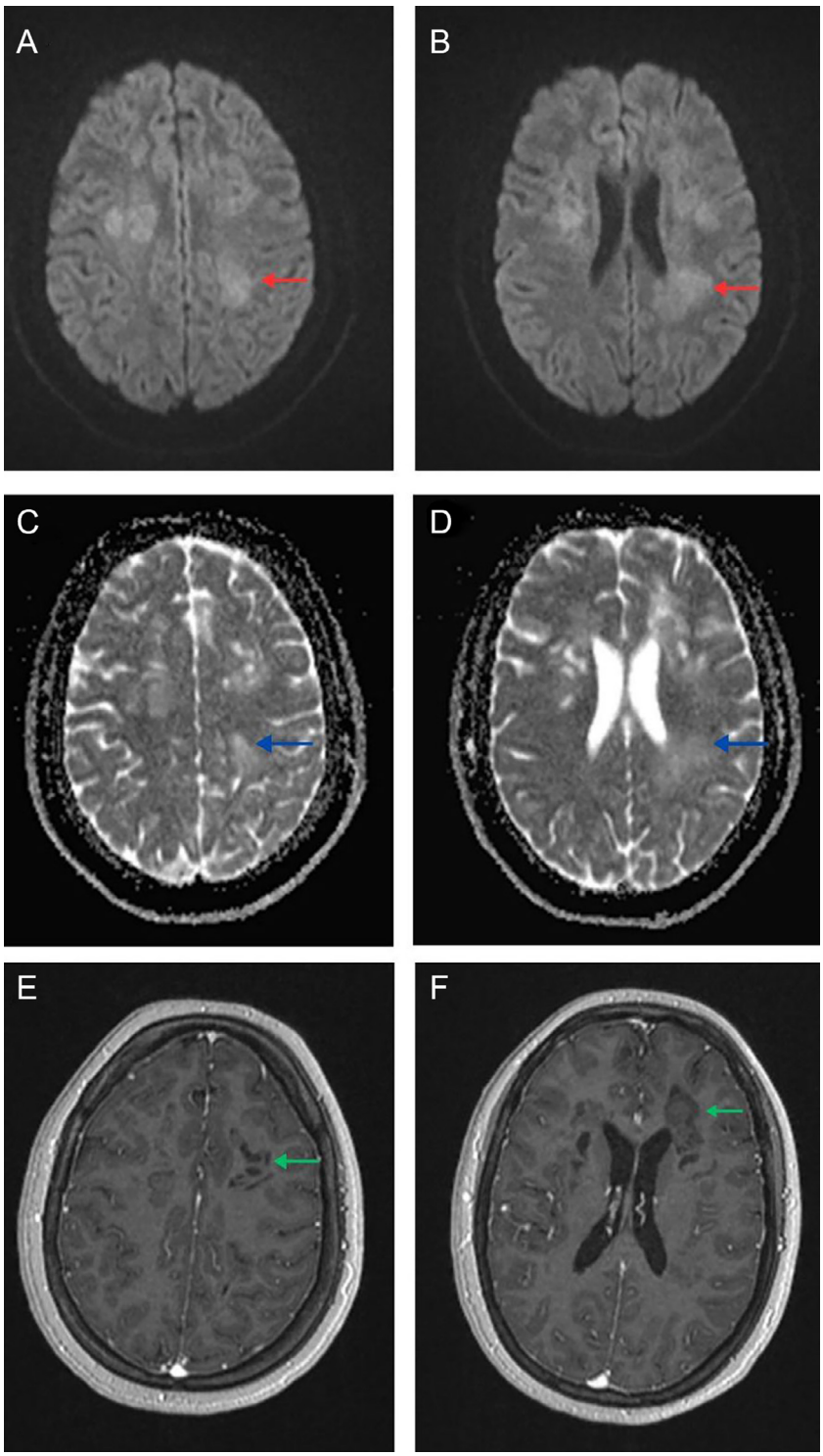

Fig. 2 – Axial diffusion-weighted images (A and B) and ADC Map (C and D) showing no diffusion restriction (red arrows) with high ADC (blue arrows). Axial postcontrast T1 weighted images (E and F) showing no enhancement of the lesions (green arrows).

disorders [5]. Cocaine-induced leukoencephalopathy is a rare condition, with only a few cases reported in the literature.

The clinical presentation of this condition is nonspecific and can be vary widely, with symptoms including behavioral changes, confusion, memory loss and inattention [6–8]. Spastic hemiparesis, ataxia [9] and mental status alteration [10] have also been reported.

Brain MRI typically shows bilateral, multiple hyperintensities on Fluid-attenuated inversion recovery (FLAIR) and T2-weighted images, often confluent, involving the

periventricular and subcortical withe matter, with or without sparing of U fibers. The posterior fossa may also be involved in some cases [8]. Affected regions may exhibit high signal intensity on diffusion-weighted images and can show variable enhancement pattern on postcontrast images, sometimes appearing patchy [10]. Balo's concentric sclerosis pattern has also been reported in some cases in the literature [11,12]. The radiological features can resemble those of heroin-induced toxic leukoencephalopathy, except that the occipital predominance and the involvement of the cerebellum and brainstem are rarely seen.

When encountering similar clinical and radiological presentations, it is important to exclude other differential diagnoses such as acute disseminated encephalomyelitis (ADEM), posterior reversible encephalopathy syndrome (PRES), and other metabolic and infectious disorders. In our case, the absence of fever and the lack a parainfectious or postvaccinal process did not support acute disseminated encephalomyelitis as a differential diagnosis.

There is no official consensus on the clinical management of cocaine-induced leukoencephalopathy. However, most case reports have utilized methylprednisolone, typically administered at doses of 1000 mg to 2000 mg daily within 3-5 days [5,8,13]. The outcome is highly variable, ranging from a fatal course [3] to complete recovery [13]. Intravenous immunoglobulin, plasma exchange, and cyclophosphamide have also been used, with variable outcomes [4,13].

In addition to the drug itself, reports in the literature raised the involvement of Levamisole in cocaine-related leukoencephalopathy [3,4,14]. In 2003, Levamisole was identified as a cocaine adulterant [15]. Originally used as an anthelminthic in human and veterinary medicine, Levamisole was later found to have immunomodulating properties. It has been used to treat colorectal cancer and inflammatory conditions such as rheumatoid arthritis, aphthous ulcers, and nephritic syndrome [15].

Levamisole has immune-modulating properties by affecting monocyte chemotaxis and enhancing macrophage functions, which may contribute to potential immune-mediated neuronal toxicity [16]. It has been recognized to cause several side effects, including multiple leukoencephalopathy [16].

Cases of levamisole-induced multifocal leukoencephalopathy present with clinical, biological and radiological findings similar to those of cocaine-induced leukoencephalopathy [16,17]. Vitt et al. confirmed the involvement of levamisole in a case of a 63 years old woman who presented with cocaine-induced multifocal leukoencephalopathy. Urine toxicology was positive for cocaine, and chromatography-tandem mass spectrometry confirmed the presence of levamisole [4]. Unfortunately, levamisole detection was not available in our case.

Conclusion

Given the high prevalence of cocaine users, recognizing multifocal leukoencephalopathy is crucial for a better clinical management of this condition. The potential involvement of levamisole opens the door to a better understanding and management of cocaine induced multifocal leukoencephalopathy.

Patient consent

Written informed consent was obtained from the patient to publish this manuscript.

REFERENCES

[1] Zimmerman JL. Cocaine intoxication. Crit Care Clin 2012;28(4):517–26.
[2] Kondziella D, Danielsen E R, Arlien-Soeborg P. Fatal encephalopathy after an isolated overdose of cocaine. J Neurol Neurosurg Psychiatry 2007;78(4):437–8.
[3] D BP, Cynthia C, Lynch Kara L. Multifocal inflammatory leukoencephalopathy associated with cocaine abuse: is levamisole responsible? Clin Toxicol 2012;50(6):534–5.
[4] Vitt JR, Chow BEG, Daniel S, et al. Confirmed case of levamisole-associated multifocal inflammatory leukoencephalopathy in a cocaine user. J Neuroimmunol 2017;305:128–30.
[5] Treadwell SD, Robinson TG. Cocaine use and stroke. Postgrad Med J 2007;83(980):389–94.
[6] Willems R, You SJ, Vollme F, et al. Toxic Leukoencephalopathy due to suspected levamisole-adulterated cocaine. Clin Neuroradiol 2024;34:503–6. doi:10.1007/s00062-023-01358-z.
[7] Ali Y, Valenzuela R, Kattah J. Sever toxic leucoencephalopathy following cocaine abuse. Neurology® 2013;80. doi:10.1212/WNL.80.7_supplement.P06.202.
[8] Tollens N, Post P, Martins Dos Santos M, et al. Multifocal leukoencephalopathy associated with intensive use of cocaine and the adulterant levamisole in a 29-year old patient. Neurol. Res. Pract. 2022;4:38. doi:10.1186/s42466-022-00202-y.
[9] Vitturi BK. Cocaine-induced multifocal leukoencephalopathy. Acta Neurol Belg 2020. doi:10.1007/s13760-020-01449-5.
[10] Eshan S, Bedross A, Chandra G, et al. Cocaine-induced toxic leukoencephalopathy: a case report. Cureus 2024;16(2):e54574. doi:10.7759/cureus.54574.
[11] Pessini LM, Kremer S, Auger C, et al. Tumefactive inflammatory leukoencephalopathy in cocaine users: report of three cases. Mult Scler Relat Disord 2020;38:101496. doi:10.1016/j.msard.2019.101496.
[12] Grasso D, Borreggine C, Castorani G, et al. Balò's concentric sclerosis in a case of cocaine-levamisole abuse. SAGE Open Med Case Rep 2020;8. doi:10.1177/2050313X20940532.
[13] Abdilla Y, Cauchi M, Vella N. Cocaine-induced toxic leucoencephalopathy with complete clinical recovery. BMJ Case Rep CP 2019;12:e229134.
[14] Vosoughi R, Schmidt BJ. Multifocal leukoencephalopathy in cocaine users: a report of two cases and review of the literature. BMC Neurol 2015;15:208.
[15] Larocque A, Hoffman RS. Levamisole in cocaine: unexpected news from an old acquaintance. Clin Toxicol 2012;50:231–41.
[16] I Xu, W Zhou, S Li, G Zhou et al. Clinical and MRI characteristics of levamisole-induced leukoencephalopathy in 16 Patients. J Neuroimaging, 19(4), 326–331
[17] Yan R, Wu Q, Ren J, et al. Clinical features and magnetic resonance image analysis of 15 cases of demyelinating leukoencephalopathy induced by levamisole. Exp Ther Med 2013;6(1):71–4.