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Short communication

Ischemic stroke associated with the use of a synthetic cannabinoid (spice)

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ABSTRACT

Synthetic cannabinoids, i.e. "spice", are psychoactive drugs with increasing use worldwide. Spice may have harmful neuropsychiatric and physical side effects.

Here, we present the case of a 25-year-old man with ischemic stroke after smoking spice on the previous evening. Diagnostic work-up was negative for other common causes of stroke. Toxicology screen unveiled the cannabimimetic ADB-FUBINACA in the drug sample and in patient's urine. The cardiac sympathomimetic effect of spice might have triggered an unnoticed episode of tachyarrhythmia and resulted in stroke via cardioembolic etiology.

Thus, in absence of other risk factors, a careful patient history of spice use is recommended for patients with acute neurological deficits.

1. Introduction

Synthetic cannabinoids, also known as "spice", are psychoactive drugs, and their use is increasing worldwide (Muller et al., 2015). Spice causes psychotropic effects, i.e., alterations in mood, sleep, or perception that are usually stronger than those that result from inhaling marijuana. Spice is also associated with higher rates of toxicity and hospital admissions than natural marijuana (Mills et al., 2015). Synthetic cannabinoids include several hundred agonists, each displaying varying affinities for the cannabinoid (CB)-type receptors CB1 and CB2 (Mills et al., 2015). Synthetic cannabinoids have higher affinity and potency than THC for the CB1 receptor (Mills et al., 2015). Additional ingredients, e.g. tocopherol (vitamin E), are included to hinder the detection and analysis of the contents (Muller et al., 2015). The mode of action of the psychoactive drug can result in neuropsychiatric side effects, e.g., anxiety attacks, agitation, paranoia and delusions (Muller et al., 2010a,b, 2015). The sympathomimetic effect of synthetic cannabinoids and additive substances like clenbuterol can also result in harmful cardial side effects, e.g., palpitations, tachycardia, or myocardial infarction (Bhanushali et al., 2013; Gunderson et al., 2012; Hermanns-Clausen et al., 2013; Kazory and Aiyer, 2013; Lank et al., 2013; Mir et al., 2011; Weaver et al., 2015). There are only few reports of ischemic stroke after spice use (Freeman et al., 2013; Takematsu et al., 2014).

Here, we present the case of a 25-year-old man who manifested stroke symptoms the next morning after smoking spice the evening before and describe the extended analysis of the substance.

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2. Case description

A 25-year-old patient presented with left severe hemiparesis (no movement of the limbs against gravity) and left hypaesthesia, moderate dysarthria, and visual neglect. The exact onset of symptoms was unknown because he woke up symptomatic. He had smoked three grams of a product called "Freeze" that was later analysed to contain synthetic cannabinoids the previous evening. The patient denied having taken any drugs other than spice during the previous months. Since the age of 13, he had been drinking alcohol (mild irregular consumption up to 2 times/week) and smoking cigarettes (10/d; 10 pack years). Additionally, since the age of 17, he had been taking spice. Until he was 23 years old, he had also been irregularly using cannabis, amphetamines, cocaine, heroin, opioids, and lorazepam.

Initial magnetic resonance imaging (MRI) showed acute ischemic infarction in the region of the basal parts of the right middle cerebral artery, with a demarcation in T2w and fluid-attenuated inversion recovery (FLAIR) sequences (Fig. 1). A magnetic resonance angiography (Fig. 1) and ultrasound examination revealed an occlusion of the proximal right middle cerebral artery. Follow-up cerebral CT scans showed a right cerebral brain oedema and haemorrhagic transformation of the lentiform nucleus but no signs of herniation.

The patient received standardized stroke unit management, including intensive respiratory and cardiac care, fluid and metabolic management, and blood pressure control.

The extensive diagnostic work-up, including thrombophilia and vasculitis screening, transoesophageal echocardiography, and an analysis of his spinal fluid was negative for other common causes of stroke. During the course of his hospital stay, his neurologic symptoms improved. However, after nine days, the patient was discharged to a rehabilitative centre with neurologic sequelae of moderately severe right arm paresis, slight paresis of the right leg with hypaesthesia, and dysarthria.

3. Detection of spice

The patient was able to provide a package of a product that later was shown to contain synthetic cannabinoids. He had inhaled the spice from this package the evening before the onset of stroke. It was labelled "Freeze" (Supplemental Figures), the brand he liked to use regularly. Analysis of the drug sample by gas chromatography showed that it was positive for the cannabimimetic ADB-FUBINACA.

The patient's urine sample was positive for the potent synthetic cannabinoids ADB-FUBINACA and MDMB-CHMICA, as detected by liquid chromatography/tandem mass spectroscopy. The urine screening was negative for the screening for benzodiazepines, amphetamines, mephedrone, morphine/opiate/heroin, barbiturates, ecstasy/3,4-methylenedioxy-methamphetamine, methylenedioxypyrovalerone, methadone, cocaine metabolites, methamphetamine, tetrahydrocannabinol, fentanyl, tricyclic antidepressants and buprenorphine. The additional serum screening showed no pathological findings for barbiturates, benzodiazepines, tricyclic antidepressants, and ethanol suggesting that the patient may have not taken other psychoactive drugs.

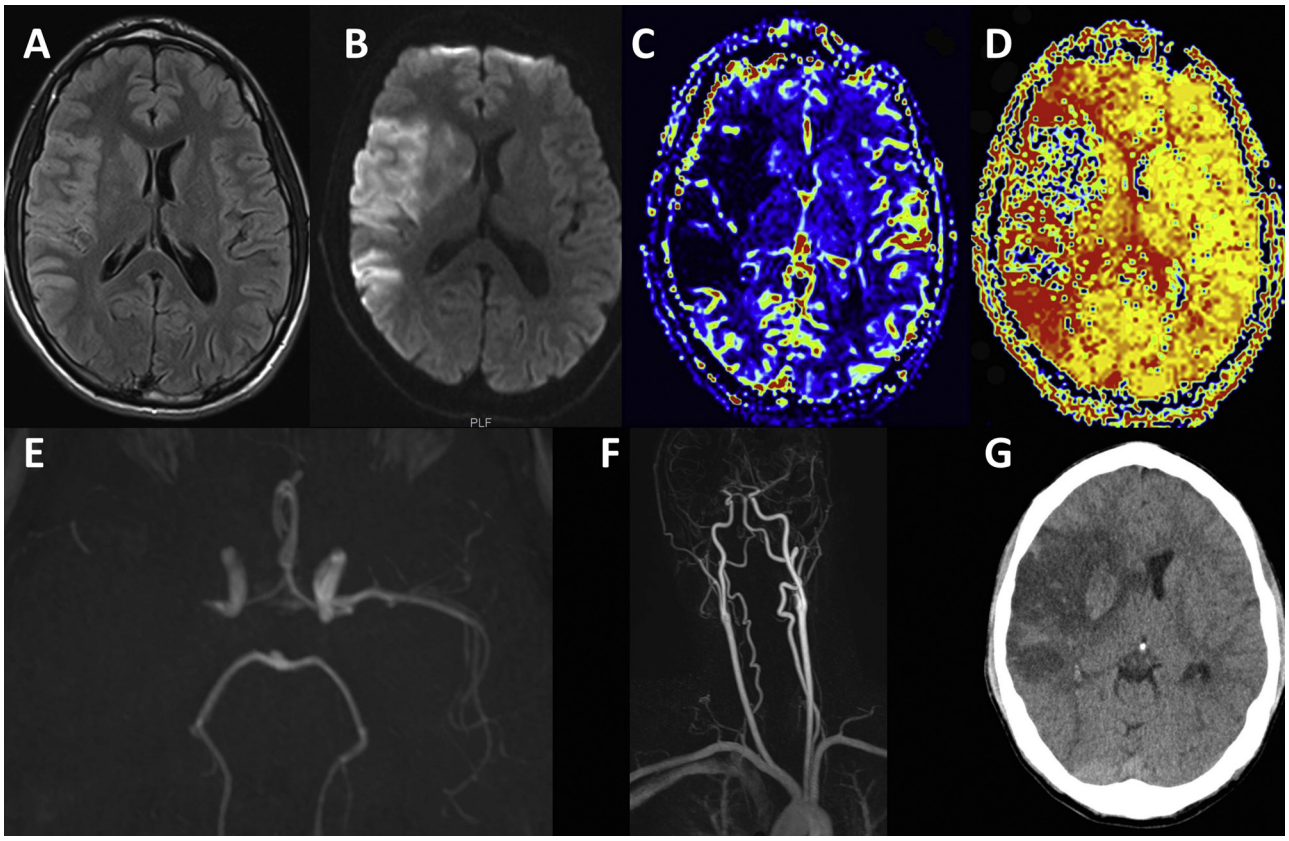

Fig. 1. Magnetic Resonance Imaging (MRI) on admission and Computed Tomography (CT) Scan 48 h after admission.
On admission FLAIR imaging (A) showed swelling with beginning stroke demarcation. Though mismatch could not be recognized (B DWI imaging, C/D contrast enhanced perfusion imaging CBV and TTP map) intra-arterial or intravenous therapy could not be initiated. Angiographic imaging (E time-of-flight, F contrast enhanced MRI angiography) confirmed occlusion of the right middle cerebral artery. In follow-up (G multi slice CT after 48 h) stroke demarcation according to the perfusion deficit and DWI lesion was obvious.
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