## **ARTICLE IN PRESS**

#### Journal of Clinical Neuroscience xxx (2015) xxx-xxx



Contents lists available at ScienceDirect

# Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn



# Case Report Synthetic cannabinoids revealing adrenoleukodystrophy

## Avi Fellner\*, Felix Benninger, Ruth Djaldetti

Department of Neurology, Rabin Medical Center, Beilinson Hospital, 39 Jabotinski Street, Petah Tikva 49100, Israel Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

## ARTICLE INFO

Article history: Received 16 July 2015 Accepted 23 July 2015 Available online xxxx

Keywords: Adrenoleukodystrophy Cannabinoids Leukodystrophies MRI Seizures

## ABSTRACT

We report a 41-year-old man who presented with a first generalized tonic-clonic seizure after recent consumption of a synthetic cannabinoid. MRI showed extensive bilateral, mainly frontal, white matter lesions. Blood analysis for very long chain fatty acids was compatible with adrenoleukodystrophy, and a missense mutation in the ABCD1 gene confirmed the diagnosis. We hypothesize that cannabinoid use might have contributed to metabolic decompensation with subacute worsening of the underlying condition.

© 2015 Elsevier Ltd. All rights reserved.

### 1. Case report

A 41-year-old man presented to the emergency department with a first generalized tonic-clonic seizure. On arrival he was confused and disoriented with disinhibited behavior and frontal release signs. Spastic quadriparesis, bilateral ankle clonus and bilateral extensor plantar response were noticed.

The patient's family reported learning difficulties from childhood and an acute depressive episode with a single suicide attempt 4 years earlier. He smoked cannabis on a regular basis and was recently consuming a synthetic cannabinoid street drug termed "Nice Guy". During the month prior to admission, behavioral changes were noted with easy irritability and aggressive outbursts as well as bizarre incoherent behavior, including shaving half of his face and talking to himself.

Toxic screen on admission was positive for benzodiazepines and tetrahydrocannabinol. Blood tests were unremarkable, except for an elevated creatine kinase [1,928 units/l (normal range: 20–200 units/l)]. MRI following head CT scan showed hyperintense symmetric bilateral, mainly frontal, lesions, with symmetric linear restricted diffusion and gadolinium enhancement in part of the lesion (Fig. 1).

Human immunodeficiency virus testing was negative. Cerebrospinal fluid (CSF) analysis showed four white cells, elevated protein level of 74 mg/dl (normal range: 15–45 mg/dl), and glucose of 76 mg/dl (normal range: 40–70 mg/dl), and was negative for venereal disease research laboratory test, treponema pallidum

\* Corresponding author. Tel.: +972 54 541 1771; fax: +972 3 937 6355. *E-mail address:* avi.fellner@gmail.com (A. Fellner).

http://dx.doi.org/10.1016/j.jocn.2015.07.020 0967-5868/© 2015 Elsevier Ltd. All rights reserved. hemagglutination test, cryptococcal antigen, polymerase chain reaction for John Cunningham virus and toxoplasma. CSF showed two monoclonal bands which were stronger in the CSF than in the serum. Free light chain analysis in the serum demonstrated normal kappa to lambda ratio. Total body positron emission tomography-CT scan was normal. Electroencephalogram showed bilateral frontal slowing in the theta range.

The patient was treated with antiepileptic medication without recurrent seizures. Motor weakness resolved spontaneously. He was left with bilateral extensor plantar response, frontal disinhibition and incoherent behavior.

Blood analysis for very long chain fatty acids levels demonstrated increased C24:22 ratio of 1.663 and increased C26:22 ratio of 0.092, compatible with the diagnosis of adrenoleukodystrophy (ALD). A missense mutation in the ABCD1 gene confirmed the diagnosis.

#### 2. Discussion

We present a case of leukodystrophy in a patient who came to medical attention after a first epileptic seizure following synthetic cannabinoid consumption. Synthetic cannabinoids abuse is associated with seizures [1] and leukodystrophy diagnosis in this case could be incidental. Nevertheless, we hypothesize that cannabinoids use might have contributed to metabolic decompensation with subacute worsening of the underlying condition. Lesions in cerebral ALD involve the parieto-occipital lobes or, as in this case, the frontal lobes [2]. The demyelinating lesions of ALD are initially not of active inflammatory origin, with absence of gadolinium

Please cite this article in press as: Fellner A et al. Synthetic cannabinoids revealing adrenoleukodystrophy. J Clin Neurosci (2015), http://dx.doi.org/ 10.1016/j.jocn.2015.07.020

## **ARTICLE IN PRESS**



**Fig. 1.** Axial brain CT scan showing bilateral hypodense confluent lesion involving periventricular frontal areas (A) and the corpus callosum, with mild peripheral contrast enhancement (B). Axial MRI showing hyperintense bilateral symmetric lesion on T2-weighted imaging (C), with symmetric linear restricted diffusion (not shown) and gadolinium enhancement in part of the lesion on T1-weighted imaging (not shown) and on fluid attenuated inversion recovery sequence (D).

enhancement. Patients often have no neurologic deficits, except mild progressive cognitive impairment, until the disease turns to an active inflammatory state with gadolinium enhancement of the lesions followed by rapid clinical deterioration [2]. Gadolinium enhancement of the lesions in our patient may represent progression from indolent ALD to clinically overt disease possibly triggered by synthetic cannabinoid abuse.

## **Conflicts of Interest/Disclosures**

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

### References

- Harris CR, Brown A. Synthetic cannabinoid intoxication: a case series and review. J Emerg Med 2013;44:360–6.
- [2] Kemp S, Berger J, Aubourg P. X-linked Adrenoleukodystrophy: clinical, metabolic, genetic and pathophysiological aspects. Biochim Biophys Acta 2012;1822:1465–74.