Int J Clin Exp Med 2019;12(2):2068-2071
www.ijcem.com /ISSN:1940-5901/IJCEM0085860

Case Report

Drug abuse and epileptic seizure in a patient with hippocampus gangliocytoma: a case report

Yanyan Zhang, Ping Liu

Department of Neurology, The First Affiliated Hospital, School of Medical, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, China

Received September 22, 2018; Accepted November 8, 2018; Epub February 15, 2019; Published February 28, 2019

Abstract: The relationship between drug abuse and regional lesions in the brain is rarely discussed and the specific association between drug abuse and hippocampal tumors has yet to be investigated. We report here an unusual case of a 27-year-male drug addict with a hippocampal tumor and the primary symptom of epilepsy. The patient underwent surgical treatments, and the pathological findings confirmed a gangliocytoma (World Health Organization [WHO] I) that was associated with focal cortical dysplasia (FCD type IIIB). Postoperative recovery was good and during the follow-up period, which exceeded 1 year, the patient's seizures were controlled and he did not take any more drugs. The present study indicates that the drug abuse of this patient may have been associated with his hippocampal gangliocytoma.

Keywords: Drug abuse, epilepsy, gangliocytoma, focal cortical dysplasia, surgery

Introduction

Drug abuse is a serious social health problem worldwide and the increasing number of novel drugs has created new challenges for the prevention and treatment. A variety of factors play key roles in drug abuse including social, family, genetic, and psychological variables [1]. The classic reward circuitry, mainly including the nucleus accumbens, ventral tegmental area, and prefrontal cortex, is the main underlying neuroanatomic structure for drug addiction. However, more and more evidence suggests that hippocampal plasticity as well as hippocampus-dependent learning and memory also play the important roles in the development and maintenance of drug abuse and addiction [2]. Methamphetamine (METH), or crystal meth, poses greater danger than other illegal drugs owing to its acute complications, long-term neurotoxicity, and drug dependency [3]. The hippocampus seems to be especially vulnerable to METH. Dopamine oxidation, oxidative stress, excitotoxicity, neuroinflammation, and increased blood-brain barrier (BBB) permeability have been proven as mechanisms for neuronal dysfunction in the hippocampus [4, 5].

On the other hand, it has been known that temporo-mesial structures (namely limbic lobe), including hippocampus, are the main locations for long-term epilepsy associated tumor (LEAT) [6]. Patients often have long histories (often two years or more) of drug-resistant epilepsy, and the tumors are generally slow growing low grade and cortically based. LEAT and focal cortical dysplasia (FCD) frequently coexist [7]. It is now grouped as FCD type IIIb in the updated International League Against Epilepsy (ILAE) classification [8].

To the best of our knowledge, the relationship between drug abuse and hippocampal tumors has never been reported. The present study describes the case of a METH addict with a hippocampal tumor whose primary symptom was long term epilepsy.

Case report

A 27-year-old male patient presented in our neurological department due to one bout of tetany and escalation of repeated attacks of unconsciousness over the past three years. The frequency of repeated attacks occurred

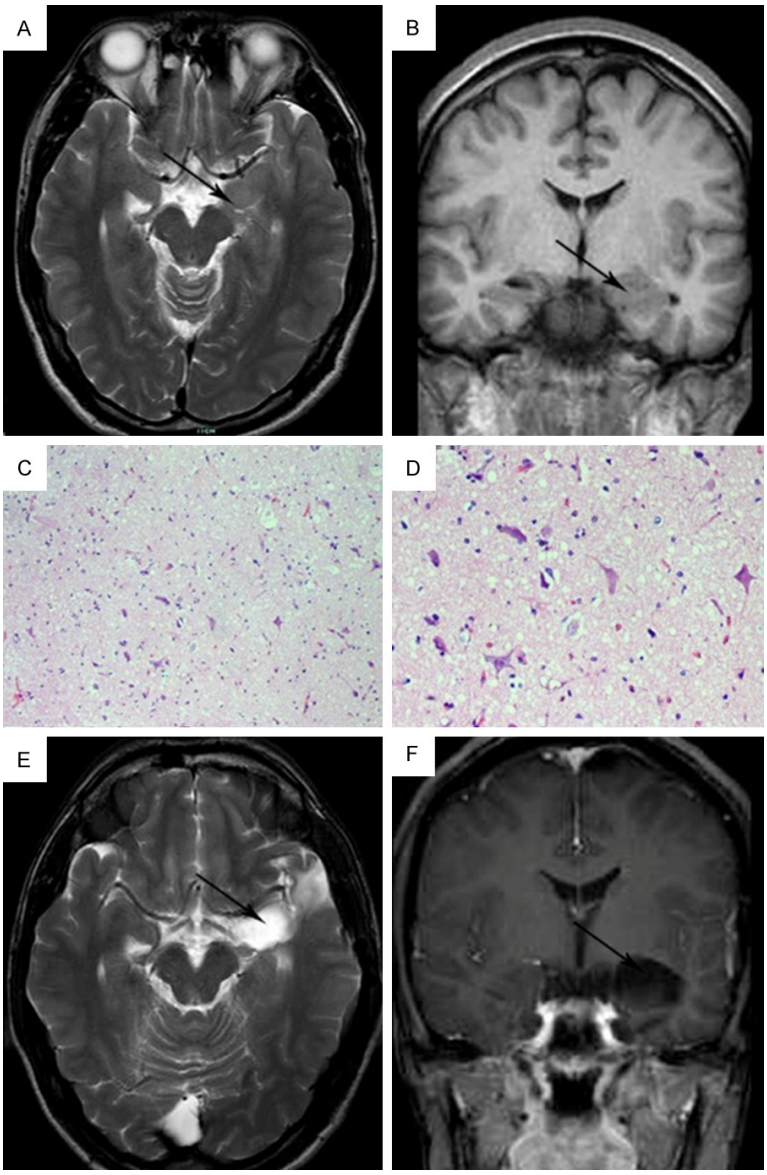

Figure 1. Clinical materials of the case. (A, B), Head MRI prior to the operation revealed swelling in the left anterior hippocampus with a homogenous signal increase on axial T2-weighted images (A: arrow) and signal decrease on coronal T1-weighted images (B: arrow). (C, D), Histopathological findings (C: 10*20, D: 10*40) showed actively proliferating ganglion cells and the presence of heterocysts. (E, F) One year after the operation, secondary MRI revealed post-operative changes in the left hippocampus with no contrast enhancement.

from once to several times per day, and lasted a few seconds per attack, and the symptoms didn't arouse the patient's attention. One month prior to his visit, his symptoms worsened, with limbs' twitching when the attack occurred. Depakin was prescribed to control his seizures, yet no obvious effect was achieved. The patient had a history of taking METH for more than four years, including episodes of drug abuse and instances of withdrawal and relapse over the last year. The patient did not complain about memory or any other cognitive impairment, and got a full score of 30 on Mini-mental State Examination (MMSE). His physical examinations were also normal. Spikes showed on the whilst scalp electroencephalography (EEG) of temporal lobe. Moreover, brain magnetic resonance imaging (MRI) scan revealed swelling in the left anterior hippocampus (**Figure 1A**, **1B**) and the enhanced head MRI scan showed that left amygdala and hippocampal region had lesions with mass effect. Therefore, low-grade gliomas were initially suspected. The further head magnetic resonance spectroscopy scan revealed slight choline increases in left hippocampus which indicated the lesion of either low-grade astrocytoma or brain glial tumor.

The patient underwent a surgery for tumor resection. Using intraoperative electrophysiological stimulation under general anesthesia, the lesion was localized to the hippocampal head and the epileptogenic foci were resected. The procedure was successfully completed and no abnormal electrophysiological discharges were detected after surgery.

The histopathological examination confirmed the diagnosis of grade I gangliocytoma (World Health Organization [WHO] classification) which was correlated to FCD type IIIb (**Figure 1C**, **1D**). In the meantime, Depakin was applied for antiepileptic treatment after surgery and the patient had good compliance with no other drugs taken. The patient had MRI follow up in

one year, which showed no enhancement in the left hippocampus (**Figure 1E**, **1F**). Since then he has stopped taking Depakin. Recently we followed him up by telephone, and found that the patient is doing well without drug abuse, and there has been no seizure attack after the operation.

Discussion

Long-term epilepsy associated tumors (LEAT) are proven to be one of major cause of focal epilepsies, especially in children and young adults. The biologic behavior of LEAT is generally benign, and low-grade tumors. They are more inclined to epileptogenic than high-grade tumors. Epilepsy associated with LEAT is poorly controlled by antiepileptic drugs while it is extremely responsive to surgical treatment [6]. The mechanisms of the epileptogenesis of LEAT are complicated, with key factors including local glutamate and GABA receptors change, neuroinflammation, alterations in BBB, as well as associated cortical dysplasia [6]. The patient had a three year history of epilepsy. His EEG scans showed that the epileptic discharges were localized to the left temporal lobe, while his brain MRI scans suggested the possibility of a hippocampal tumor. Surgery confirmed the diagnosis of a left hippocampal gangliocytoma with focal cortical dysplasia (FCD Type IIIb).

Gangliocytoma is a quite rare, benign intraparenchymal neuronal tumor comprised mainly of ganglion cells. The most frequent site is the temporal lobe, and seizures are the most common symptoms [9]. FCD, a neuronal migration disorder characterized by abnormalities of the laminar structure of the cortex, is also a frequent cause of drug resistant focal epilepsy [10]. When the cortical lamination abnormalities are associated with a primary brain tumor, such as our patient, FCD type IIIb is diagnosed according to the classification of FCD by an ILAE task force [8]. Additionally, the gangliocytoma associated FCD was considered belonging to the range of LEAT with regard to his post-surgical seizure-freedom.

In addition, it was noted that the patient had a history of drug abuse over several years. Research on drug abuse and addiction has primarily focused on two neural circuits: the limbic system and the dopaminergic reward circuitry. Experimental studies have also shown that the hippocampus is part of the brain's reward circuit that underlies addiction. Martins, T and his co-workers have found that acute high dose of METH can transiently increase BBB permeability in adult mice brain. The hippocampus was shown to be the most susceptible brain region to METH, comparing to frontal cortex and striatum [5]. METH can also induce neuroinflammation, characterized by astrocytic and microglia reactivity, and neuronal dysfunction in the mice hippocampus [4].

Above all, drug abuse seems to share some common pathophysiological mechanisms with tumor associated epilepsy. Thus, the drug abuse in the case might be correlated with the development of his hippocampal tumor. Changes in neuronal function and neurotransmitters caused by hippocampal tumors may activate the mesolimbic dopamine system and lead to the abuse of drugs. Accordingly, tumor resection could deactivate the mechanism above, and further plays the roles of not merely controlling tumor-related seizures but also aiding in detoxification. The patient was followed-up for more than one year after resection with no further seizures or drug use, which supports our hypothesis that the tumor was well correlated to patient's drug abuse. However, long-term follow-up on the case is necessary.

In conclusion, this is the case of a drug addict with a hippocampal gangliocytoma associated with FCD whose primary symptom was epilepsy. This study provides novel avenues for research on the mechanisms underlying the relationship between drug abuse and hippocampal tumor.

Acknowledgements

The authors wish to thank the patient for participating in this study. This work was supported by the Zhejiang province education department scientific research projects, NO: Y201430731.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Ping Liu, Department of Neurology, The First Affiliated Hospital, School of Medical, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, China. E-mail: 1511011@zju.edu.cn

References

[1] Ajonijebu DC, Abboussi O, Russell VA, Mabandla MV, Daniels WMU. Epigenetics: a link between addiction and social environment. Cell Mol Life Sci 2017; 74: 2735-2747.

[2] Kutlu MG, Gould TJ. Effects of drugs of abuse on hippocampal plasticity and hippocampus-dependent learning and memory: contributions to development and maintenance of addiction. Learn Mem 2016; 23: 515-533.

[3] Gouzoulis-Mayfrank E, Hartel-Petri R, Hamdorf W, Havemann-Reinecke U, Muhlig S, Wodarz N. Methamphetamine-related disorders. Dtsch Arztebl Int 2017;114: 455-461.

[4] Goncalves J, Baptista S, Martins T, Milhazes N, Borges F, Ribeiro CF, Malva JO, Silva AP. Methamphetamine-induced neuroinflammation and neuronal dysfunction in the mice hippocampus: preventive effect of indomethacin. Eur J Neurosci 2010; 31: 315-326.

[5] Martins T, Baptista S, Goncalves J, Leal E, Milhazes N, Borges F, Ribeiro CF, Quintela O, Lendoiro E, Lopez-Rivadulla M, Ambrosio AF, Silva AP. Methamphetamine transiently increases the blood-brain barrier permeability in the hippocampus: role of tight junction proteins and matrix metalloproteinase-9. Brain Res 2011; 1411: 28-40.

[6] Giulioni M, Marucci G, Martinoni M, Marliani AF, Toni F, Bartiromo F, Volpi L, Riguzzi P, Bisulli F, Naldi I, Michelucci R, Baruzzi A, Tinuper P, Rubboli G. Epilepsy associated tumors: review article. World J Clin Cases 2014; 2: 623-641.

[7] Thom M, Blumcke I, Aronica E. Long-term epilepsy-associated tumors. Brain Pathol 2012; 22: 350-379.

[8] Blumcke I, Thom M, Aronica E, Armstrong DD, Vinters HV, Palmini A, Jacques TS, Avanzini G, Barkovich AJ, Battaglia G, Becker A, Cepeda C, Cendes F, Colombo N, Crino P, Cross JH, Delalande O, Dubeau F, Duncan J, Guerrini R, Kahane P, Mathern G, Najm I, Ozkara C, Raybaud C, Represa A, Roper SN, Salamon N, Schulze-Bonhage A, Tassi L, Vezzani A, Spreafico R. The clinicopathologic spectrum of focal cortical dysplasias: a consensus classification proposed by an ad hoc task force of the ILAE diagnostic methods commission. Epilepsia 2011; 52: 158-174.

[9] Tureyen K, Senol N, Sav A. Gangliocytoma associated with focal cortical dysplasia in a young-adult: a case report. Turk Neurosurg 2008; 18: 259-263.

[10] Palmini A, Najm I, Avanzini G, Babb T, Guerrini R, Foldvary-Schaefer N, Jackson G, Luders HO, Prayson R, Spreafico R and Vinters HV. Terminology and classification of the cortical dysplasias. Neurology 2004; 62: S2-S8.