Received: 28 December 2021 | Revised: 29 January 2022 | Accepted: 6 February 2022

DOI: 10.1002/ccr3.5460

CASE REPORT

Clinical Case Reports Open Access WILEY

Epilepsia partialis continua associated with ketotic hyperglycemia and tuberculous meningoencephalitis: A case report

Cordule Balola[1] | **Fabrice Nzabara**[2] | **Christian Tshongo Muhindo**[3,4] | **Cirhuza Cikomola**[3,4,5] | **Ghislain Balemba Maheshe**[2,4] | **Marius Baguma**[1,4,5]

[1]Neurology Ward, Department of Internal Medicine, Hôpital Provincial Général de Référence de Bukavu (HPGRB), Bukavu, Democratic Republic of the Congo

[2]Radiology Ward, Department of Internal Medicine, Hôpital Provincial Général de Référence de Bukavu (HPGRB), Bukavu, Democratic Republic of the Congo

[3]Diabetology and Endocrinology Ward, Department of Internal Medicine, Hôpital Provincial Général de Référence de Bukavu (HPGRB), Bukavu, Democratic Republic of the Congo

[4]Faculty of Medicine, Université Catholique de Bukavu (UCB), Bukavu, Democratic Republic of the Congo

[5]Center for Tropical Diseases and Global Health (CTDGH), Université Catholique de Bukavu (UCB), Bukavu, Democratic Republic of the Congo

Correspondence
Marius Baguma, Neurology Ward, Department of Internal Medicine, Hôpital Provincial Général de Référence de Bukavu (HPGRB), Avenue Michombero 2, 285 Bukavu, Democratic Republic of the Congo.
Email: baguma.akonkwa@ucbukavu.ac.cd

Funding information
None.

Abstract

We report the case of an 18-year-old girl who presented with several episodes of simple partial motor seizures compatible with the diagnosis of epilepsia partialis continua. In addition to ketotic hyperglycemia, tuberculous meningoencephalitis was diagnosed based on clinical, biological, and brain imaging findings. The seizures ceased after normalization of glycemia.

KEYWORDS

case report, cortical laminar necrosis, epilepsia partialis continua, hyperglycemia, ketosis, tuberculosis

1 | BACKGROUND

Epilepsia partialis continua (EPC) is a rare seizure disorder characterized by continuously repeated fragments of epileptic seizures lasting more than 1 h, with preserved consciousness.[1] It is a rare form of focal status epilepticus.[2] Its prevalence is estimated to be less than one per one million population.[3] Although no etiology has been identified in about a quarter of patients with EPC, this disorder is often an indicator of a serious underlying pathology, including central nervous system (CNS) inflammation or infections, cerebrovascular diseases, neoplasms, or metabolic disorders.[2] Non-ketotic hyperglycemia is among the most frequent metabolic causes of EPC in adulthood.[1,3] EPC is very uncommon in hyperglycemia-associated ketosis. To our knowledge, EPC has been reported in only two cases of ketotic hyperglycemia.[4,5]

Here, we report the case of an 18-year-old girl with type 1 diabetes who developed simple partial motor status epilepticus compatible with a diagnosis of EPC. Investigations

showed hyperglycemia associated with ketosis, along with clinical, biological, and radiological signs compatible with a diagnosis of tuberculous meningoencephalitis. EPC episodes resisted anticonvulsant drugs but regressed after the initiation of anti-tuberculosis treatment and disappeared after lowering blood glucose levels.

2 | CASE PRESENTATION

An 18-year-old female patient with a medical history of severe protein-calorie malnutrition during childhood, and poorly controlled type 1 diabetes mellitus treated with insulin therapy for 2 years, was admitted to the emergency ward of the Hôpital Provincial Général de Référence de Bukavu (HPGRB), a tertiary hospital located in Bukavu, in the eastern Democratic Republic of the Congo (DRC). The patient complained of a sudden onset of simple partial motor seizures, restricted to the left side of the face, with repetitive regular clonic jerks of the lips and cheek associated with eyes and head deviation, lasting approximately 1–3 min and occurring every 5–15 min. There was no loss of consciousness. These movements were preceded by hypersialorrhea as the only prodromal symptom. No triggering factors were identified. The patient reported involuntary weight loss over a few months, as well as persistent fever and recurrent headaches for approximately 4 weeks. One week before the onset of seizures, they had taken 1 g of acetaminophen two to three times daily and an antimalarial drug (a combination of 80 mg of artemether and 480 mg of lumefantrine) as one tablet twice daily for 3 days, without cessation of symptoms. The neurological examination results were normal between the attacks.

Our biological investigations showed high blood glucose levels (>600 mg/dl), mild hyponatremia (132 mmol/L), and a urine dipstick positive for 3+ ketones. The rest of the biological investigations, including complete blood count, C-reactive protein, and renal function, were unremarkable (see Table 1). The patient's fundus oculus was normal. A diagnosis of EPC secondary to hyperglycemia was confirmed. Insulin therapy was administered to the patient along with an antiepileptic drug (carbamazepine extended-release, 200 mg twice daily). Despite this treatment, no improvement was observed; therefore, the carbamazepine was replaced with 100 mg of phenobarbital (Gardenal®) twice a day and clonazepam (Rivotril®, 0.5 mg) once a day. However, the patient continued to present attacks. A brain CT scan performed a week later showed a spontaneously hyperdense lesion (50–60 HU) of the cortex in the right ascending frontal gyrus, which was not enhanced after contrast agent injection (Figure 1). This image was suggestive of a cortical laminar necrosis. The lumbar puncture revealed increased pressure of the cerebrospinal fluid (CSF), which was hematic. Microscopic examination showed over one thousand red blood cells per mm^3, but no pleocytosis. Biochemical analysis of the CSF showed low glucose (151 mg/dl, corresponding to a CSF/plasma ratio <0.5) and an elevated protein level (1.2 g/L). No abnormal or tumoral cells were observed on pathological examination.

According to the clinical, paraclinical, and epidemiological context, tuberculosis (TB) meningoencephalitis was suspected to be the most plausible etiology. Therefore, first-line anti-TB treatment was empirically initiated (associating rifampicin, isoniazid, pyrazinamide, and ethambutol) combined with corticosteroids (prednisolone 1 mg/kg once a day). A few days later, the frequency of seizures regressed but did not completely cease. A retrospective analysis of the frequency of seizures revealed that all of them occurred when blood glucose levels were above 300 mg/dl. Insulin therapy was therefore intensified, leading to better glycemic control (below 180 mg/dl), and a few days later, all abnormal involuntary movements disappeared while the patient was still undergoing anti-TB treatment.

The brain CT scan revealed controlled results 1 month after the initiation of anti-TB therapy. It showed persistence of the frontal cortical lesions. However, another lumbar puncture revealed clear CSF, and the pressure was normal. The biochemical and pathological analyses of the patient's CSF were unremarkable. The antiepileptic drugs were discontinued, and the patient was discharged from the hospital under continued insulin therapy and TB treatment. When they were seen for a follow-up 2 months later, they reported no recurrence of seizures despite several subsequent episodes of hyperglycemia.

3 | DISCUSSION

This case report describes a patient admitted for EPC in the context of hyperglycemia associated with ketosis. EPC is an uncommon complication of non-ketotic hyperglycemia.[1,3] Hyperglycemia is often associated with other metabolic disturbances, such as hyponatremia or hyperosmolality, which may contribute to the occurrence of seizures. Furthermore, hyperglycemia may induce an accumulation of glutamate (an excitatory amino acid neurotransmitter), and lower gamma-aminobutyric acid (GABA) levels, both of which result in a lower seizure threshold.[5] However, partial seizures in general, and EPC in particular, are very unusual in hyperglycemia associated with (acido)ketosis, as ketosis (and the related intracellular acidosis) increases the seizure threshold.[6]

The etiology of EPC in the present case report could not be confidently determined. Although hyperglycemia

TABLE 1 Summary of the patient's laboratory tests

Laboratory tests	Normal values	April 27	May 16	May 30	July 26
Complete blood count					
White blood cells ($\times 10^3/\mu l$)	4.00–10.00	5.20	6.30	–	7.8
Neutrophils ($\times 10^3/\mu l$)	1.50–7.00	2.63	3.24	–	5.87
Lymphocytes ($\times 10^3/\mu l$)	1.50–4.50	2.23	2.48	–	1.46
Monocytes ($\times 10^3/\mu l$)	0.20–1.00	0.30	0.47	–	0.46
Eosinophils ($\times 10^3/\mu l$)	0.10–0.50	0.04	0.09	–	0.01
Red blood cells ($\times 10^6/\mu l$)	4.20–5.70	4.75	4.82	–	4.91
Hemoglobin (g/L)	13.0–18.0	12.8	12.7	–	13.1
Hematocrit (%)	40.0–52.0	39.9	37.2	–	37.7
Platelets ($\times 10^3/\mu l$)	150–450	268	266	–	286
C-Reactive protein (mg/L)	<3.0	<3.0	–	–	<3.0
Erythrocyte sedimentation rate (mm/h)	<20	23	–	–	16
Electrolytes					
Sodium (mmol/L)	135–155	132	138	–	122
Potassium (mmol/L)	3.5–5.1	4.0	4.0	–	5.8
Chloride (mmol/L)	96–115	95	105	–	92
Calcium (mmol/L)	1.10–1.40	1.13	1.24	–	1.22
Magnesium (mg/dl)	1.60–2.50	1.8	2.1	–	1.7
Creatinine (mg/dl)	0.6–1.40		1.32	–	1.22
Blood urea nitrogen	8.0–23.0		26	–	22
Blood glucose (mg/dl)	60–110	>600	452	152	562
Malaria thick blood film	Negative	Negative	–	–	–
Serologies					
Human immunodeficiency virus	Negative	Negative	–	–	–
Viral hepatitis B	Negative	Negative	–	–	–
Viral hepatitis C	Negative	Negative	–	–	–
Syphilis	Negative	Negative	–	–	–
Urine Dipstick					
pH	4.5–8.0	6	–	–	–
Specific gravity	1.015–1.025	1.015	–	–	–
Glucose	Negative	3+	–	–	–
Proteins	Negative	Negative	–	–	–
Ketones	Negative	3+	–	–	–
Leucocytes	Negative	1+	–	–	–
Blood	Negative	Negative	–	–	–
Cerebrospinal fluid					
Opening pressure (cmH_2O)	15–20	28	–	16	–
Aspect	Clear	Hematic	–	Clear	
Leucocytes ($/mm^3$)	≤5	0	–	0	–
Red blood cells ($/mm^3$)	0	>1000	–	0	–
Glucose (mg/dl)	–	151	–	108	–
Ratio cerebrospinal fluid glucose/glycemia	≥0.67	0.36	–	0.71	–
Proteins (g/L)	0.15–0.45	1.2	–	0.43	–

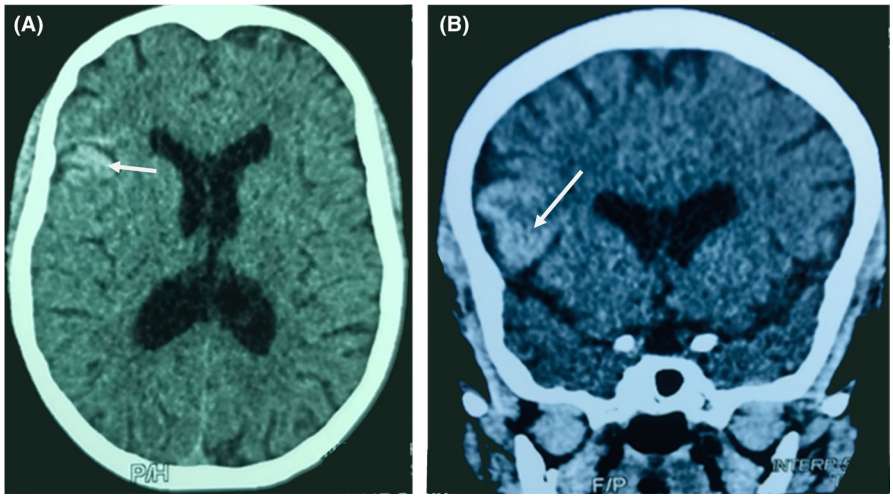

FIGURE 1 Brain CT-Scan of the patient shown in the (A) axial plane and (B) coronal plane, showing a spontaneously hyperdense lesion (50–60 HU) of the cortex in the right ascending frontal gyrus (arrows), compatible with a diagnosis of cortical laminar necrosis

appeared to be the most probable factor, it is likely that the latter was just a triggering factor in the context of a pre-existing brain (inflammatory) lesion. In fact, in most patients with hyperglycemia-related EPC, the brain imaging (usually brain MRI) results do not show significant structural lesions, and these patients' CSF analyses are unremarkable.[4] A few studies, however, have reported unusual MRI abnormalities consisting of focal cortical ribbon enhancement.[7] Furthermore, EPC, as a (partial) status epilepticus, independent of its underlying etiology, may induce cortical laminar necrosis secondary to hypermetabolic neural damage.[8] The brain CT scan lesion observed in this case report was compatible with the diagnosis of cortical laminar necrosis. However, the persistence of this lesion 2 months later, even after the seizures ceased, makes the hypothesis of seizure-related cortical changes unlikely.

Tuberculosis meningoencephalitis was another plausible etiology of the EPC in this case report. In fact, the precarious socioeconomic status of the patient constitutes a risk factor for contracting TB.[9,10] Furthermore, the clinical picture (notable weight loss, prolonged fever, and chronic headaches), as well as the hematic aspect of the CSF and elevated proteins above 1 g/L in the CSF, constituted indirect arguments for this diagnosis.[11] The persistence of the cortical laminar necrosis lesion several weeks after the initiation of anti-TB treatment does not rule out the diagnosis of TBC encephalitis, as previous studies have shown that cortical laminar necrosis lesions may persist for several months.[12]

As in most hyperglycemia-related EPC,[7] antiepileptic drugs proved ineffective in controlling seizures. It is recommended to focus on etiological treatment in the presence of EPC. The reduction in the frequency of seizures after the initiation of first-line anti-TB treatment was another argument for a tuberculous origin. However, despite the administration of both antiepileptic drugs and anti-TB treatment, the seizures persisted until the patient's glycemia was decreased to below 200 mg/dl. This is typically seen in cases of hyperglycemia-related EPC.[7,13] Therefore, it seems likely that in this case report, hyperglycemia may have been a triggering factor in the brain previously aggressed by tuberculosis.

Finally, the findings presented in this case report should be interpreted by considering its limitations. The major limitations include its retrospective design and the lack of a definitive microbiologic confirmation of tuberculosis and electrophysiologic investigations (no electroencephalography was performed due to logistic and financial reasons: no EEG machine was available at the time of the patient's hospitalization, and they could not afford the costs of a transfer to another hospital that could perform it).

4 | CONCLUSION

In conclusion, EPC is a very uncommon neurological manifestation of ketotic hyperglycemia. The present case report emphasizes the need for further etiological investigations (e.g., biological tests and neuroimaging) in patients presenting with hyperglycemia-related EPC in order to identify potential coexisting underlying causes. The normalization of glycemia, along with the initiation of an appropriate etiological treatment, is essential in the key treatment of EPC.

ACKNOWLEDGEMENT

None.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

CB, CT, CC, and MB were the clinicians in charge of the patient's care during the course of their illness. FN and GM realized and interpreted the brain CT scan images. CB and MB reviewed the medical records and drafted the first version of the manuscript. All authors have substantially reviewed the manuscript and approved the final version.

ETHICAL APPROVAL

All procedures in this study were performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments, and following national and institutional ethical standards.

CONSENT

Written informed consent was obtained from the patient for publication of this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

All data used in this case report are presented in the manuscript.

ORCID

Cordule Balola https://orcid.org/0000-0002-3927-5891
Fabrice Nzabara https://orcid.org/0000-0002-7575-7695
Christian Tshongo Muhindo https://orcid.org/0000-0002-9511-7994
Cirhuza Cikomola https://orcid.org/0000-0002-0856-5992
Ghislain Balemba Maheshe https://orcid.org/0000-0003-2227-5999
Marius Baguma https://orcid.org/0000-0002-4934-4846

REFERENCES

1. Mameniškienė R, Wolf P. Epilepsia partialis continua: a review. *Seizure*. 2017;44:74-80. doi:10.1016/j.seizure.2016.10.010
2. Mbizvo GK, Lentell IC, Leen C, et al. Epilepsia partialis continua complicated by disseminated tuberculosis and hemophagocytic lymphohistiocytosis: a case report. *J Med Case Rep*. 2019;13:191. doi:10.1186/s13256-019-2092-x
3. Racz A, Elger CE. The causes of epilepsia partialis continua. In: Trinka E, Guerrini R, Shorvon S, Schachter S, eds. *The Causes of Epilepsy: Common and Uncommon Causes in Adults and Children*, 2nd edn. Cambridge University Press; 2011:961-967. doi:10.1017/9781108355209.130
4. Van OJ, Koehn T, Duginski T. Epilepsia partialis continua secondary to diabetic ketoacidosis. *Neurology*. 2019;92:4-6.
5. Placidi F, Floris R, Bozzao A, et al. Ketotic hyperglycemia and epilepsia partialis continua. *Neurology*. 2001;57(3):534-537. doi:10.1212/WNL.57.3.534
6. Singh BM, Strobos J. Epilepsia partialis continua associated with nonketotic hyperglycemia: clinical and biochemical profile of 21 patients. *Ann Neurol*. 1980;8(2):155-160. doi:10.1002/ana.410080205
7. Tsai J-P, Sheu J-J, Hsieh KL. Unusual magnetic resonance imaging abnormality in nonketotic hyperglycemia – related epilepsia partialis continua. *Ann Indian Acad Neurol*. 2018;21(3):225-227. doi:10.4103/aian.AIAN_386_17
8. Donaire A, Carreno M, Gómez B, et al. Cortical laminar necrosis related to prolonged focal status epilepticus. *J Neurol Neurosurg Psychiatry*. 2006;77(1):104-106. doi:10.1136/jnnp.2004.058701
9. Harling G, Castro MC. A spatial analysis of social and economic determinants of tuberculosis in Brazil. *Health Place*. 2014;25:56-67. doi:10.1016/j.healthplace.2013.10.008
10. Harling G, Ehrlich R, Myer L. The social epidemiology of tuberculosis in South Africa: a multilevel analysis. *Soc Sci Med*. 2008;66(2):492-505. doi:10.1016/j.socscimed.2007.08.026
11. Marx GE, Chan ED. Tuberculous meningitis: diagnosis and treatment overview. *Tuberc Res Treat*. 2011;2011:798764. doi:10.1155/2011/798764
12. Komiyama M, Nishikawa M, Yasui T. Cortical laminar necrosis in brain infarcts: chronological changes on MRI. *Neuroradiology*. 1997;39:474-479.
13. Çokar Ö, Aydın B, Özer F. Non-ketotic hyperglycaemia presenting as epilepsia partialis continua. *Seizure*. 2004;13:264-269. doi:10.1016/S1059-1311(03)00155-9

How to cite this article: Balola C, Nzabara F, Tshongo Muhindo C, Cikomola C, Maheshe GB, Baguma M. Epilepsia partialis continua associated with ketotic hyperglycemia and tuberculous meningoencephalitis: A case report. *Clin Case Rep*. 2022;10:e05460. doi:10.1002/ccr3.5460