Unveiling epilepsia partialis continua as an early indicator of HIV encephalitis

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Abstract

A young male with no known addictions and comorbidities presenting with recurrent clonic-myoclonic movements, initially localized to the left corner of the mouth and left upper limb, evolving into epilepsia partialis continua, despite appropriate sequential antiepileptic medications, subsequently progressed to refractory status epilepticus. He was tested positive for HIV infection and his neuroimaging revealed nonenhancing lesions, a novel finding in HIV-related encephalitis. We managed him with intravenous immunoglobulin along with multiple antiepileptic medications and highly active antiretroviral therapy (ART), and he exhibited a rapid clinical recovery over 3 weeks. This case highlights the importance of initiating immunomodulatory therapy promptly at presentation and underscores the challenges of managing drug interactions between antiepileptic drugs and antiretroviral therapy (ART), emphasizing the need for careful selection of medications in HIV-infected individuals.

Key words: Epilepsia partialis continua, highly active antiretroviral therapy, HIV infection, immunoglobulins, immunomodulators, nonenhancing lesions

Introduction

Seizures in HIV often stem from various factors, including opportunistic infections such as toxoplasmosis, tuberculosis, and cryptococcosis, along with neoplastic lesions like central nervous system (CNS) lymphoma, and the development of HIV encephalopathy.[1] Hereby, we report a case of epilepsia partialis continua (EPC) in the setting of HIV with subsequent generalization leading to refractory status epilepticus necessitating unique management strategies.

Case Report

A young male in his early 20s, without any comorbidities, presented with recurrent-involuntary clonic-myoclonic movements at the left corner of his mouth and left upper limb, each episode lasting 45–50 min and at times 2–3 hours, without any impairment in consciousness. Despite administration of antiepileptic medications (phenytoin, levetiracetam, and oxcarbazepine), he remained unresponsive for 2 days. Initial evaluation revealed abnormal speech characterized by hypotonic, scanning dysarthria, bilateral lower motor neuron 7th nerve palsy (with the left side more affected than the right), and focal myoclonic jerks involving the left angle of the mouth and distal left upper limb, suggestive of EPC. Given the distinct clinical presentation, potential diagnoses including Rasmussen's encephalitis, autoimmune encephalitis, and focal cortical lesions (such as dysplasia or space-occupying lesions) involving the right motor cortex were considered. The patient's complete blood count and biochemical parameters were within the normal range. However, brain magnetic resonance imaging (MRI) revealed hyperintensity and subtle dedifferentiation of gray-white interface at the precentral gyrus, respectively, as depicted in Figure 1a and b. Cerebrospinal fluid assessments, including cytology, biochemistry, adenosine deaminase levels, and panels for autoimmune encephalitis, malignant cells, toxoplasmosis, cryptococcosis, as well as multiplex polymerase chain reaction testing for herpes simplex virus, *Cytomegalovirus*, Epstein–Barr virus, and pneumococcal, all returned negative.

The patient was managed with intravenous immunoglobulin (IVIG) and 2 g/kg over 5 days, along with antiepileptic drugs (AEDs; tablet oxcarbazepine 750 mg BD, tablet levetiracetam 1.5 g BD, and tablet perampanel 6 mg OD). The electroencephalogram revealed right frontocentral spike and wave discharges occurring periodically at a frequency of 1 Hz, with phase reversal observed at C4, as illustrated in Figure 2a and b.

Furthermore, the patient tested positive for HIV through enzyme-linked immunosorbent assay testing, with an HIV RNA load of 163,771 IU/mL and a CD4 cell count of 95 cells/cumm.

On the 5th day, the patient experienced status epilepticus, necessitating endotracheal intubation, mechanical ventilation, and intravenous midazolam infusion, in addition to the administration of five AEDs. Subsequent brain MRI scans revealed an increase in the previously observed lesions, as depicted in Figure 1c-f. Based on the clinical and radiological findings, the patient underwent additional treatment with IVIG at a dosage of 1 g/kg over a period of 4 days, alongside tablet perampanel 6 mg once daily, tablet lacosamide 200 mg, tablet levetiracetam 1 g, and tablet oxcarbazepine 750 mg twice daily. Additionally, after a week, the patient was started on tablet tenofovir

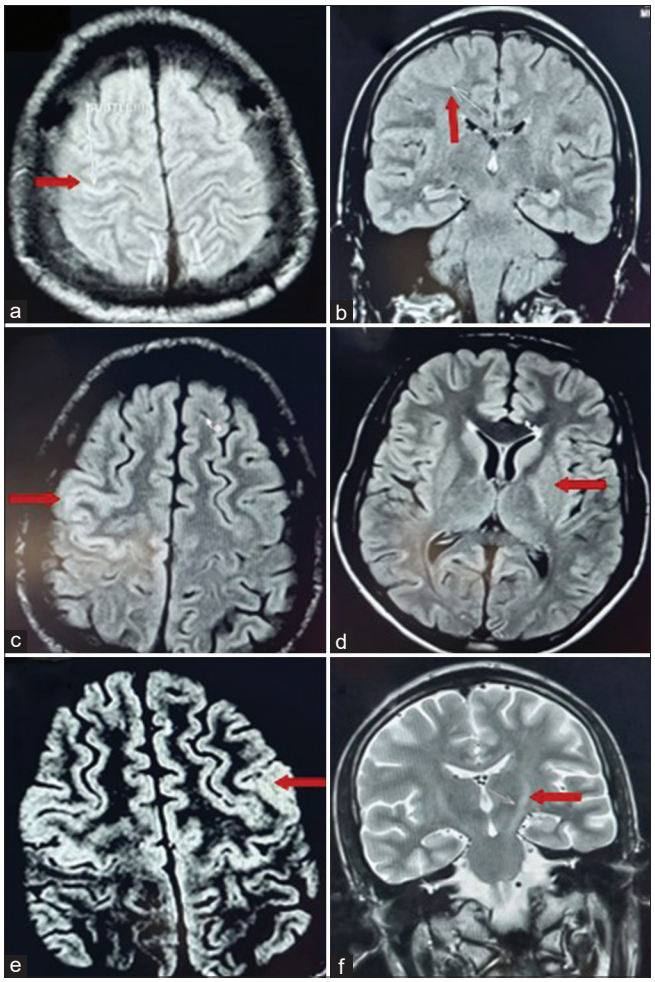

Figure 1: Magnetic resonance imaging brain: (a and b) Arrows highlight the hyperintensity and subtle dedifferentiation of the gray-white interface at the precentral gyrus in axial and coronal views, respectively. (c and d) Arrows point to hyperintensities in the entire right motor cortex and the left globus pallidus on axial sequences. (e) Arrow indicates the hyperintensity in the left motor cortex on an axial sequence. (f) Arrow emphasizes the hyperintense signal involving the left corticospinal tract on the coronal T2 sequence

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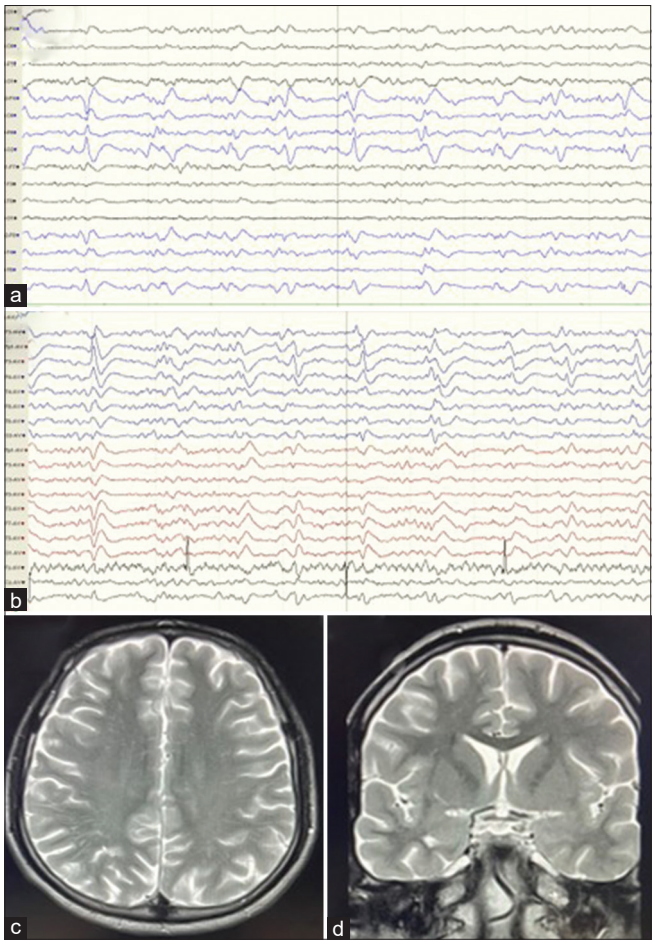

Figure 2: (a) Longitudinal montage shows right frontocentral spike and wave discharges, occurring periodically at frequency of 1 Hz with phase reversal at C4. (b) Average montage shows epileptiform discharges with maximum amplitude at C4. (c and d) Axial and coronal T2 sequences show significant resolution of lesions

300 mg, tablet lamivudine 300 mg, and tablet efavirenz 600 mg once daily, as well as tablet co-trimoxazole DS once daily.

Over the subsequent week, the seizures ceased, and gradual clinical improvement was observed. A follow-up brain MRI conducted 6 weeks later demonstrated complete resolution of the previously identified lesions, as illustrated in Figure 2c and d.

Discussion

EPC is defined as a variant of simple focal motor status epilepticus, characterized by stereotyped, arrhythmic repetitive muscle jerks affecting single muscles, muscle groups, an entire limb, or larger parts of the unilateral body, persisting over prolonged periods of time;[2] this is a rare presentation of HIV. It is well known that HIV enters the CNS by migrating through infected monocytes and macrophages, which then initiate a series of neuroinflammatory responses leading to HIV encephalitis (HIVE). With the increasing number of chronic HIV patients on highly active antiretroviral therapy (HAART), the occurrence of CNS involvement from neoplasms and opportunistic infections has declined, yet the rate of HIV-associated cognitive and neurological impairments is rising despite HAART treatment, largely attributed due to HIVE.[3] Sinha *et al*. and Sempere *et al*. noted that seizures were the initial presentation in 4% and 8.2% of HIV patients, respectively. Furthermore, they found that opportunistic infections were responsible for seizures in 93.9% of patients.[1,4] The present case displays several notable features; given the patient's low CD4 count and high viral load, the differential diagnosis also included CNS tuberculosis, toxoplasmosis, cryptococcal infection, CNS lymphoma, and Rasmussen's encephalitis, which were subsequently ruled out. Initially, it presented as EPC with subsequent generalization. This progression led to deterioration in the sensorium, culminating in refractory status epilepticus. In contrast, Bartolomei *et al*. reported a case involving isolated focal myoclonic jerks affecting the left upper limb, with rare secondary generalization. Treatment for this case included prednisolone, carbamazepine, and antiretroviral therapy (ART), resulting in a gradual, prolonged recovery over a 6-month period, ultimately leading to radiological resolution.[5] We administered IVIGs along with antiepileptics and antiretrovirals, resulting in a smooth clinical recovery over a short period of 3 weeks. The use of IVIG is novel, and this approach aimed to eliminate circulating immunosuppressive factors while providing antibodies to combat the condition. Schmitt *et al*. documented neurological symptoms in HIV-infected children treated with IVIG alone or in combination with Zidovudine (AZT). Although the study suggested a beneficial effect of IVIG on neurological deterioration, the small sample size limits definitive conclusions. Combining immunomodulation with aggressive ART is vital in managing EPC within the context of HIV infection.[6]

Additionally, neuroimaging of the brain revealed noncontrast-enhancing lesions that appeared hyperintense on T2/ Fluid-Attenuated Inversion Recovery (FLAIR), with no significant changes on T1 sequence. These signal changes have not been previously reported in HIV-related encephalitis.

Drug interaction between enzyme-inducing AEDs and ARTs is a major challenge. Older-generation AEDs such as carbamazepine, phenytoin, phenobarbital, and primidone are potent inducers of hepatic enzymes, which can decrease the plasma concentration of protease inhibitors or nonnucleoside reverse transcriptase inhibitors. Pharmacokinetic interactions may lead to virologic failure, posing clinical implications for disease progression and the development of antiretroviral (ARV) resistance. In resource-limited settings, where such regimens are necessary for seizure control, patients may undergo pharmacokinetic assessments to ensure the efficacy of the ARV regimen.[7]

Levetiracetam is the preferred choice of AED in HIV-infected patients due to its broad-spectrum activity, ease of use, minimal drug interactions, and favorable side effect profile. Other favored choices include lamotrigine, lacosamide, gabapentin, and pregabalin.[8] In settings where newer AEDs are unavailable, valproic acid may be the treatment of choice in terms of an AED, as it does not cause enzyme induction-associated ARV failure. However, its side effect profile presents other challenges.[7]

We also tabulated previous case reports about EPC on presentation in HIV-positive patients as in Table 1.

Conclusion

Timely evaluation for acute-onset EPC must include HIV

Table 1: Epilepsia partialis continua on presentation in HIV-positive patients

Author	Ferrari *et al*.[9]		Bartolomei *et al*.[5]	Ramanujam *et al*.[10]	Present case
Year	1998		1999	2016	2021
n	2		1	1	1
Age (years)	39	36	54	14	21
Gender	Male	Male	Male	Male	Male
Semiology of seizure	EPC - right UL	EPC - left UL	EPC- distal right upper limb	Generalized tonic-clonic seizure followed by EPC involving the left half of the body	Complex partial seizure followed by EPC involving distal left upper limb
MRI brain	Bilateral frontal cortical and subcortical	Right frontal cortical	Left precentral sulcus	Right parieto-occipital cortex and thalamus	Right precentral sulcus, followed by bilateral precentral sulcus
EEG	Spike wave discharges - left frontal	Normal	Irregular theta rhythm over left frontocentral region	PLEDS - right frontocentral region	PLEDs - right frontocentral region
CSF study					
Cytology (per mm^3, pred. cells)	No cells	Normal	No cells	400, neutrophils	Normal
Protein	Normal	68	Normal	120	Normal
Glucose	Normal	Normal	Normal	60	Normal
PCR	JCV+	JCV+	Negative	CMV positive	Negative
CD4 T cell count	60	270	-	51	95
HIV RNA	-	-	-	-	163,771
Management ART AED	Didanosine Clonazepam	Details N/A	Dideoxycytidine, indinavir, lamivudine Carbamazepine	Acyclovir, meropenem	Tenofovir, lamivudine, Efavirenz Perampanel, oxcarbazepine Levetiracetam Lacosamide
Outcome	Death	Death	Improved, resolution of MRI changes	Death	Improved, resolution of MRI changes

EPC=Epilepsia partialis continua; MRI=Magnetic resonance imaging; EEG=Electroencephalogram; CSF=Cerebrospinal fluid; PCR=Polymerase chain reaction; CMV=CJohn cunningham virus; UL=Upper limb

screening. Early immunomodulation with AEDs is vital for positive outcomes, yet caution is warranted for drug interactions in HIV-infected patients.

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Conflicts of interest

There are no conflicts of interest.

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