

Stroke-induced epilepsy partialis continua

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Abstract

Objective: Focal status epilepticus requires timely diagnosis and treatment. Stroke is a common cause of epileptic seizures, but stroke-induced epilepsy partialis continua (SIEPC) is a rare type of focal status epilepticus with unknown management and prognosis. The aim of the study was to present a single-center case series of patients admitted to a third-level referral hospital diagnosed with SIEPC. **Methods:** We performed a retrospective review assessing all in-hospital consultations from July 2021 to July 2022 describing patients who presented with a diagnosis of SIEPC during hospital admission. Patients received standard diagnostic approaches (including electroencephalographic assessment) and treatment protocols. We defined EPC as focal, continuously repeated seizures with preserved consciousness lasting at least 1 h, confirmed with electroencephalography. **Results:** We identified 1054 patients seen by the neurology department as in-patient consultations. We found 268 patients with a diagnosis of stroke or epilepsy and then excluded 265 patients due to an alternate diagnosis. We finally identified three patients with (SIEPC). **Conclusions:** Although cerebrovascular disorders are a common cause of hospital admission, and SIEPC is rare, this condition is relevant to the practicing clinician. This study draws attention to this distinct clinical entity with variable presentation, diagnosis, treatment, and prognostic issues.

Keywords: Stroke. Focal status epilepticus. Epilepsia partialis continua. Stroke-induced epilepsy partialis continua.

Epilepsia partialis continua inducida por ictus

Resumen

Objetivo: El status epilepticus requiere un diagnóstico y tratamiento temprano. El ictus es una causa común de crisis epilépticas, pero la epilepsia partialis continua inducida por ictus es un tipo raro de status epilepticus focal con tratamiento y pronóstico desconocido. Presentar una serie de casos unicéntrica de pacientes admitidos a un hospital de referencia de tercer nivel con diagnóstico de epilepsia partialis continua inducida por ictus. **Métodos:** Realizamos una revisión retrospectiva, recopilando todas las interconsultas desde Julio del 2021 hasta Julio del 2022 que describieran pacientes quienes tuvieran un diagnóstico de epilepsia partialis continua inducida por ictus durante el ingreso hospitalario. Los pacientes recibieron abordajes diagnósticos (incluyendo realización de electroencefalograma) y terapéuticos estandar. Definimos epilepsia partialis continua como episodios convulsivos continuos focales con estado de consciencia preservado con duración mayor a una hora, confirmado por electroencefalografía. **Resultados:** Identificamos 1054 pacientes que fueron vistos por el

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servicio de neurología como interconsultas hospitalarias. A partir de dichos pacientes, encontramos 268 con diagnóstico de ictus o epilepsia, y excluimos 265 pacientes debido a diagnósticos alternativos. Finalmente, identificamos tres pacientes con epilepsia partialis continua inducida por ictus. Conclusiones: A pesar de que las enfermedades cerebrovasculares son una causa frecuente de admisión hospitalaria, y la epilepsia partialis continua inducida por infarto es rara, esta condición es relevante para el médico practicante. Este estudio llama la atención hacia esta distinta entidad clínica con presentación variable, y dificultades en el diagnóstico y tratamiento

Palabras clave: Ictus. Status epilepticus focal. Epilepsia partialis continua. Epilepsia partialis continua inducida por ictus.

Introduction

Epilepsia partialis continua (EPC) is part of the focal status epilepticus spectrum. Standardized management for this condition remains unknown. Stroke-induced EPC (SIEPC) is a rare disorder with unknown frequency. We aim to describe a single-center case series regarding this uncommon condition, emphasizing clinical outcomes.

Methods

We considered consecutive adult patients (≥ 18 years) with a history of stroke or epilepsy admitted to the Hospital Civil Fray Antonio Alcalde (Guadalajara, Mexico) from July 1, 2021, to July 1, 2022. Inclusion criteria were: ≥ 18 years, with an admission diagnosis of previous or acute stroke, history of post-stroke epilepsy, and SIEPC. Exclusion criteria were generalized status epilepticus and epilepsy before stroke. We identified 1052 patients seen in-hospital consultation using the electronic health record. During this period, 268 patients presented with the diagnosis of stroke or epilepsy. We identified eight patients with post-stroke epilepsy and excluded five due to generalized epilepsy diagnosis. We finally included three patients with a diagnosis of SIEPC (Fig. 1).

Patients received standard diagnostic (including electroencephalographic assessment) and treatment protocols. A board-certified neurologist made the diagnosis on clinical grounds and supported by brain imaging and electroencephalogram (EEG). We defined EPC as continuously repeated motor seizures with preserved consciousness lasting at least 1 h, confirmed with an electroencephalogram. We analyzed the following sociodemographic variables: age, gender, stroke risk factors (dyslipidemia, hypertension, diabetes, and atrial fibrillation), clinical symptoms, EEG findings, radiological findings in computerized tomography (CT) or magnetic resonance imaging (MRI), stroke localization, pharmacological treatment, the use of mechanical ventilation, clinical outcome, and follow-up.

Results

After a systematic search, we identified eight patients with post-stroke epilepsy. Three of these presented with SIEPC ($< 1\%$ frequency [0.28%]) (Table 1). All three patients had clinical, radiological, and electrophysiological findings consistent with SIEPC.

Patient 1

A 49-year-old right-handed female experienced right hemifacial weakness. After 26 days of this event, she presented to the emergency room with repeated right hemifacial seizures, aphasia, and preserved awareness. Her medical history was relevant for Type 2 diabetes mellitus and hypothyroidism. Unenhanced brain computed tomography (CT) was unremarkable. MRI showed subacute infarction involving the left frontocortical and superior frontal gyrus (Fig. 2). The ictal standard scalp EEG reported the presence of continuous focal epileptiform discharges in the left centroparietal region and no secondary generalization. We treated her with levetiracetam, valproate, lacosamide, and carbamazepine (doses shown in Table 1). On 8-month follow-up, she remained seizure-free with levetiracetam and valproate. After extended workup, the stroke was classified as an embolic stroke of unknown source.

Patient 2

A 49-year-old right-handed female presented to the emergency room after experiencing lingual motor seizures with motor left faciobrachial progression. She had a history of hypertension, obesity, and dyslipidemia. CT scan revealed an intracerebral hemorrhage (ICH) in the right frontal lobe at the level of the precentral gyrus. Brain MRI showed a lesion at the same level (T2 hypointensity with isointense center and a “popcorn” appearance with associated perilesional edema) consistent with a cerebral cavernous venous malformation (cavernoma) (Fig. 3). The ictal standard scalp EEG showed right frontocentral discharges (F4-C4) with propagation to the contralateral

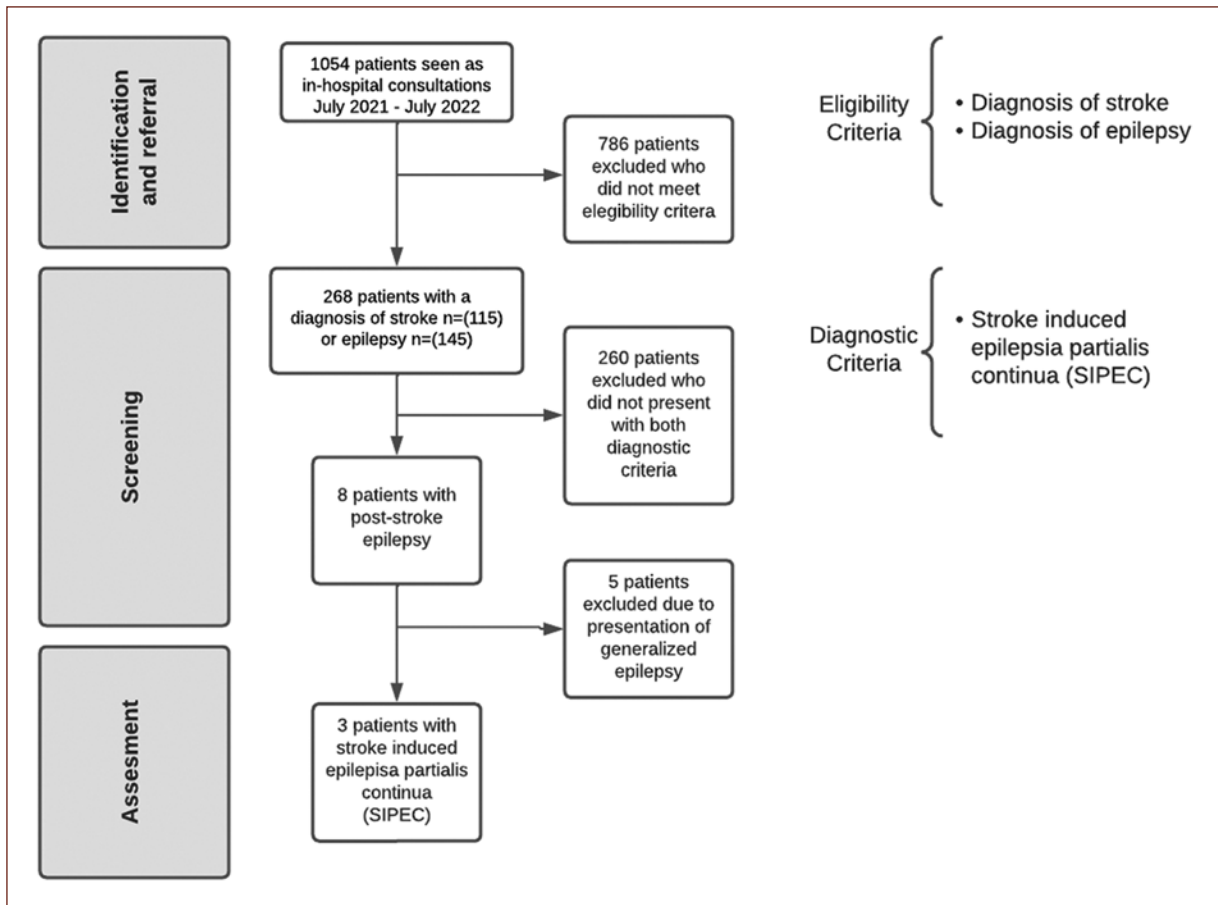


Figure 1. Flowchart.

hemisphere. At admission, we treated her with oxcarbazepine and levetiracetam (doses shown in Table 1). The patient responded well to pharmacotherapy.

The lesion was surgically removed, and the patient remained seizure-free on 2-month follow-up.

Patient 3

A 72-year-old right-handed male presented to the emergency department with left hemiparesis and rhythmic, ipsilateral, and clonic movements (synchronic, face-arm-leg). He had a history of type 2 diabetes, hypertension, and chronic kidney disease. A brain CT scan showed a right temporal-occipital gyrus infarction consistent with a posterior cerebral artery territory stroke (Fig. 4). The ictal standard scalp EEG showed irregular rhythm, right hemispheric slowing, and lateralized periodic discharges (LPDs). The abnormal left-sided movements stopped abruptly after a benzodiazepine challenge but reinitiated acutely after a few minutes. The patient remained awake throughout the hospital

admission and was treated with a combination of levetiracetam, phenytoin, clonazepam, and valproic acid with marked improvement (doses shown in Table 1). The patient was discharged against medical advice and was lost to follow-up. This patient's stroke was classified as cryptogenic due to an incomplete workup.

Discussion

EPC was first described by Yakovlevich Kozhevnikov in 1894 but lacks a universally accepted definition¹. It is a subtype of focal status epilepticus defined as continuous regular or irregular muscular clonic twitching affecting a limited body part for at least an hour². Consciousness is typically preserved, and the twitching most commonly involves the face, arms, or both³. The diagnosis is usually supported with an EEG; however, it may be normal⁴. EPC is uncommon, but when identified, a common underlying cause is stroke⁴⁻⁶.

Stroke is the most common cause of epilepsy in older adults, accounting for approximately 20% of the

Table 1. Demographic and clinical information of patients with stroke-induced epilepsy partialis continua

Case	Sex	Age	Medical history	Clinical presentation	Imaging	Radiologic diagnosis	Abnormal EEG	Treatment	Pharmaco resistant epilepsy	Death
1	F	49	Type 2 diabetes and hypothyroidism	Hemifacial seizures with accompanying aphasia	MRI	IS	+	Levetiracetam (2 g every 12 h), Valproate (600 mg every 8 h), Carbamazepine (200 mg every 6 h), Lacosamide (200 mg every 12 h)	+	-
2	F	49	Hypertension, obesity, dyslipidemia	Lingual seizures with accompanying motor faciobrachial progression	MRI	ICH	+	Levetiracetam (1 g every 12 h), Oxcarbazepine (600 mg every 12 h)	-	-
3	M	72	Type 2 diabetes, hypertension, and chronic kidney disease	Hemiparesis with accompanying rhythmic clonic movements (synchronous, face-arm-leg)	CT	IS	+	Levetiracetam (1 g every 12 h), Phenytoin (100 mg every 8 h), Clonazepam (0.25 mg every 8 h), Valproate (1 g every 8 h)	+	-

MRI: magnetic resonance imaging; CT: computed tomography; EEG: electroencephalogram; IS: ischemic stroke; ICH: intracerebral hemorrhage.

cases^{7,8}. The incidence of post-stroke status epilepticus is 0.1-0.9%⁹. Stroke is also the most common cause of status epilepticus in people over 60 years¹⁰. The risk of seizures is highest in the first week after stroke¹¹. Early seizures (< 14 days after stroke) have a 35% increased risk of later epilepsy, but the risk of epilepsy after late seizures (> 14 days after stroke) increases to 90%¹². The stroke subtype is also a significant predictor of seizures and epilepsy. Hemorrhagic stroke patients have a higher incidence of seizures compared to ischemic stroke. A symptomatic post-stroke seizure has a > 60% probability of seizure recurrence¹³. Large infarcts with cortical involvement increase the risk of epilepsy, and the localization of the lesion determines seizure type¹⁴.

SIEPC is rare, the frequency of this condition is unknown, and few studies have focused on determining its incidence. A prospective study conducted by Bentes et al. showed an incidence of 1.7% among 151 patients with stroke. However, the study sample was small, with no similar studies¹⁵.

The differential diagnosis for this rare condition includes cluster seizures (> 3 seizures in 24 h) and other abnormal movement disorders such as hemiballismus and hemichorea¹⁶. A benzodiazepine challenge (clonic movement cessation after IV administration of short-acting benzodiazepine) may help distinguish these entities.

Management of EPC remains to be seen. Studies are highly heterogeneous, with variable clinical responses to antiseizure drugs¹⁵. However, anti-seizure medications (ASMs) such as levetiracetam, carbamazepine, and lacosamide have shown promising responses with seizure resolution. These results, although showing adequate responses, should be taken with caution, since only one patient was included for each study¹⁷⁻¹⁹. Other approaches such as vagus nerve stimulation, transcranial brain stimulation, and alcohol; performed in four, one, and one patient, respectively; have also been used in EPC unresponsive to medical therapy²⁰⁻²².

SIEPC response to ASMs is varied and presents a worse clinical response than EPC due to other etiologies. In a study conducted by Phabphal et al., all patients with EPC due to metabolic etiologies responded well to ASMs, but only 81% of the patients with SIEPC responded well to ASMs³. In our case series, all patients required two or more ASMs to achieve clinical response. Levetiracetam was administered to all patients, with favorable outcomes; only one patient (Case 3) could not be evaluated in the follow-up but showed partial resolution within hospitalization. Previous studies have shown adequate clinical responses with the use of levetiracetam in SIEPC secondary to traumatic

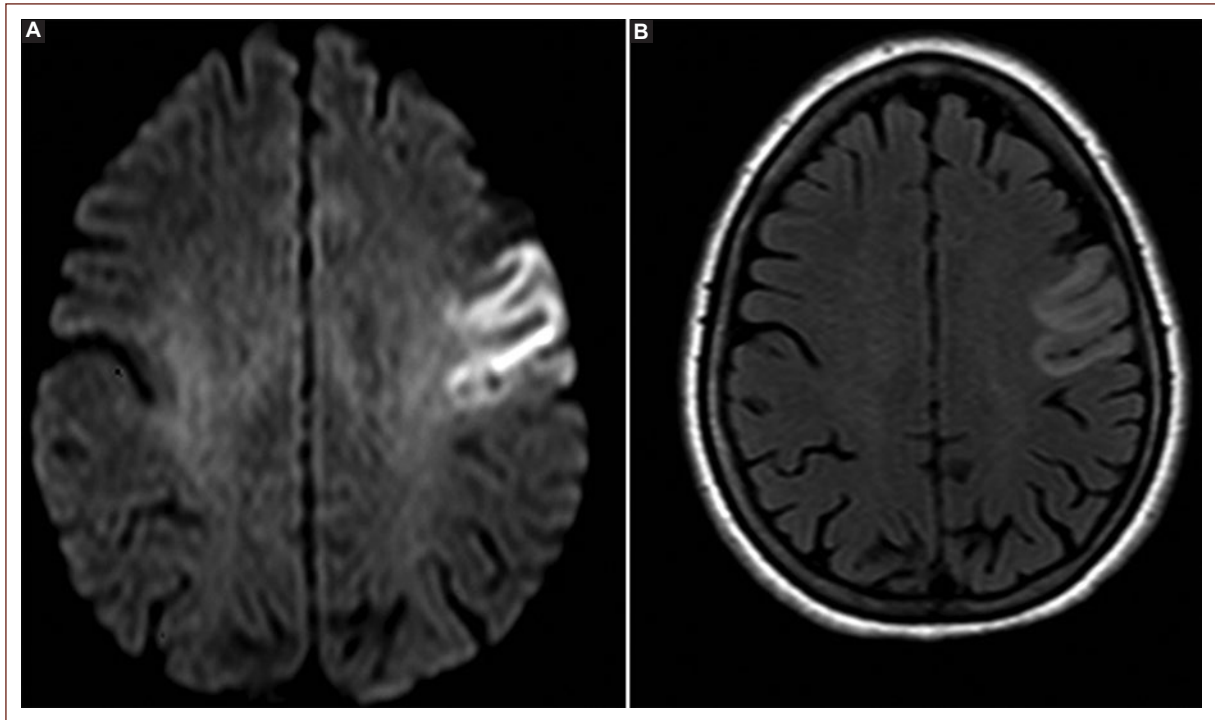


Figure 2. Diffusion-weighted image (A) shows diffusion restriction in the left superior frontal gyrus. Fluid-attenuated inversion recovery magnetic resonance imaging (B) confirms subacute infarction involving the left superior frontal gyrus.

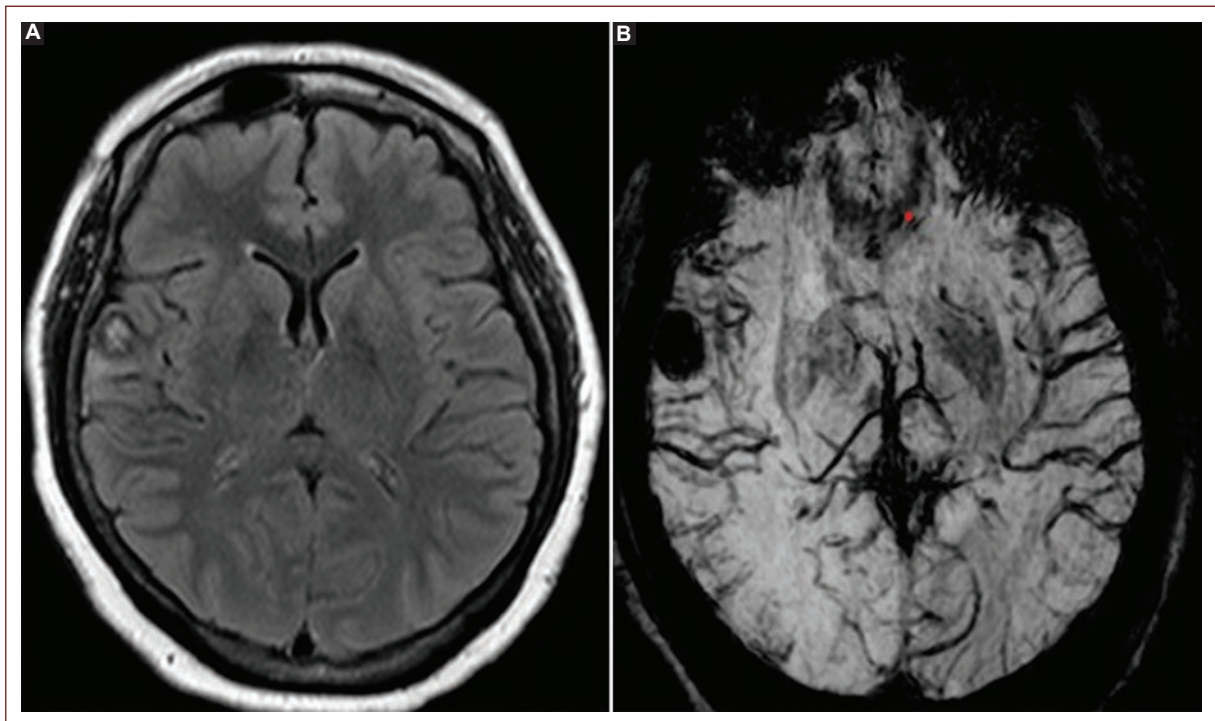


Figure 3. Fluid-attenuated inversion recovery magnetic resonance imaging (MRI) (A) shows a hypointense lesion with an isointense center (popcorn appearance) and perilesional edema in the right parietal operculum. Susceptibility-weighted angiography MRI (B) reveals a hypointense lesion in the right parietal operculum.

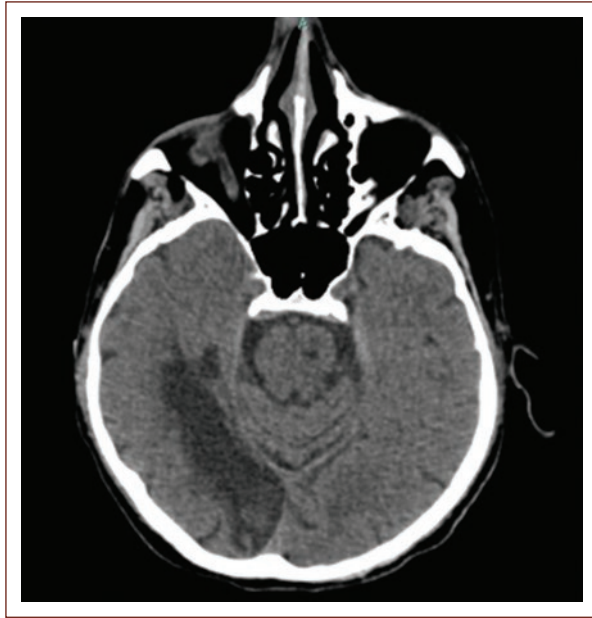


Figure 4. Brain computed tomography shows a hypointense lesion in the right temporo-occipital gyrus.

hemorrhagic intracerebral hemorrhage²³, venous sinus thrombosis²⁴, and ischemic stroke^{25,26}. One of the limitations of these studies is that all were one patient-case reports; therefore, further studies should be conducted to confirm these findings. Other therapies used for SIEPC include fosphenytoin and clobazam²⁷. The dose of ASMs could also impact the patient's outcome; in our series, we used either a dose of 1 g of levetiracetam every 12 h or 2 g every 12 h, similar to the doses used by Brigo et al²⁶. and Haase et al²⁸. Unfortunately, other case reports of SIEPC do not specify dosing.

In our case series, SIEPC secondary to ischemic stroke required more than two ASMs to achieve clinical response, contrary, SIEPC secondary to ICH only required two ASMs to achieve seizure resolution. Previously, Haase et al. showed similar results of seizure resolution of SIEPC secondary to ICH with the use of levetiracetam²³.

Timing between seizure onset and treatment administration could also impact the clinical response of the patients since previous studies have shown that delayed treatment is related to longer duration of the episodes²⁸. This could be explained by the greater momentum gained with the longer duration of the episodes⁶. Hyperglycemia may also contribute to worse clinical outcomes^{28,29}. However, more studies should be conducted to confirm this hypothesis.

Our study has strengths and limitations. We acknowledge that it was a single-center retrospective design, and the small sample size may be a substantial limitation of our study. As an in-hospital consultation department, most patients are admitted to the geriatric or internal medicine ward. Patients with subtle clinical manifestations in other departments may be unrecognized.

Stroke is a prevalent neurological disorder in in-hospital admissions, and this complication must be correctly identified. Our study includes many screened patients with epilepsy or stroke. All patients were treated directly by us, and we were directly involved in the diagnosis and treatment. In this study, the frequency of SIEPC was low. However, cerebrovascular disease is a common cause of hospital admission, making this disorder clinically relevant. The lack of diagnostic criteria and treatment protocols for SIEPC is striking.

Conclusion

Stroke-induced epilepsy partialis continua is rare. However, given the high prevalence of stroke as a common cause for hospital admissions, it is essential for practicing physicians to be aware of this condition. This study draws attention to this distinct clinical entity with variable presentation, diagnosis, treatment, and prognostic issues. We need a precise diagnostic strategy for this patient population, and more studies are required to guide adequate management.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type

of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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