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A 73-Year-Old Woman with Respiratory Failure and Stimulus-Induced Rhythmic, Periodic, or Ictal Discharges (SIRPIDs) in the Absence of a Detectable Brain Insult Diagnosed and Monitored by Continuous Electroencephalogram (EEG) and Treated with Valproate, Carbamazepine, and Clonazepam

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 73-year-old
Final Diagnosis: SIRPIDs
Symptoms: Stimulus-induced jerks in the head and right arm • right gaze deviation
Medication: Valproate • Carbamazepine • Clonazepam
Clinical Procedure: Continuous video-electroencephalogram
Specialty: Neurology
Objective: Rare phenomenon

Background: Stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs) commonly occur in critically ill patients and can be distinguished from spontaneous epileptic seizures by continuous electroencephalogram (CEEG) monitoring. There are no current treatment guidelines for SIRPIDs. This report is of a 73-year-old woman with respiratory failure and without any detectable gross brain lesions. She had developed SIRPIDs, which were diagnosed through CEEG monitoring. She responded well to valproate, carbamazepine, and clonazepam.

Case Report: A 73-year-old woman was admitted to the intensive care unit (ICU) with a chest infection. After 3 days, this infection was complicated by respiratory failure and coma, for which she was intubated. After that, recurrent brief episodes of abnormal head and right upper limb jerky movements with right gaze deviation occurred. Nurses noticed that these episodes occurred exclusively upon physical interaction with the patient, and lasted up to 3 minutes. No focal findings were noted on neurological examination. The brain computed tomography (CT) scan revealed no acute brain insult. CEEG revealed SIRPIDs, which abated with midazolam boluses, followed by infusion at 15 mg/hour. Later, they were controlled by valproate, carbamazepine, and clonazepam in succession, guided by CEEG data.

Conclusions: This report shows the importance of CEEG monitoring to diagnose SIRPIDs and monitor treatment response. It also suggests that SIRPIDs can occur even in the absence of gross brain pathology. Although there are no current treatment guidelines for SIRPIDs, the use of valproate, carbamazepine, and clonazepam can help control them, as evidenced in this case.

Keywords: Benzodiazepines • Case Reports • Continuous EEG • Critical Care • Critical Illness • Electroencephalography • Respiratory Insufficiency • SIRPIDs • Video-EEG

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Background

Continuous electroencephalogram (CEEG) is a practical and convenient method of brain monitoring that is being increasingly utilized in refractory-status epilepticus cases and critically ill patients with impaired mental status [1-3]. CEEG monitoring is of particular importance in comatose patients, as most of these patients' seizures are subclinical [4].

Stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs) are an electroencephalographic (EEG) finding, with or without clinical manifestations, seen in the critical care setting. They were first described by Hirsch et al in 2004 [5]. SIRPIDs are a relatively common phenomenon that may occur in 12% to 22% of patients undergoing EEG recordings in the intensive care unit (ICU) [5-7]. SIRPIDs are seen in patients with a broad range of underlying etiologies, including intracranial hemorrhages, cerebral infarcts, traumatic and anoxic brain injuries, neurodegenerative diseases such as Creutzfeldt-Jakob disease, and, rarely, toxic-metabolic disturbances [5-10]. However, the exact underlying pathophysiology of SIRPIDs remains unknown [5,11].

SIRPIDs commonly occur in critically ill patients, are elicited by stimulation, and can be recognized and distinguished from epileptic seizures by CEEG monitoring [5,7]. There are no current treatment guidelines for SIRPIDs, and their therapeutic significance remains unclear [11,12]. We present a case report of a 73-year-old critically ill woman with a chest infection and respiratory failure without any detectable brain insult, who developed SIRPIDs, which were diagnosed with CEEG monitoring and resolved by valproate, carbamazepine, and clonazepam.

Institutional approval was not required for a case report. Informed consent was obtained from the patient's family to have the case details published. We reviewed the electronic medical records to investigate this clinical case, including hospital course, vital signs, laboratory findings, radiological images, and treatments. This case study was performed and reported in line with the CARE (CAse REports) criteria.

Case Report

A 73-year-old woman known to have diabetes mellitus, hypertension, chronic kidney disease, and pulmonary hypertension presented with a history of cough and chills. She had an oxygen saturation of 90% on a 15 liter/minute face mask. Chest X-ray revealed bilateral infiltrates, right-lung opacity, and shifting of the trachea to the right side. Thus, she was admitted to the ICU as a case of pneumonia. After 3 days, she was comatose and intubated as she developed type 2 respiratory failure. During her ICU admission, the patient developed recurrent attacks of abnormal head and right upper limb jerky movements. The attacks were first noticed by the ICU nursing staff and were exclusively brought about upon physical interaction with the patient, such as measuring vital signs, manipulating the endotracheal tube, and administering drugs. The neurology team was consulted and found no focal findings on neurological examination. The jerky right upper limb and head movements were consistently induced by applying painful stimuli, and lasted for up to 3 minutes.

Several brain computed tomography (CT) scans were conducted throughout the patient's ICU stay, and revealed no acute gross lesions or acute ischemia (**Figure 1**). MRI was not done, because the patient was unstable, comatose, and intubated. CEEG was done in the ICU and revealed SIRPIDs that occurred each time the stimulation-induced movements developed. These SIRPIDs evolved in amplitude, sharpness, frequency (stimulus-induced lateralized rhythmic delta activity; SI-LRDA), and, later, in morphology (**Figure 2, Video 1**). The SIRPIDs ceased upon treatment with midazolam boluses followed by infusion at 15 mg/h. The patient was placed on valproate, carbamazepine, and clonazepam, in succession, guided by CEEG data. The patient was then weaned off the midazolam infusion over 24 hours, with no recurrence of the SIRPIDs.

A chest and abdominal CT scan showed bilateral lung infiltrates and a large mass herniating from the abdomen to the right chest cavity. An abdominal guided biopsy was taken and showed an inflammatory necrotic mass. Bronchoscopy was conducted, along with biopsy and aspiration; the results revealed a necrotic mass superimposed by a candida infection. Thus, antifungal therapy was started. Unfortunately, after 23 days of admission, the patient developed asystole and died.

Discussion

We report an interesting case of fungal pneumonia complicated by respiratory arrest, followed by neurological sequelae upon stimulation, with a negative brain image explained by CEEG as SIRPIDs, which were resolved by valproate, carbamazepine, and clonazepam. This report demonstrates the diagnostic role of CEEG monitoring in capturing SIRPIDs and evaluating the response to treatment. Also, this case suggests that brain insult is not mandatory for a finding of SIRPIDs. Thus, healthcare providers in neurology departments should be aware of the importance of CEEG in critically ill patients, as it can help capture SIRPIDs.

SIRPIDs, an EEG pattern found in critically ill encephalopathic patients, are consistently induced and reproduced by physical stimuli. They can appear trivial or unnoticeable if video-EEG is not used [13,14]. The ICU nurse caring for our patient noticed

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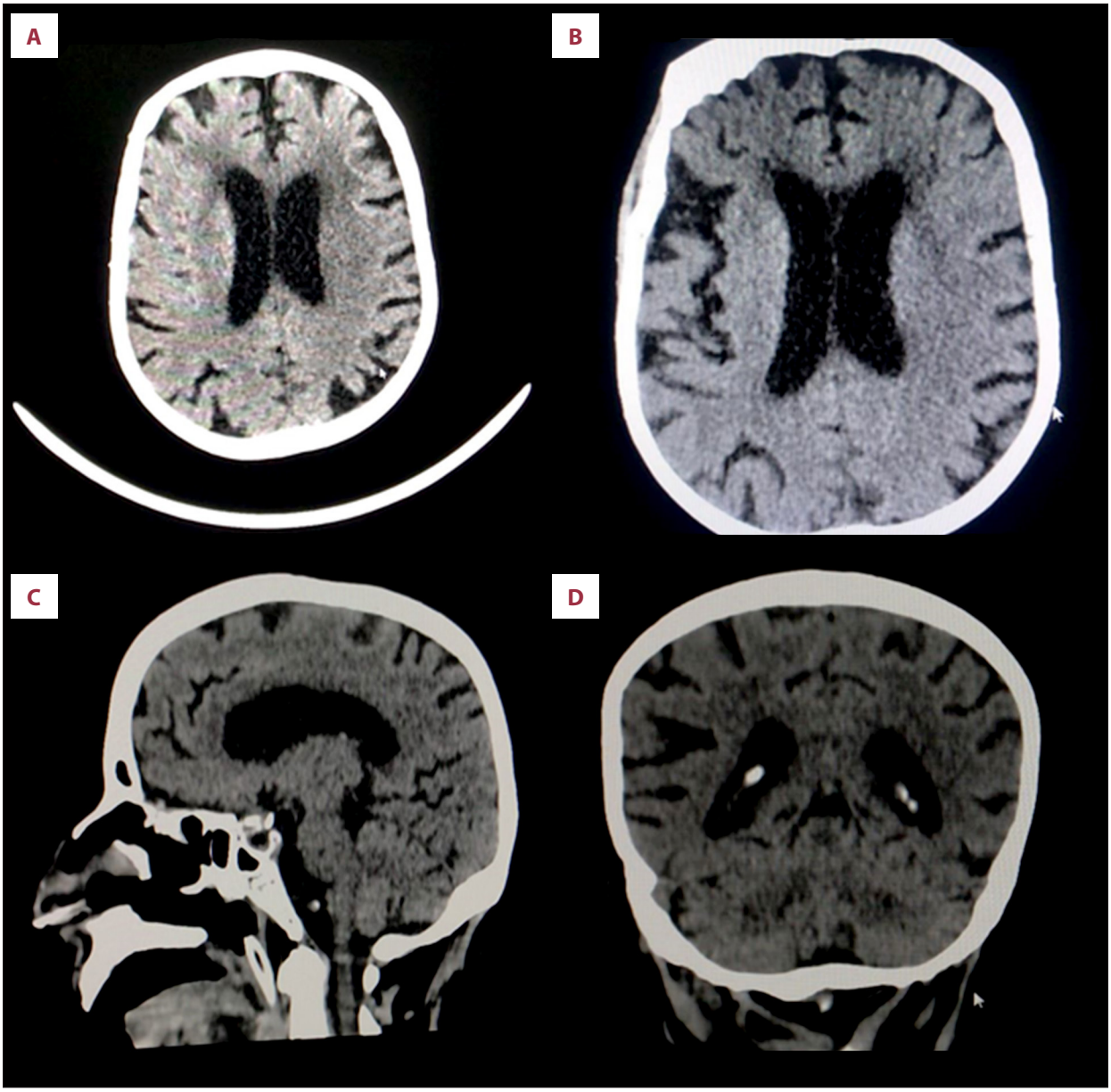

Figure 1. Multiple images of brain computed tomography scan (CT scan) without intravenous contrast show age-related brain atrophic changes with neither acute brain lesions nor acute ischemic changes: (**A, B**) axial sections; (**C**) sagittal section; (**D**) coronal section.

the recurrent jerking associated with stimulating the patient, but only video-EEG confirmed that this was a case of SIRPIDs. Most of the time, SIRPIDs and most seizures of any kind in critically ill patients are not associated with observed clinical seizure activity, although they might be infrequently correlated with clinical manifestations, and thus, can only be detected by CEEG [5,7,15-18]. In a case series by Hirsch et al (2008), only 5% of SIRPIDs were associated with clinical manifestations, including focal clonic activity (affecting body parts like hand, arm, or face) [19]. In the present report, SIRPIDs were associated with clinical correlates, as our patient developed recurrent brief episodes of abnormal head and right upper limb jerky movements with right gaze deviation.

Van Straten et al reported a 12.1% prevalence of SIRPIDs in retrospectively reviewed ICU patients who underwent video-EEG monitoring [7]. Factors associated with SIRPIDs included a higher prevalence of subclinical status epilepticus, longer total video-EEG recording time, and acute traumatic brain injury [7]. The most common risk factors for SIRPIDs include subarachnoid and intracranial hemorrhage [5], traumatic brain injury [7,20], and anoxic brain injury [6,21]. Other less common risk factors

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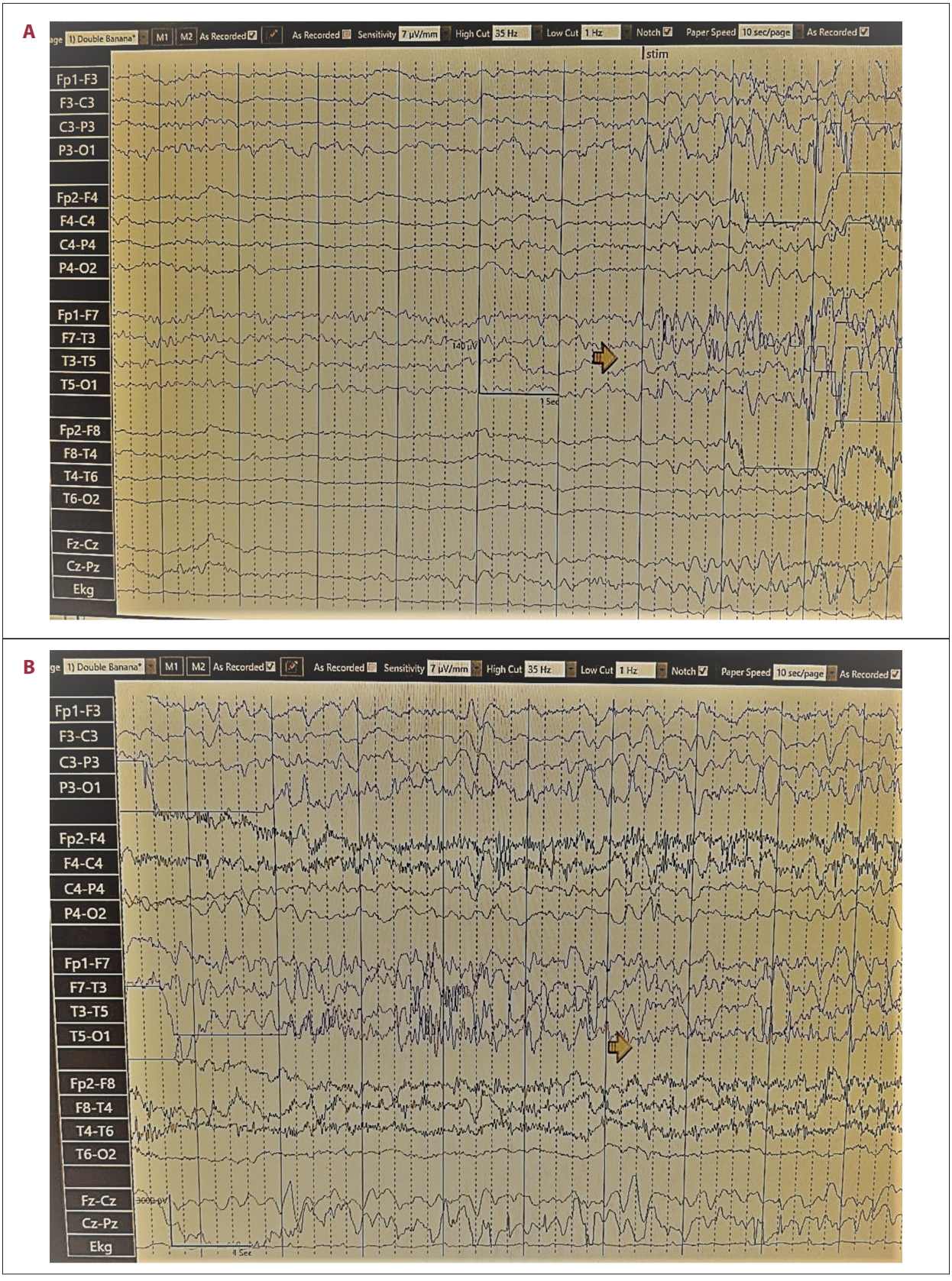

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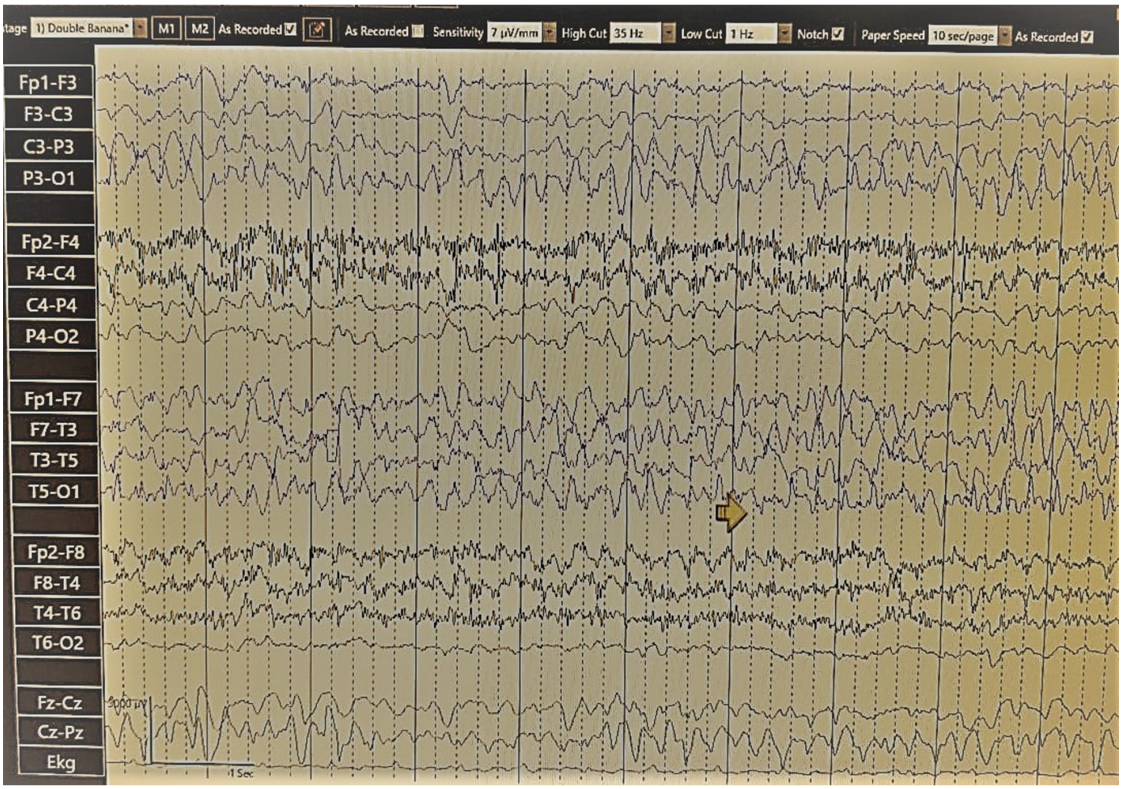

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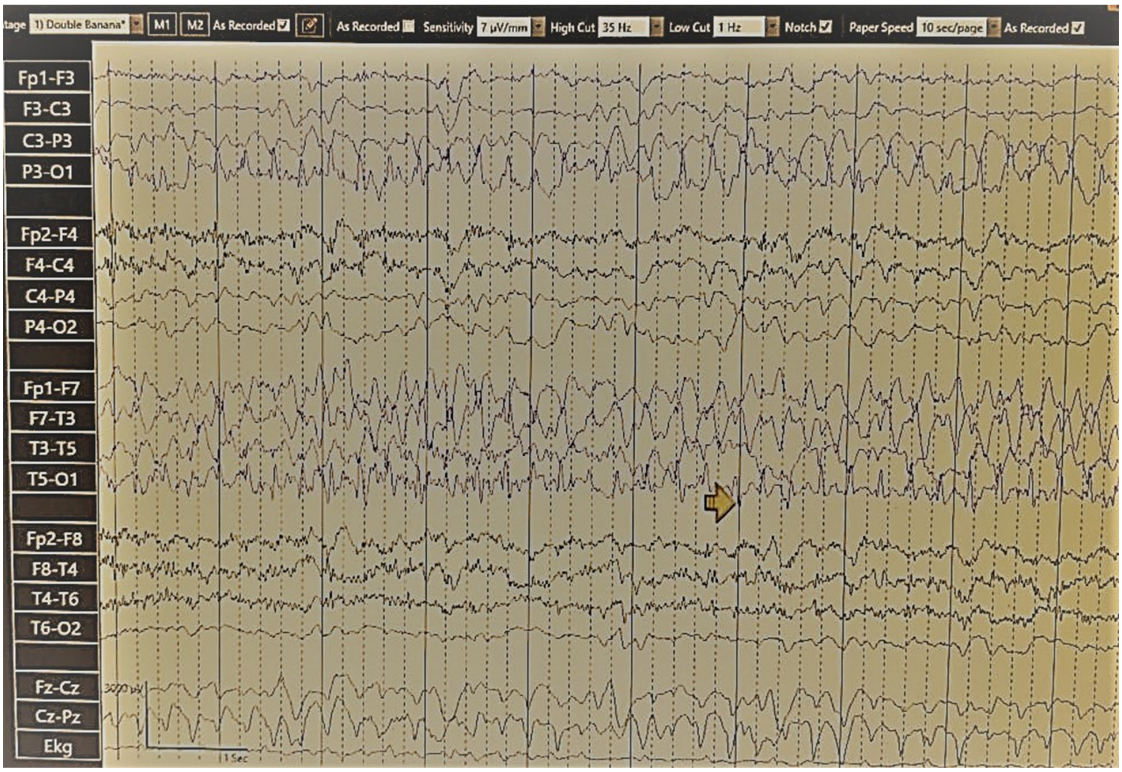

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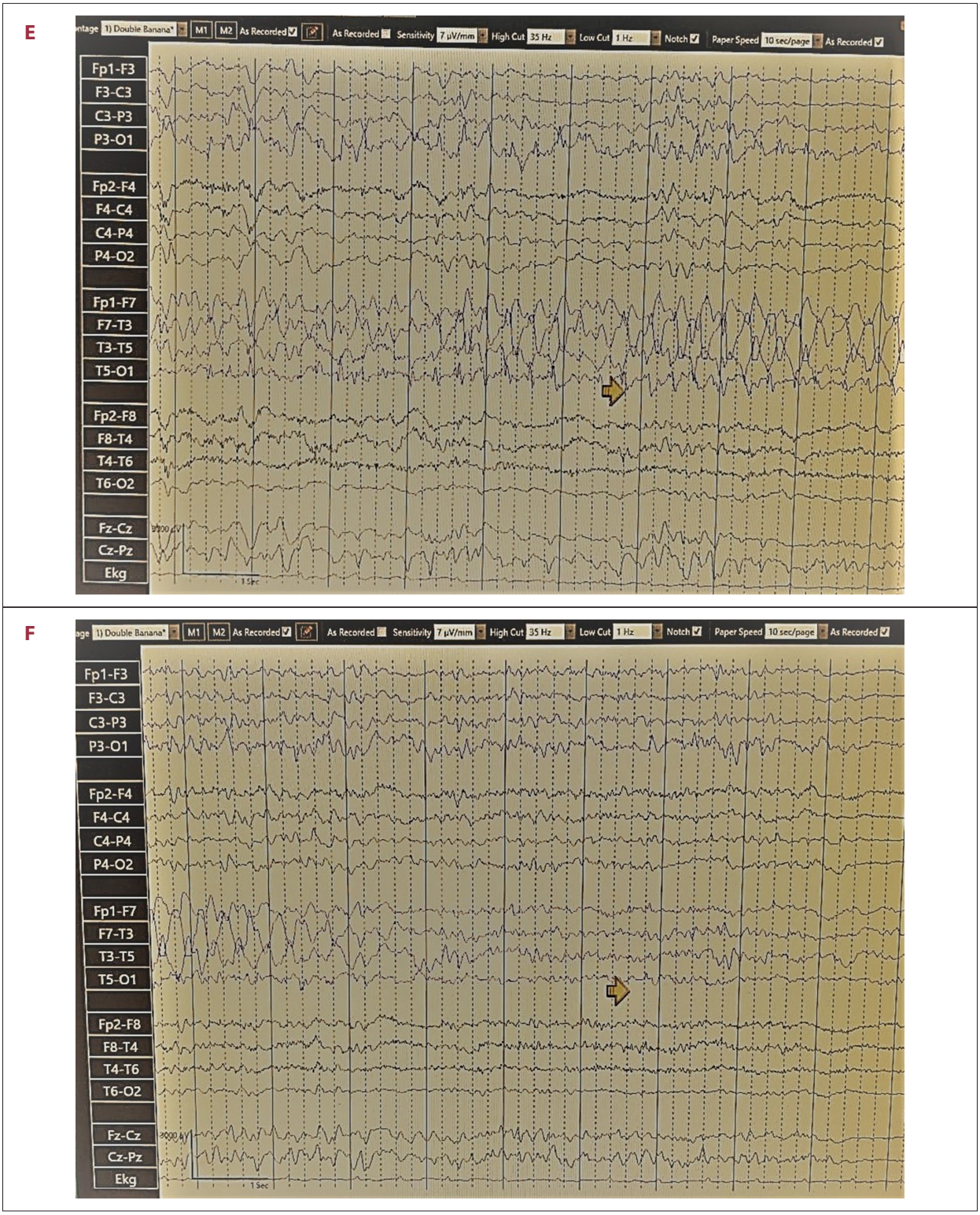

Figure 2. (**A-F**) EEG epochs from **A to F** show that upon stimulation of the patient, a left temporal theta/alpha activity appears, quickly spreads to the left parasagittal area, slows down, changes in morphology to a 3-4 Hz spike and wave discharges, and becomes higher in amplitude before it devolves. The whole activity lasts around 45 seconds. * EEG settings: Longitudinal Bipolar "Double Banana" Montage, sensitivity: 7 microvolt/mm; high cut: 35 Hz, low cut: 1 Hz; paper speed: 10 sec/page.

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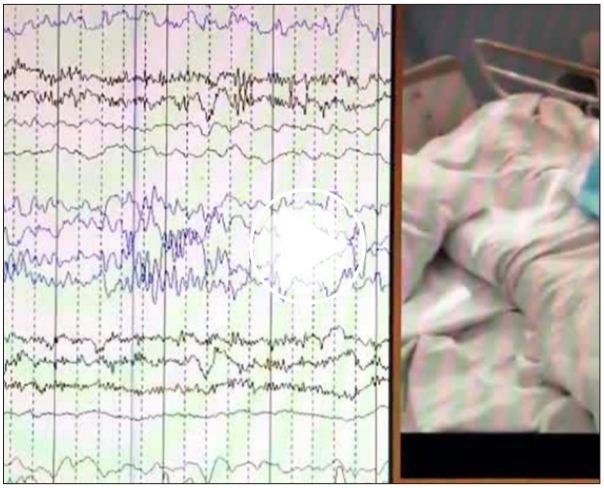

Video 1. Continuous electroencephalogram monitoring showed an ictal-appearing activity from the left-brain side induced by painful stimulation and was associated with right upper limb jerky movements. The activity started over the left side, mainly in the left temporal lobe, as stimulus-induced rhythmic 5-6 Hz theta waves that evolved over time in amplitude (became higher), in sharpness (became sharper), in frequency (slowed down to rhythmic delta activity – stimulus-induced lateralized rhythmic delta activity 'SI-LRDA'), and, later, in morphology (become spike and wave discharges).

include stroke, status epilepticus, meningitis or encephalitis, and, less frequently, toxic-metabolic disturbances [9,20]. Our case report's novelty comes from the fact that our patient had no evident gross brain pathology, and so chest infection and respiratory failure most likely caused her SIRPIDs. However, it is possible that there was brain damage that we were unable to detect, as conducting a brain MRI was not possible due to the patient's condition. In conclusion, we can suggest that detectable brain lesion is not mandatory for a diagnosis of SIRPIDs.

The pathophysiology of SIRPIDs is not well-known but probably involves dysregulation of the thalamocortical circuit in the context of a hyperexcitable cortex [9]. It is not known whether SIRPIDs are solely a sign of severe brain injury or might themselves cause neuronal damage [13]. The association of SIRPIDs with morbidity and mortality has been debatable, with some studies showing a favorable outcome while others show an association with poor prognosis [6,7,22,23]. Several studies have reported that EEG reactivity to comatose patients' stimulation appears to be a positive sign of recovery of consciousness and good outcome [22,23]. On the other hand, Alvarez et al suggested a poor outcome in postcardiac-arrest patients who displayed SIRPIDs on EEG [6]. Other studies could not find a significant association between SIRPIDs and clinical outcomes [7,21].

In our patient, SIRPIDs ceased with midazolam first and then were controlled entirely with multiple anti-epileptic drugs, including valproate, carbamazepine, and clonazepam. Our patient, unfortunately, died due to her critical medical condition. In cases described by Kaplan and Duckworth, in which SIRPIDs were associated with impaired mental status, and in cases where SIRPIDs were persistent or associated with clinical activity, treatment with benzodiazepines and other anti-epileptic drugs resulted in improved level of consciousness, the return of verbal interaction, and regression of the SIRPIDs [15].

Conclusions

This report illustrates the importance of CEEG monitoring to diagnose SIRPIDs, even in the absence of a detectable brain insult, and to monitor the response to treatment. We suggest that gross brain pathology is not mandatory for a finding of SIRPIDs. Thus, when subtle findings are noticed on accidental stimulation of the patient, CEEG monitoring can help capture SIRPIDs. Although there are no current treatment guidelines for SIRPIDs, the use of valproate, carbamazepine, and clonazepam can be helpful.

Department and Institution Where Work Was Done

This case report was conducted at King Abdullah University Hospital, Jordan University of Science and Technology, Irbid, Jordan.

Availability of Data and Materials

The datasets are available from the corresponding authors.

Conflict of Interest

None.

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