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Psychiatric disorders secondary to nonconvulsive status epilepticus of frontal origin. Two clinical case reports

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Nonconvulsive status epilepticus (NCSE) is common but often under-diagnosed. Due to the absence of specific symptoms, it is frequently misdiagnosed as a psychiatric disorder, which delays treatment. The cases of two patients who exhibited psychiatric symptoms and subtle cognitive disturbances (without confusion) as the sole manifestation of frontal lobe NCSE are reported. Both patients were initially treated as psychiatric disorders (depression and anorexia nervosa). The correct diagnosis was established by the electroencephalographic study, in one case after the patient experienced a generalized tonic-clonic seizure and in the other, after failure to improve with supposedly adequate treatment. There are reports of patients with NCSE whose symptoms suggest a psychiatric disorder (inappropriate behavior, emotional disinhibition, perseveration, reduced speech and motivation). This can occur without altered consciousness and symptoms may fluctuate, making the correct diagnosis extremely difficult. This entity can occur at any age and without a previous history of seizures. A high level of suspicion is necessary for prompt electroencephalographic study to confirm the diagnosis. Early treatment will correct the symptoms and significantly improve quality of life for patients and their families.

Key words: Behavior, Electroencephalography, Epilepsy, Frontal lobe, Status epilepticus, Psychiatric disorder

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Trastornos psiquiátricos secundarios a estados epilépticos no convulsivos de origen frontal. A propósito de dos casos clínicos

El estado epiléptico no convulsivo (EENC) es una entidad frecuente, aunque muchas veces subdiagnosticada. Debido

a la ausencia de síntomas específicos es frecuentemente confundida inicialmente con trastornos psiquiátricos, lo que retarda el tratamiento. Presentamos dos pacientes que manifestaron síntomas psiquiátricos y trastornos cognitivos sutiles (sin confusión) como única manifestación de un estado epiléptico no convulsivo de origen frontal. Ambos fueron tratados inicialmente como un trastorno psiquiátrico (depresión mayor y anorexia nerviosa). El diagnóstico correcto fue establecido con el estudio electroencefalográfico, realizado luego de que uno de los pacientes experimentara una crisis convulsiva y el otro no evidenciara mejoría con el tratamiento psiquiátrico. Existen reportes de pacientes con EENC cuyos síntomas sugieren un trastorno psiquiátrico (conducta inapropiada, desinhibición afectiva, perseverancia, reducción del lenguaje y desmotivación). Esto puede ocurrir sin compromiso de conciencia, y los síntomas pueden ser fluctuantes, lo que hace en ocasiones el diagnóstico muy difícil. Esta entidad puede ocurrir a cualquier edad y sin historia previa de crisis. Es necesario un alto nivel de sospecha para indicar la realización de un estudio electroencefalográfico para confirmar el diagnóstico. Un tratamiento precoz corregirá los síntomas y mejorará significativamente la calidad de vida del paciente y su familia.

Palabras clave: Comportamiento, Electroencefalografía, Epilepsia, Lóbulo frontal, Estado epiléptico, Trastorno psiquiátrico

INTRODUCTION

Nonconvulsive status epilepticus (NCSE) is a heterogeneous entity with a variety of clinical manifestations, so that many consider it to be a diagnostic challenge¹. Whereas convulsive status epilepticus is easily recognizable because of the evident clinical manifestations of underlying ictal activity, NCSE can easily be overlooked because specific symptoms suggestive of epileptic etiology are often absent. The diagnosis of NCSE is based on correlation of clinical

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symptoms with electroencephalographic activity. These symptoms can be expressed as a sudden change in behavior and/or mental status, associated with the presence of ictal discharges on the electroencephalogram.

In recent years, reports of patients with ictal psychiatric phenomena as the only manifestation of NCSE have been increasingly more frequent. In most cases they express simple partial NCSE, if consciousness is unimpaired, or complex NCSE, if impaired consciousness is present. However, in some cases these symptoms may be the clinical manifestation of a state of absence (idiopathic generalized epilepsy).

Case report 1

A 40-year-old woman with a history of left frontal glioma surgery was seen in the emergency room for a generalized tonic-clonic seizure. In the interview, a noteworthy finding was a history of behavior changes, frequent memory lapses, lack of initiative and emotional indifference starting a month earlier. During the admission neurological examination, she was oriented in time and space and capable of reversing series but she said that she felt "different, slower and found it hard to think." Cerebral magnetic resonance imaging revealed no brain tumor recurrence and continuous video monitoring electroencephalography (VM-EEG) was carried out. During the examination, localized recurrent seizures were evident in the left frontal region, starting with fast, low-voltage activity on the frontopolar electrode (Fp1) that spread rapidly to the rest of the left frontal cortex. As the seizures progressed, the activity described decreased in frequency and increased in voltage, culminating in a wave-like, multiple spike pattern at about two cycles per second. These seizures lasted 40 to 60 seconds and recurred every 1-2 minutes. Between seizures, slow, continuous, frequent left frontal interictal epileptiform activity was evident (Fig. 1). Although initially there was no clear clinical manifestation, when asked to count consecutively, she persevered in repeating the same number. She was fully aware of what was happening, telling the evaluator that she "was stuck and could not move to the next number." After receiving an intravenous loading dose of phenytoin, the seizures gradually became more spaced out over a period of minutes until they completely disappeared. Family members reported that "she was herself again."

Case report 2

A 20-year-old woman with a history of anorexia nervosa and depression starting one year earlier was treated with escitalopram. Her parents described how a progressive behavior disorder started at the same time. The behavior was

characterized by abulia, lack of initiative, difficulty in planning activities and increasingly impaired memory, resulting in social isolation and poor performance. About two months later she developed a severe eating disorder. She was admitted to the intensive care unit for attempted suicide by massive escitalopram ingestion. One month before admission, the patient underwent an electroencephalogram (EEG) at the request of her treating psychiatrist. The EEG showed abundant interictal bifrontal synchronous epileptiform activity that generalized secondarily in bursts lasting up to six seconds. Antiepileptic treatment was not given because of the absence of clinical seizures. The day she was admitted to the clinic, the EEG was repeated, which revealed frequent bifrontal synchronous epileptiform activity. The patient was then connected to a video monitoring EEG to evaluate the presence of subclinical seizures and eventually correlate them with possible subtle clinical manifestations. During the examination, recurrent electrographic seizures with synchronous bifrontal activity 6-12 seconds long were evident, which occurred successively for over an hour (Fig. 2). Concomitant with this activity, the patient reported periods of "partial connection with her surroundings" in which she lost fragments of conversation, showed slowed thought and had trouble formulating responses, a condition that has occurred intermittently in the course of the past year. Treatment was started with lamotrigine in escalating doses up to 300 mg a day. After a month of treatment (100 mg lamotrigine), the patient reported a decrease of about 80% in the events "in which she slows down" and her parents noticed significant behavioral improvement, "She manages to focus on one activity and she understands what she reads." The control EEG showed only occasional synchronous bifrontal interictal epileptiform activity in bursts of 1-2 seconds duration. Valproic acid 1 g a day was added, with which the "events" described by the patient disappeared completely and the EEG normalized.

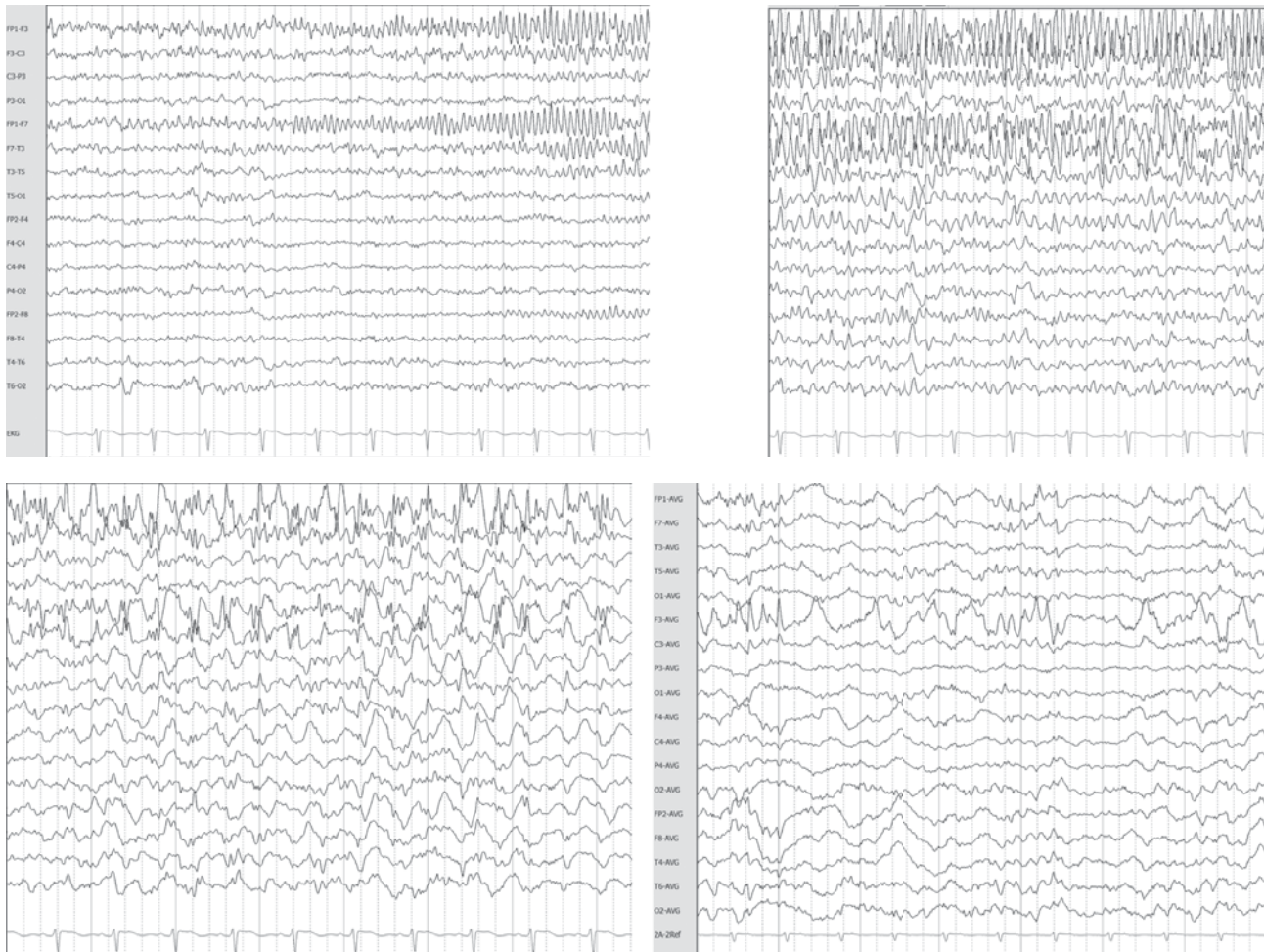
DISCUSSION

The psychiatric manifestations of NCSE cover a wide psychopathology spectrum. In some cases, symptoms may be so subtle that they are recognized only by friends or relatives. The frequent absence of confusion or motor symptoms is among the factors responsible for the common delay in diagnosis.

The characteristics of the different types of NCSE will be examined below.

Simple partial NCSE

Simple partial NCSE is characterized clinically by the presence of symptoms in the absence of impaired



EEG

Recurrent epileptic seizures that initiate with rapid, low-voltage activity in the beta range on electrode Fp1. As the seizure progresses, the voltage increases and the frequency decreases, later evolving into a polyspike type pattern with irregular waves located in the left frontal region with maximum frontopolar negativity. Between seizures, slow waves and left frontal seizure-like activity are present

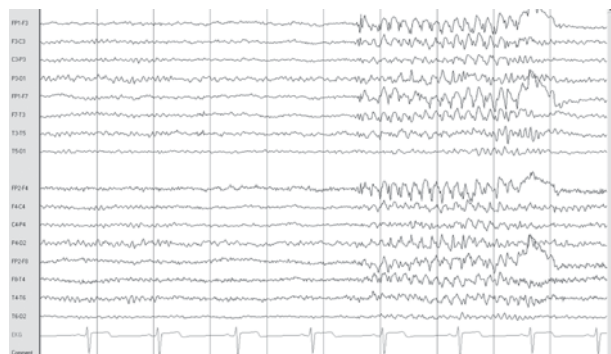
Figure 1

Partial simple status epilepticus of frontal origin

consciousness in one of the following areas: somatosensory, visual, auditory, vegetative, mental, cognitive, affective or behavioral. Behavioral changes are one of the clinical manifestations of simple partial NCSE, though little known about them because they occur without impaired consciousness.

Some authors use the term "continuous aura"^{2, 3} to describe prolonged episodes of sensory symptoms identical to the aura experienced as the initial manifestation of epileptic seizures, which can last from hours to days. While this term is not found in current glossaries of epileptic symptoms, in the opinion of some authors^{2, 4} it may be an

appropriate clinical description to refer to this subtype of simple partial NCSE. This diagnosis is sometimes difficult to prove because the findings of surface electroencephalograms often are falsely negative. However, well-documented cases in the literature support the ictal nature of this phenomenon. Reported cases include patients who have experienced prolonged episodes of ictal fear^{4, 5} and psychological or vegetative symptoms³. A "dreamy state" is also described in seizures originating in medial temporal structures, consisting of a feeling of having previously experienced the same situation (*déjà vu*).⁶ In cases of ictal activity located in the amygdala, the findings of the surface EEG may be falsely negative, so recordings with sphenoidal electrodes (under



EEG

Recurrent epileptic seizures characterized by spike-and-wave onset, at about 4-5 cps, of synchronous bilateral frontal origin that evolves into a rhythmic theta pattern at the same location with a tendency to generalization. This activity occurred successively in bursts of 6 to 12 seconds duration

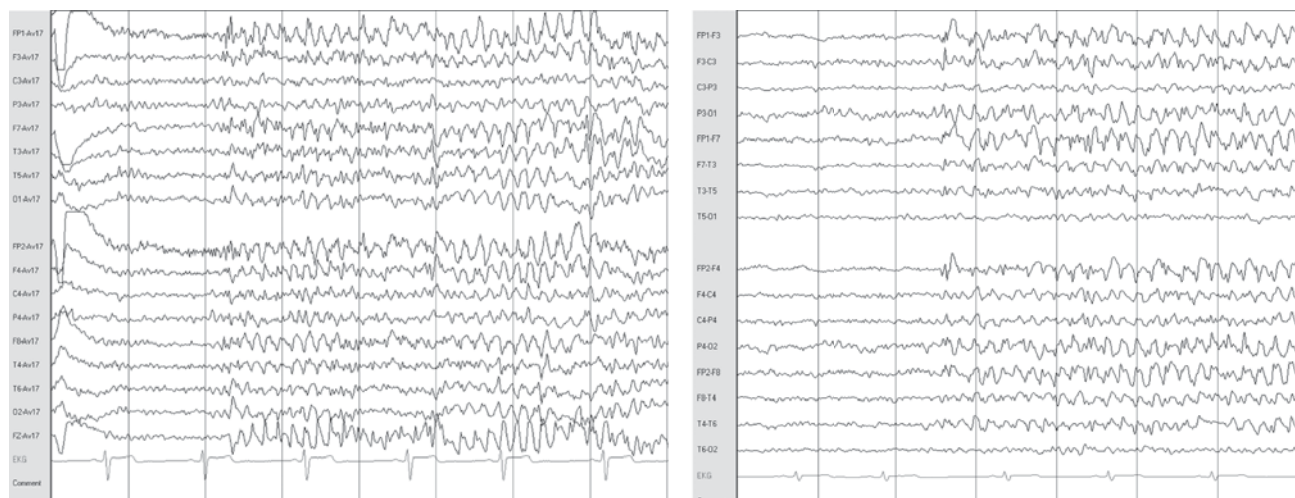


Figure 2

Nonconvulsive status epilepticus of frontal origin

fluoroscopic view) are needed to demonstrate seizure activity.⁷

In contrast to simple partial NCSE originating in the temporal lobe, frontal simple partial NCSE often occurs without confusion.^{8,9} This entity has been recognized since the 1970s with different names, such as "absence status with focal characteristics," "prolonged cyclic epileptic seizures," "frontal prolonged ictal confusion," "frontal nonconvulsive confusional status," "complex partial status of frontal origin" and "frontal status."

In 1988, Rohr-Le Floch et al.⁸ reported a series of 60 patients with NCSE, of which 18 had NCSE of frontal origin. It is noteworthy that 57.5% of these patients did not exhibit confusion. The most common clinical manifestation in these patients is the euphoric-like behavior disorder and difficulty in planning complex tasks associated with certain clinical features such as collusion and inappropriate laughter, which

are not evidenced in any state of absence or NCSE originating in the temporal lobe.

Thomas et al.¹⁰ later identified two types of NCSE of frontal origin in a series of ten patients. Type I: In seven patients there was no clear alteration of consciousness. The clinical manifestations of these patients were disorders of mood and behavior, either through a hypomanic state with affective disinhibition, increased verbal fluency or, conversely, a state of emotional indifference with diminished facial expression, reduced verbal fluency and decreased emotivity and spontaneous activity. After episodes of simple partial NCSE, most patients were able to recall what had occurred during the episode. Simple automatisms are often observed, such as picking at clothes and scratching. No oroalimentary or manual automatisms are evident. In all these patients, the electrical pattern consisted of unilateral frontal ictal activity. Type II: Three patients presented with a confusional state and temporospatial disorientation, evident

behavioral disorder and perseverance. In two patients, the ictal pattern consisted of recurring seizures that affected both frontotemporal regions. The remaining patient showed recurrent seizures of bilateral central frontal origin. In this series, 6 of the 10 patients had frontal lesions.

Simple partial NCSE may also present with visual hallucinations or, less often, auditory hallucinations. In contrast to what occurs with "psychotic" hallucinations, the hallucinations of NCSE are perceived as "unreal".¹²

According to several authors, NCSE of frontal origin is often underdiagnosed and confused with primarily psychiatric disorders, resulting in a delay in starting treatment.^{10, 11}

Absence type NCSE

Absence type NCSE is characterized by sudden onset, without aura, often accompanied by palpebral or perioral myoclonus that varies in severity.^{13, 14} Patients may appear alert and cooperative, but although verbal function is maintained, their language is slow and they often answer with monosyllables or stereotyped words. The descriptions of patients who have been in this condition are illustrative: "My mind slows down, I can understand but it takes me longer to respond, I lose fragments of conversation ... as if I were in a trance ...".¹³ Most cases occur in patients whose epilepsy persists as a primarily generalized form in adulthood, or whose epilepsy disappears and is later reactivated as an absence type NCSE. There is also a so-called adult "de novo" absence that usually occurs later in life, on average at an age of about 50 years. It has been described as a consequence of discontinuing benzodiazepines.¹⁶

On the other hand, there are isolated reports of cases of ictal catatonia as an expression of NCSE.¹⁵ Kanemoto et al.¹⁷ described the case of a 78-year-old patient who presented with a history of mutism, which had started one week earlier, alternating with episodes of psychomotor agitation. On examination, the patient was awake but had a fixed gaze. He occasionally responded to questions using appropriate, but fragmented, language. His limbs remained in a passive, atypical pattern. He had no neurological deficit, history of epilepsy or previous psychiatric history. The EEG showed continuous epileptiform activity in the form of spike-and-wave discharges of generalized distribution (1.5-2 Hz), consistent with an absence type NCSE. A detailed interview with his wife revealed that he had discontinued benzodiazepines. Diazepam administration resulted in resolution of his abnormal behavior and catatonic symptoms. What was most remarkable about this case, aside from the symptoms, was that EEG made the diagnosis possible. This examination should be made in all patients presenting sudden onset catatonia, especially if it occurs "de novo" in older patients.

DIAGNOSIS

Patients with epilepsy often present seizures with cognitive and psychiatric symptoms; these symptoms often are not recognized by clinicians as a manifestation of an ictal phenomenon. This is reflected by the fact that NCSE is often confused with a psychiatric condition, which delays the onset of antiepileptic therapy.^{10, 11}

Since the diagnosis of NCSE requires electroencephalographic study, high-grade initial clinical suspicion is needed. This entity can be easily overlooked if not considered in the differential diagnosis of patients presenting with subtle cognitive or behavioral changes. Under ideal circumstances, any patients with these symptoms should be studied by EEG. However, this is not always possible for a variety of reasons. For this reason, Husain et al.¹⁸ made a study to assess whether clinical characteristics could be identified that might predict which patients are at the greatest risk presenting NCSE. The study shows that the presence of abnormal eye movements (repeated blinking, nystagmus, gaze aversion) in combination with the presence of remote risk factors for seizures (previous strokes, neurosurgical intervention, history of meningitis, brain tumors) have a high combined sensitivity for predicting NCSE.

Neuroimaging studies can also be useful in the diagnosis of NCSE. In some cases, focal abnormalities in cerebral magnetic resonance imaging can be observed as a result of local edema (hyperintensity on T2) or enhanced local perfusion (hyperintensity on diffusion sequences). These changes resolve spontaneously after the cessation of seizure activity. SPECT may also be useful in demonstrating a hyperperfusion focus in NCSE cases of focal origin.¹⁰

In young patients, especially patients with mild mental retardation and brain scans that show no significant injury, it is important to rule out ring chromosome 20 syndrome.¹⁹

CONCLUSIONS

NCSE is a heterogeneous condition, with a number of subtypes and varied electroclinical manifestations. The frequency of NCSE is thought to be higher than reported and it is probably often underdiagnosed or diagnosed late. NCSE should always be considered in the differential diagnosis of patients presenting with cognitive or behavioral disorders of sudden onset. Electroencephalographic study is essential for the early diagnosis and prompt treatment of NCSE.

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