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Non-convulsive status epilepticus characterised exclusively by a language disorder induced by non-ketotic hyperglycaemia

Stefano Pro, Franco Randi, Patrizia Pulitano, Edoardo Vicenzini, Oriano Mecarelli

Department of Neurology and Psychiatry, Sapienza University of Rome

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ABSTRACT – Non-ketotic hyperglycaemia is an endocrine emergency characterised by elevated blood glucose levels and high plasma osmolarity. While hypoglycaemia-induced seizures are usually generalised, hyperglycaemia-induced seizures are often focal and secondary to the presence of brain lesions. Moreover, in the few studies in which language disorders of epileptic origin have been reported as a clinical manifestation of non-ketotic hyperglycaemia, the disorders were usually not isolated but were followed by partial motor seizures. We describe a patient who presented with non-convulsive partial status epilepticus and whose only sign was a fluctuating language disorder induced by non-ketotic hyperglycaemia. There were no accompanying brain lesions and the patient responded optimally to diazepam. Neurophysiological EEG evaluation was fundamental for the diagnosis.

Key words: non-ketotic hyperglycaemia, partial status epilepticus, transient language disorders

Non-ketotic hyperglycaemia (NKH) is an endocrine emergency characterised by elevated serum glucose levels and high plasma osmolarity, but without, or only very slight, ketoacidosis. NKH may initially manifest through a wide range of neurological symptoms, including headache, somato-sensory disturbances, visual hallucinations, choreoathetosis, hemiballismus, coma and seizures (Chung *et al*., 2005).

While hypoglycaemia-induced seizures, which are usually generalised, have been extensively described in the literature, hyperglycaemia-induced seizures are often focal and secondary to brain lesions in cases of cortical venous infarction, although the exact mechanism of focal motor seizures without a localised lesion is unknown (Stahlman *et al*., 1988). Epilepsia partialis continua with an ictal EEG manifestation, believed to

Correspondence:
S. Pro
Department of Neurology and Psychiatry/Neurophysiopathology Unit, Sapienza University of Rome,
Viale Regina Elena 336,
00185 Rome, Italy
<stefanopro1974@libero.it>

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originate in the frontal lobe, has previously been described in NKH in one patient with a temporal epileptic focus (Cokar *et al*., 2004). Some cases with focal origin from the occipital origin have also been described (Moien-Afshari and Tellez-Zenteno, 2009). Only one case presenting pure alexia with agraphia and without motor manifestations, although with transient brain alterations, has been published to date (Kutluay *et al*., 2007).

We describe a patient affected by NKH presenting with non-convulsive partial status epilepticus whose only symptom was a fluctuating language disorder. There were no accompanying brain lesions and the patient responded very well to diazepam.

Case study

A 52-year-old male patient was admitted to our hospital after three days of transient, short episodes of language disturbance and incoherent speech. The patient had a low educational level (five years) and a history of an impulse-control disorder, including compulsive gambling and the purchasing of sweets, as reported by his wife. Moreover, there was no history of pre-, peri- or postnatal causative factors known to influence brain insults or developmental deficits. In the year prior to hospitalisation, several routine blood examinations had shown a slight increase in the patient's glycaemia (130-150 mg/dL); he had thus started treatment with oral anti-diabetic drugs, although the level of compliance and dietary control were poor.

When the patient was first examined upon admission to the emergency room, he was awake and cooperative, but displayed incoherent speech and an aggressive attitude. When questioned, he was able to understand and execute simple verbal orders, but he could not repeat words or sentences. This disturbance fluctuated, with moments in which the patient's speech worsened or ceased completely, alternating with short spells of normal verbal output. When verbal output was normal, the patient, if questioned, was lucid and oriented. The rest of the neurological examination was unremarkable. Blood samples showed hyperglycaemia (350 mg/dL) with slightly increased osmolarity (290 mOsm/L) and with an increase in glycated haemoglobin (12.8%). Chest X-rays, cerebral computed tomography (CT), magnetic resonance imaging (MRI) and carotid ultrasound were all normal. The hyperglycaemia was treated with subcutaneous insulin (V IU//tid) until glycaemic control was achieved.

The day following the patient's admission, the language disturbance persisted with the same fluctuating characteristics of short periods of complete speech arrest, alternating with incoherent speech and apparent language normality. Comprehension, as assessed by the responses to verbal orders, when possible, was preserved. Following a psychiatric examination which revealed some degree of persecutory ideation and in view of the patient's clinical history, a presumptive diagnosis of a psychiatric disorder was made and the patient was given haloperidol (5 mg *i.v.*) twice, four hours apart, although with no beneficial effect. Blood glucose had, by then, dropped to 135 mg/dL.

A standard EEG (S/EEG) was then performed. After initially detecting only a slight slowing of the background activity at rest, an electroclinical seizure was recorded after two minutes of hyperventilation *(figure 1)*. The seizure, which lasted 60 seconds, was characterised by the presence of fast activity over the left temporal region with a frequency of 14-15 Hz *(figure 1A)*, followed by high voltage, irregular sharp and slow waves *(figure 1B)* and an abrupt termination with minimal EEG background slowing and gradual recovery *(figure 1C)*. The patient presented speech arrest during EEG epileptic discharges, as described above, with recovery after almost one minute following discharge termination. Given the fluctuating nature of the symptoms, which never totally resolved, the patient underwent continuous EEG monitoring, aimed at quantifying the epileptic activity immediately thereafter. A total number of 202 epileptic discharges, with a mean discharge duration of 120±90 seconds and a total duration of 309.55 minutes, were recorded over a period of 15 hours (900 minutes). No other alteration was observed during interictal phases. Given the total duration of the EEG discharges, non-convulsive partial status epilepticus was diagnosed and the following morning (*i.e.* on the third day) the patient was given a bolus of diazepam (10 mg *i.v.* over 3 minutes), while still under EEG monitoring and in the presence of persisting fluctuating symptoms. Following the administration of the benzodiazepine, EEG-documented regression of the epileptic activity was observed after one minute from the end of injection and speech gradually improved until it completely recovered. Although this episode was interpreted as an acute symptomatic seizure, given the outcome of the psychiatric examination, the patient was placed on carbamazepine monotherapy, titrated up to final dosage of 600 mg/day. The choice of this therapy was based, in part, on the effects it has on mood stabilisation. At discharge, the patient's neurological examination and S/EEG were completely normal with good representation of background alpha rhythm, his blood glucose levels had returned to normal (120 mg/dL) and hypoglycaemic agents combined with strict dietary control were again prescribed.

Ten months later, the patient was seizure-free, without any language disorders, and had a normal S/EEG. The patient was compliant to therapy and carbamazepine fell within the therapeutic range (6.8 ng/mL).

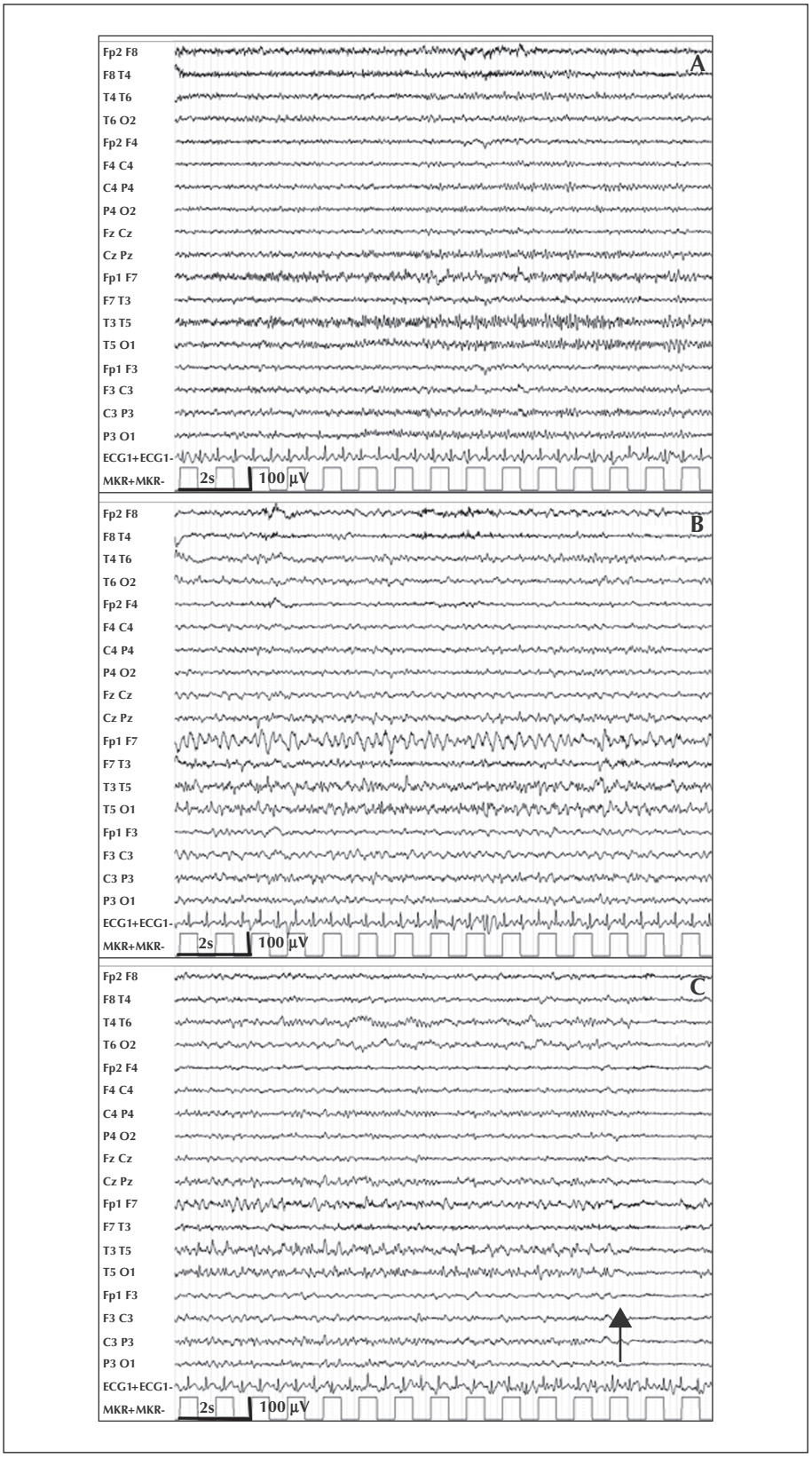

Figure 1. Ictal EEG during hyperventilation showing fast activity over the left temporal region, with a frequency of 14-15 Hz (**A**), followed by high voltage and irregular sharp-and-slow waves (**B**) and an abrupt termination (arrow) (**C**). No differences in speech disturbance were present during the epileptic discharge. Recovery was not prompt after the end of discharge, requiring almost one minute.

The patient's blood glucose levels ranged from 160 to 185 mg/dL, although compliance with the dietary restrictions and oral anti-diabetic treatment remained poor. Neuropsychological testing, including the Bender-Gestalt test, Toulouse-Pieron test, WAIS-R test and Rorschach test, revealed a low intellectual level (IQ: 70), with "reduced criticism and reaction to external stimuli and normal verbal output". No compulsive gambling, shopping or other psychiatric symptoms were reported by his wife.

Discussion

Hyperglycaemia in diabetic patients may induce epileptic seizures, especially of focal origin (Stahlman *et al*., 1988). Epileptic seizures occur in up to 25% of cases of non-ketotic hyperglycaemia, and in 50% of cases at the onset of diabetes, with blood glucose levels ranging widely from 265 to 900 mg/dL (Scherer, 2005).

Seizures are usually resistant to antiepileptic drugs if blood glucose is not kept under control (Lavin, 2005). Some authors have suggested that a focal cerebral lesion (pre-existing or acute) is a predisposing factor for focal seizures in patients with non-ketotic hyperglycaemia (Siddiqi *et al*., 2002). However, Schwechter *et al*. (2003) documented that hyperglycaemia may *per se* be proconvulsant, even in the absence of organic brain lesions. A decrease in GABA levels and KATP channel conduction during hyperglycaemia, followed by an increase in neuronal excitability induced by high extracellular glucose concentrations, have been hypothesized as precipitating factors (Moien-Afshari and Tellez-Zenteno, 2009).

The patient we describe presented non-ketotic hyperglycaemia with partial non-convulsive status epilepticus clinically characterised exclusively by a fluctuating language disorder. With regards to the possible pathogenesis of this disorder, it should be borne in mind that the patient did not present any organic brain lesion, as demonstrated by normal CT and MRI. The episode presented by our patient may thus be interpreted as a case of acute recurrent symptomatic seizures, secondary to non-ketotic hyperglycaemia. Changes in neurotransmitter-mediated mechanisms coupled with cerebral metabolic dysfunction might induce these epileptic manifestations in a patient with an alteration in glycaemia, but would not be sufficient to induce a stupor or coma.

Our case is a very rare presentation of non-convulsive status epilepticus characterised exclusively by a language disorder. To our knowledge, there is only one previous description of NKH-induced partial status epilepticus characterised solely by a language disorder. In 2007, Kutluay *et al*. described a man with pure alexia without agraphia. The brain MRI scan, performed upon admission, revealed cortical swelling and an increased signal in the temporo-occipital and middle temporal *gyrus* FLAIR sequences. A follow-up brain MRI scan, performed one month later, was normal. The transient MRI abnormalities observed in this patient were probably due to the partial status epilepticus itself.

In such cases, the differential diagnosis between epileptic and non-epileptic seizures may be difficult for both the neurologist and the psychiatrist: in our patient, for example, the paroxystic fluctuating language disturbance was initially misinterpreted as a psychotic state. We recommend that an EEG evaluation, particularly by means of serial or continuous recordings, be performed to identify non-convulsive status epilepticus, particularly in cases with proconvulsant factors such as NKH, even in the absence of organic brain lesions. □

Disclosure.
None of the authors has any conflict of interest or financial support to disclose.

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