Reflex epilepsy and non-ketotic hyperglycemia

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ABSTRACT – Epileptic seizures are paroxysmal events, and it is likely that many, if not most, of them are precipitated by known or unknown factors acting on a central nervous system that is predisposed to the production of epileptic discharges by the presence of an organic lesion, a genetically determined neuronal hyperexcitability, or both. Known precipitating influences are quite varied. We report the case of a 58 years-old patient, followed for non-ketotic hyperglycemia, who presented with focal seizures exclusively induced by specific, active or passive, postures and movements of the right arm or hand. MRI was normal. Following regulation of glucose blood levels the position-induced seizures stopped and antiepileptics were not prescribed. The seizures are kept under control by regulating blood glucose. [Published with video sequences].

KEY WORDS: reflex epilepsy, non-ketotic hyperglycemia, posture-induced seizures

Case presentation

The 58 years-old patient was admitted to the emergency department with the complaint of repeated seizures during the previous 4 days, involving the right hand and forearm. During hospitalisation it was observed that the seizures began when the upper right extremity was activated, especially when the right hand was brought to slight extension and pronation and when the forearm was flexed 20 to 30 degrees from the elbow. When the position changed, the seizures stopped within the next 2 minutes. The patient had a two-years history of diabetes. He was treated with gliclazide (Diamicron®) tablets at a dose of 80 mg/day, but compliance was not optimal. At the time of hospitalisation, glucose blood level was 400 mg/dL. Administration of phenytoin failed to control the paroxysmal events.

The next day, a cranial CT scan, without contrast injection, demonstrated no lesion. On the first EEG, an epileptogenic focus of frequently repeated sharp and slow wave discharges was seen at the left fronto-temporal region (figure 1). An attempt was made to
regulate his glucose blood levels. Meanwhile, a second EEG investigation was undertaken and the patient was asked to move his right arm to a given posture and to maintain this posture as long as possible. During the EEG examination, when the patient tried to lift the right arm, partial motor seizures started when the right forearm came to semi-flexion and light pronations. A little later, secondary generalization accompanied by loss of consciousness was observed (Video sequences). Ictal EEG revealed irregular spike-slow wave discharges of high amplitude, which started from the left fronto-central region, extended to the temporal and occipital regions and then diffused to the right hemisphere, mainly in the frontal region (Figure 2A and B). On the 4th day, cranial magnetic resonance imaging (MRI) was performed, with a 1.5 Picker Edge scanner, including sagittal SE T1, axial SE T1, FSE, PD T2 and coronal Flair sequences. As for the CT scan, MRI was considered normal.

When the blood glucose levels decreased to 140 mg/dL, on the 5th day of hospitalization, the position-induced seizures ended. The patient had no other seizures during the remaining 20 days of hospitalization. During the next 2 months of follow-up, no seizures were reported, although the patient received no anti-epileptic therapy.

Discussion

Our patient presented, over 4 days, repeated motor seizures of the right arm. During that same period, his blood sugar levels were found to be high. Ictal EEG demonstrated a sharp slow wave pattern in the left fronto-temporal lobe. Paroxysmal events occurred in specific positions of the arm. We suggest that our patient presented with proprioceptive-induced reflex seizures related to his unstable blood glucose levels.

Reflex epilepsy refers to seizures that are regularly precipitated by a specific identifiable stimulus [1]. The International League Against Epilepsy (ILAE) identified reflex epilepsies as those “characterized by specific modes of seizure precipitation” and classified them as “special syndromes”. According to the provocation mechanism, “reflex” seizures can be divided into a simple and a complex group [5]. Triggering factors include: visual (photic stimulation, patterns, TV, video games, eye closure, eye fluttering, colors); auditory (music, a specific sound or voice); somatosensory (tap or touch, hot water immersion, tooth brushing); mental (calculation, problem-solving, card games, drawing); motor (movement-induced, swallowing, eye movements); and other (reading, eating) stimuli [1-4, 6].

For the study of reflex epilepsies have been two animal models used. The first model has been known since 1929 [6]. In this model, convulsions are induced by intermittent photic stimulation following strychnine application to the visual cortex. With this technique, focal cortical irritative lesions of auditory, gustatory and olfactory cortices are created [6] and seizures are induced with afferent stimuli. The second model of naturally occurring reflex epilepsy is induced by specific sensory stimulations in genetically predisposed animals [6]. Seizures associated with proprioceptive stimuli are rare [5-8]. They can result from an active or passive movement of a limb. Gowers [9] was the first to describe seizures associated with movements in humans. In their pathophysiological studies on monkeys, Chauvel and Lamarche [10] induced seizures by external stimulation, by creating a lesion in the pre-rolandic region. They demonstrated that
proprioception was the most important triggering factor. Focal motor seizures and seizures related to posture have also been reported in cases of non-ketotic hyperglycemia [7]. Neuronal response to afferent stimuli may be more sensitive to glucoses than other factors [11].

In the presence of a cortical lesion, hyperglycemia can facilitate an increase in frequency of focal motor seizures. Localized tissue hypoxia may account for focal seizure activity in diabetics. Local hypoxia leads to cell oedema, which increases movement of sodium into the cell, which in turn facilitates repetitive discharges of the cells [8]. Additionally, cellular oedema decreases the extracellular distance, leading to a decrease in the number of neurotransmitters, an increase in ephaptic transmission and lowers the seizure threshold. Brick et al. have described the focal motor seizures induced by movement in non-ketotic hyperglycemic patients [7]. No brain lesion could be seen on CT scan in any of these patients. However, in a case of non-ketotic hyperglycemia with focal seizures induced by posturing of the right hand, Siddiqi et al. [8] demonstrated, on MRI, a subacute infarct of the right frontal region. The authors noted that CT scan in early phases was unable to show the lesion, and recommended MRI to demonstrate the lesions, especially in early cases. In our case, focal motor seizures developed on posturing of the right arm. When the posture of the right hand was maintained for a long time, focal clonic seizures generalized. The particularity of our case relies on the fact that

Figure 2A-B. Ictal EEG revealed irregular spike-slow wave discharges of high amplitude, which started at the left fronto-central region, extended to temporal and occipital regions and diffused to the right hemisphere.
neither CT scan nor MRI investigations revealed a cortical lesion. Posture-related seizures remained uncontrolled despite a phenytoin loading dose, but they stopped following the regulation of glycemia.

The fact that no lesion could be seen on brain CT and MRI suggests that the seizures could result from the metabolic disturbance and this could also be the case in previously reported, non-lesional patients.

Hyperglycemia creates a hyperosmolar gradient between intracellular and extracellular neuronal compartments with subsequent dehydration, producing partial seizures [12]. Furthermore, the Krebs cycle is inhibited [7, 13]. This leads to an increase in GABA metabolism, through the succinic semialdehyde pathway. Depressed brain GABA levels presumably lower the seizure threshold. In a case with reflex seizures related to the movement of the left hand, ictal SPECT showed a focal cortical hyperperfusion during extratemporal partial seizures [14].

Which neuronal pathways are involved and how they are activated to generate reflex seizures remains unknown. Based on the fact that MRI was normal in our patient, we speculate that seizures could be related to an increase in GABA metabolism, related to glycemia, without any ischemia. Gabor [15] and Brick et al. [7] have stated that increased activity in reflex pathways might be secondary to decreased utilization possibilities of GABA in cortical or subcortical-cortical levels.

This type of reflex seizure is mostly seen in elderly patients. Hyperglycemia should therefore be thought of in such cases. Controlling hyperglycemia alone could be sufficient to end the seizures and could avoid the use of heavy antiepileptic therapy.

References