

## CASE REPORT

# Reflex seizures and non-ketotic hyperglycemia: an unresolved issue\*

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Reflex seizures are a rare form of epilepsy, the pathogenesis of which is unclear. They have been reported in the setting of non-ketotic hyperglycemia (NKH) and are considered to be neuroendocrine in origin. We report a diabetic patient with movement-induced seizures whose presentation suggests that brain ischemia may be the precipitating event in focal seizures seen in the setting of NKH. We recommend that in such instances a focal lesion such as stroke should be ruled out.

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Reflex epilepsy is a well recognized, albeit rare, form of epilepsy in which seizures are regularly elicited by some specific stimulus or event. Several forms of sensory stimuli have been recognized to be epileptogenic in susceptible individuals<sup>1</sup>. These include simple sensory stimuli such as visual patterns, light, noise and olfaction as well as proprioceptive stimuli from voluntary movements.

In spite of several accounts of reflex seizures in humans, the mechanisms underlying such seizures have not been identified. Specifically, it is not clear whether a structural, metabolic or physiological alteration in the neurons renders them more prone to repetitive discharges when stimulated by an afferent signal. We report a patient who presented with movement-induced partial seizures and was found to have an area of ischemic injury that was spatially and temporally associated with the onset of seizures.

## CASE PRESENTATION

A 66-year old, right-handed male with poorly controlled diabetes was brought to the emergency

department (ED) for spells that started 3 days prior to his presentation. They consisted of an episodic loss of awareness and inability to use his hands. His wife described the initial episode as the patient being unable to use the phone. When the handset was handed to him, he held it in his right hand but was unable to talk, appeared to be confused and minimally responsive. Over the next 2 days the patient had several similar spells. No clonic activity was observed during any of these events. Each spell lasted for about 2 minutes and the patient gradually returned to baseline. His past medical history was significant for diabetes diagnosed three years prior to this presentation. The patient denied any history of seizures or a cerebrovascular event. His medications on admission included insulin, glipizide, and paroxetine. The patient had a normal general physical and neurological examination.

Initial work up revealed a blood glucose level of 366 mg dl<sup>-1</sup> without detectable ketosis. The calculated serum osmolality was 305 mosm l<sup>-1</sup>. An initial non-contrast brain computerized tomography (CT) scan was normal, and a routine electroencephalogram (EEG) showed mild left temporal slowing.

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The description of the spells was considered to be consistent with partial seizures, and the patient was loaded with phenytoin. Over the next 24 hours, seizures persisted despite high therapeutic phenytoin levels. The patient's blood glucose level remained above 250 mg dl<sup>-1</sup>. A brain magnetic resonance imaging (MRI) study revealed a subacute infarct in the left frontal lobe adjacent to the anterior aspect of the prefrontal gyrus (Fig. 1).

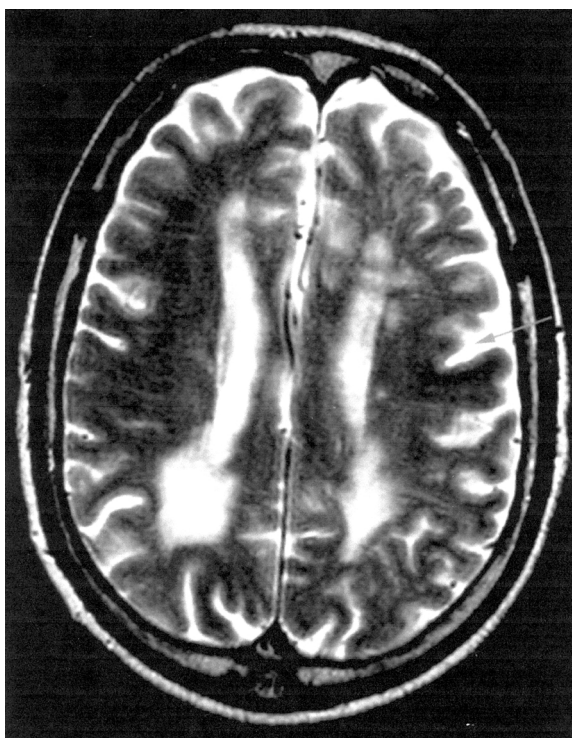


Fig. 1: MRI scan demonstrating subacute infarct in the left prefrontal area.

All seizures were stereotypic and were consistently reproducible whenever the patient tried to write. Seven seizures were captured with video-EEG monitoring. During the seizure the patient would suddenly stop talking, stare at his right hand and appear confused. Occasionally automatisms of his right upper extremity would be noted during the spell. Postictally, he would remain confused for a few minutes, unable to remember the objects presented to him. The EEG of a typical seizure showing a subtle left temporal rhythmic discharge is shown in Fig. 2.

Seizure control was achieved only after the patient became normoglycemic. The patient was discharged on tapering dose's of phenytoin. Currently, with adequate control of his blood sugar, he continues to remain seizure free and is off all antiepileptic drugs (AEDs).

## DISCUSSION

Movement-induced or proprioceptive seizures are a rarity and have been reported to be evoked by active or passive movements of an extremity, tapping of the tendons as well as posturing of a body part. Posture-induced and spontaneous focal motor seizures can occur in the setting of non-ketotic hyperglycemia (NKH), and at times are reported to be the first manifestation of a new-onset diabetes mellitus<sup>2,3</sup>.

Brick *et al.*<sup>2</sup> presented a series of five patients with NKH who had movement-induced seizures. Hennis *et al.*<sup>3</sup> reported on seven patients with diabetes, three had movement induced focal motor seizures. None of the patients in either series had brain lesions detected on CT. In both reports, voluntary movement of an extremity induced seizures. The most common seizure manifestation was clonic activity of the part of the body whose movement triggered the seizure. Since structural brain lesions have not been identified in these patients, seizures occurring in the setting of NKH have been considered to be a neuroendocrine manifestation of the metabolic disorder<sup>2</sup>.

Despite the similarity in the presentation of our patient to the patients in earlier reports, some intriguing differences remain. As compared to the simple focal clonic activity observed in most patients with NKH, the seizures in our patient consisted mainly of posturing of the right hand with brief alteration in sensorium in response to a specific movement/posture of the right hand. Only one patient in the earlier studies<sup>2</sup> had a similar presentation. Brain lesions were not seen in earlier reports, however a brain MRI scan in our patient demonstrated a subacute infarct in the left prefrontal region, but an earlier CT scan, the imaging modality used in earlier studies<sup>2,3</sup>, had not revealed the lesion. It is possible that if MRI imaging had been available to the investigators in the earlier studies, brain lesions may have been detected.

The temporal association of the ischemic event with the onset of seizures and the location of ischemia in the appropriate region of the left prefrontal cortex suggests that the stroke may have provoked the movement-induced partial seizures in this patient with NKH. Evidence of this comes from Chauvel and Lamarche<sup>4</sup> who showed that proprioception was the inciting stimulus for seizures in monkeys with experimental lesions in the prerolandic cortex. They reasoned that proprioceptive afferents appeared to trigger the hyperexcitable lesioned area of the cortex leading to generation of focal motor seizures in the contralateral limb.

Several lines of evidence indicate that localized tissue hypoxia may be a likely explanation for the



Fig. 2: EEG during movement-induced seizure.

focal seizure activity seen in diabetics. Firstly, at the cellular level, brain ischemia results in loss of activity of the sodium and potassium pumps in neurons. This leads to cellular swelling from failure to maintain an ionic balance across the cellular membrane. Such ionic imbalances have been reported to predispose the cells to repetitive discharges by increasing the sodium inside the cells<sup>5</sup>. Additionally, cellular swelling from ischemia decreases the extracellular space, which, in turn, decreases the seizure threshold by reducing the dilution of neurotransmitters in the extracellular space, decreasing efflux of the neurotransmitters from the reduced space and increasing ephaptic transmission.

Secondly, seizures are a common manifestation of ischemic stroke and estimated to occur in about 5% of patients with acute strokes<sup>6</sup>. Like the reflex proprioceptive seizures, seizures in the early stroke period are usually focal, brief and motor and do not require long term AEDs<sup>7</sup>.

Finally, metabolic derangements have been shown to precipitate epileptiform discharges in the setting of structural abnormalities. Neuffel *et al.*<sup>8</sup> have reported that in the presence of a stroke, hyperglycemia

seems to predispose the brain to ictal as well as interictal epileptiform activity. Li *et al.*<sup>9</sup> have shown that seizures can only be triggered in diabetic rat models with experimentally induced strokes once the blood glucose level reached a critical level. The hyperglycemia aggravates brain damage that leads to generation of seizure activity.

Reflex proprioceptive seizures in the setting of hyperglycemia may be a manifestation of a focal brain lesion rather than simply a neuroendocrine phenomenon. An MRI should be obtained to evaluate such a lesion. Control of seizures in this setting is possible only when the NHK is controlled and AEDs do not appear to be necessary.

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