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Atypical postictal transient subcortical T2 hypointensity in a newly diagnosed diabetic patient with seizures

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ABSTRACT – Common postictal MRI findings include transient cortical T2 hyperintensity, restricted diffusion, and gyral and/or adjacent leptomeningeal contrast enhancement. In certain uncommon pathological conditions, other signal abnormalities can be present, suggesting a different underlying pathogenic mechanism. We report the case of a 66-year-old man, recently diagnosed with diabetes mellitus type 2, presenting with new-onset visual and auditory hallucinations, "absence" seizures, and repeated peaks of hyperglycaemia without hyperketonaemia or increased serum osmolarity. EEG confirmed epileptic discharges in the right temporal region and MRI showed vast subcortical T2 hypointensity in the right temporal lobe, without any cortical hyperintensity, restricted diffusion, or contrast enhancement. Subcortical signal abnormality and EEG discharges resolved after a month of follow-up, with a small juxtacortical gliotic focus as a sequela. Peaks in hyperglycaemia have been reported to be responsible for T2 hypointense subcortical abnormalities through a proconvulsant mechanism linked to increased ketone body concentrations. Hyperosmolarity and hyperketonaemia were not evident in this case, however, transient accumulation of free radicals that alter the intercellular space can be considered the presumable cause of this finding. In summary, it is important to consider any unusual findings on postictal MRI in order to avoid errors in interpretation.

Key words: epileptic seizures, postictal, T2 hypointensity, transient subcortical MRI abnormalities, non-ketotic hyperglycaemic hyperosmolar state

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Several different signal alterations have been reported on postictal MRI, which do not necessarily represent the underlying pathologies that cause seizures. Such abnormalities tend to associate with local effects, and their transient nature is generally interpreted as direct confirmation of such effects (Hemanth *et al*., 1995; Yaffe *et al*., 1995).

Cortical-juxtacortical hyperintensities on T2-weighted (T2w) and fluid attenuated inversion recovery (FLAIR) images are the most common finding on postictal MRI, and T2 prolongation is predominantly linked to fluctuations in intra- and extracellular water, that leads to cellular swelling. In parallel, gyral restricted diffusion on diffusion weighted imaging (DWI) can be the other face of cellular swelling seen on T2w images. Apart from the T2 signal component, which is intrinsic to DWI imaging, a reversible cytotoxic oedema (pathogenically different from that of ischaemia) has been reported to be responsible for restricted diffusion in the postictal state. Whereas T1-weighted (T1w) non-contrast-enhanced images may be reported as normal, gyral or adjacent leptomeningeal enhancement after contrast administration can be present. Reasons for contrast enhancement include increased perfusion due to transient hypermetabolism, together with an alteration of blood-brain barrier permeability due to a combination of hypoxia, hypercarbia, and lactic acidosis. Permanent signal alteration may be present also, but not within the immediate postictal phase. During follow-up MRI, a T2w hyperintense focus of gliosis commonly results in a sequela of seizures, usually at the juxtacortical level.

Here, we report the case of an adult male in his sixties, with no previous neurological history, who had new-onset focal seizures and atypical postictal MRI findings, in the context of *de novo* diabetes mellitus type II.

Case study

A 66-year-old man with unremarkable neurological history presented with several episodes of auditory hallucinations and "absence" episodes lasting for 1-2 minutes, with the longest episode lasting for six minutes within the last few weeks. Only recently, and because of such symptoms, a blood panel was performed, revealing repeatedly increased fasting glucose levels, with glycaemia up to 313 mg/dL. The only reported therapy the patient was receiving was ASA at 100 mg/day, *per os*, for reasons that were poorly defined. On the day of admission, while talking with his wife, the patient experienced a visual hallucination in which he was convinced he was talking with his daughter, who was not present at that moment. The hallucination lasted for about three minutes, followed by aggressive behaviour, laughter, and slow speech. As a consequence, medical assistance was sought and the patient was admitted to the general hospital emergency department, where blood pressure, ECG, and neurological examination were reportedly normal. A blood panel revealed glycaemia at 266 mg/dL, HbA1c at 137.2 mmol/mol, a slightly low sodium level (134 mEq/L), and no ketoacidosis or ketonuria. Calculated serum osmolarity was 292 mOsm/L, within the uppermost range of normality. Brain CT was unremarkable.

The patient was consequently discharged by the emergency department with a presumable diagnosis of focal epileptic seizures and was admitted the same day to our institution where further examinations were performed. During an EEG recording using the standard 10-20 system, right-sided electrographic discharges without any clinical concomitant were recorded (*see figure 1A for details*).

A 1.5 Tesla MRI study was performed the day after. Axial T2w and FLAIR sequences (acquired with right-left [RL] phase encoding) showed a vast area of subcortical hypointensity in the right temporal lobe, with no adjacent cortical swelling or hyperintensity. An analogue T2w sequence was acquired with the same technical parameters, apart from modifying phase encoding from RL to anterior-posterior (AP), to exclude artefacts, which confirmed the finding. No signal abnormality was evident on T1w sequences and after gadolinium administration, no gyral or leptomeningeal enhancement was demonstrated (*data not shown*). DWI (b value=1,000) did not show any diffusion restriction, and ADC maps were normal both at the cortical and subcortical level (*figure 2A-D*). The radiological report concluded the presence of an unusual subcortical signal alteration of the right temporal lobe as an expression of the postictal state, presumably correlating with peaks of hyperglycaemia.

No further episodes of seizures occurred during the hospital stay and the patient was later discharged with levetiracetam (500 mg *per os,* every 12 hours) as maintenance therapy, anti-diabetic therapy, and dietary recommendations. No further symptoms occurred in the following two months.

After one month of follow-up, EEG and MRI were repeated. Complete resolution of subcortical T2 hypointensity was observed, with only a small residual juxtacortical gliotic focus (*figure 2E-F*); the EEG was normal (*figure 1B*).

After six months of follow-up, the EEG remained negative for epileptic abnormalities. Considering the lack of seizures, as well as EEG epileptic discharges, the antiepileptic therapy was gradually discontinued. The patient had neither seizures nor abnormal EEG discharges when examined during a two-year follow-up visit.

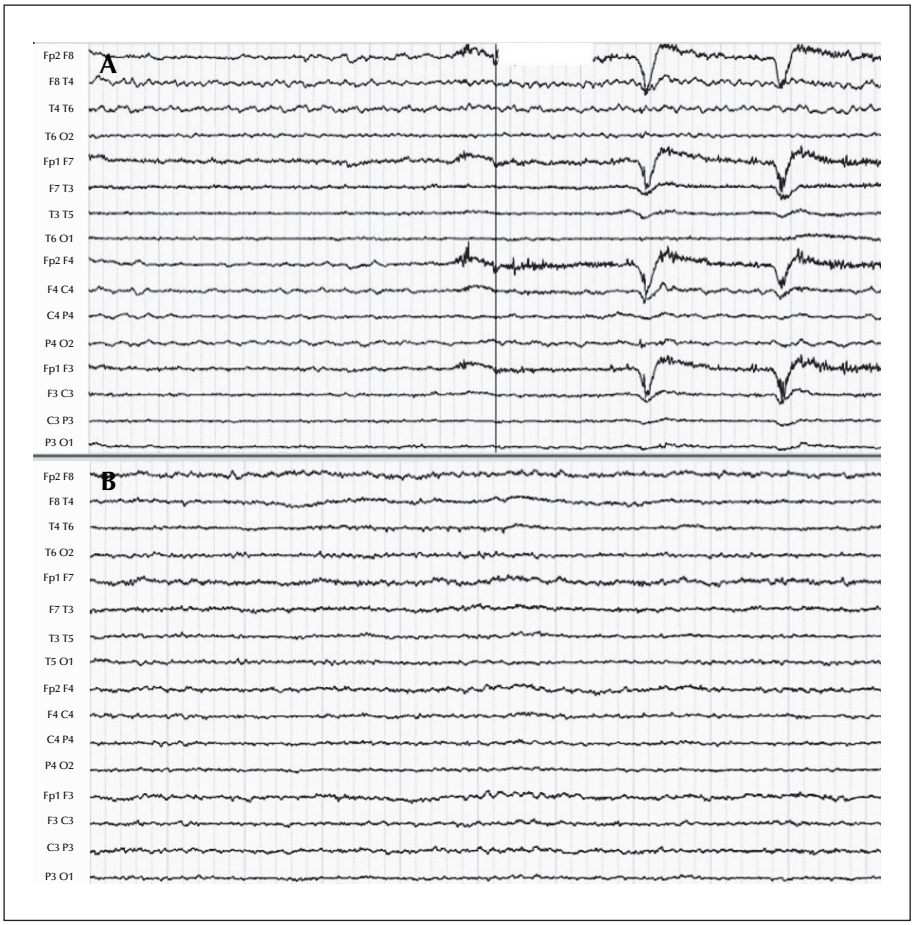

Figure 1. EEG: (A) standard 10-20 system EEG recording showing an epileptic discharge consisting of rhythmic theta activity arising from the right temporal leads. Fifteen seconds later, the discharge evolved in frequency from theta (6-Hz) to delta waves with superimposed sharply contoured waves in the right temporal region only. Two minutes later, the discharge continued, spreading over the ipsilateral and contralateral leads and slowing in the range of delta frequencies. There were no clinical concomitants. Two minutes and 48 seconds later, 8-Hz alpha activity with superimposed theta frequencies reappeared at the same leads where the epileptic discharge had occurred. (B) One-month follow-up EEG showing normal findings.

Discussion

Transient subcortical signal abnormalities, and in particular T2 hypointensity with or without associated adjacent cortical abnormality or contrast enhancement, are uncommonly reported on postictal MRI (Seo *et al*., 2003; Hung *et al*., 2010; Lee *et al*., 2016). The pathological substrate of such signal alteration is not fully understood and still under debate.

Structural modifications or accumulation of calcium/iron that could alter T2 signal, due to paramagnetic effects, can be confidently excluded because of their permanent nature, which would imply a stability of MRI findings. On the other hand, a temporary increase and/or accumulation of free radicals that might alter T2 signal is the mostly likely explanation for this subcortical phenomenon. Cellular swelling with or without associated vasogenic oedema may conversely mask this effect at the adjacent cortical level, resulting in iso- or well-known T2 hyperintensity, which is commonly shown on postictal MRI (Cianfoni *et al*., 2013).

Several pathological entities have been reported to be responsible for transient subcortical signal abnormalities, *e.g*. meningitis, encephalitis, leptomeningeal metastases, and alteration of blood glucose levels (Lee *et al*., 2002; Seo *et al*., 2003; Raghavendra *et al*., 2007; Putta *et al*., 2014).

In particular, hyperglycaemic peaks, through an unclear proconvulsant effect of high glucose levels, may lower the seizure threshold and consequently provoke epileptic seizures. The main explanation for this effect derives from a reduction in gamma-aminobutyric (GABA) levels, produced by increments of plasmatic ketone bodies that stimulate activity of the glutamic acid decarboxylase enzyme within the Krebs cycle (Hennis *et al*., 1992; Placidi *et al*., 2001).

A non-ketotic hyperglycaemic (NKH) hyperosmolar state can present with seizures (Hennis *et al*, 1992), yet

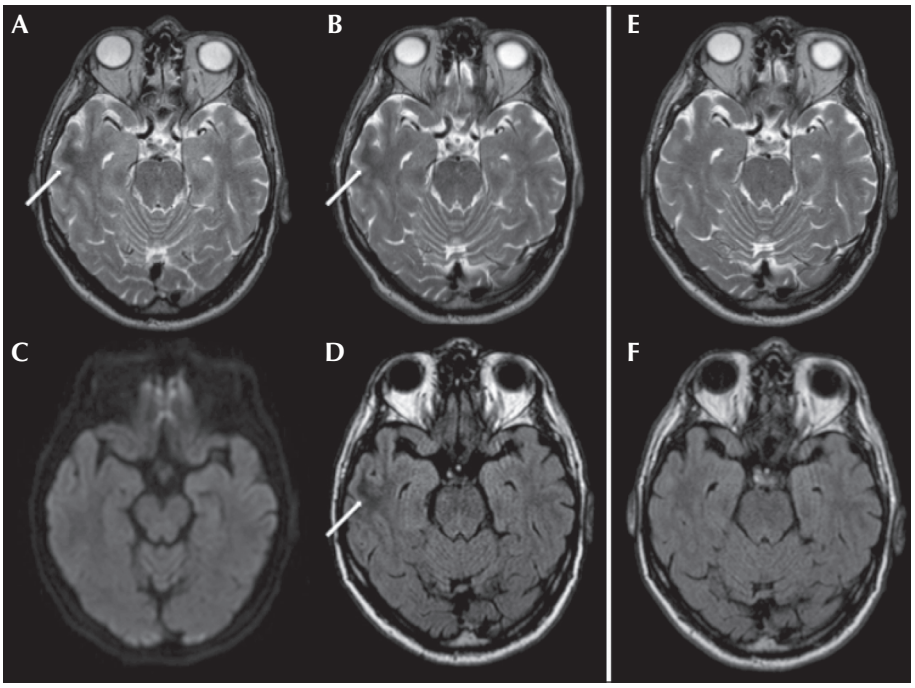

Figure 2. (A-D) Baseline MRI axial T2w with RL phase encoding (A), AP phase encoding (B), DWI b1000 (C), and FLAIR (D), showing right temporal subcortical hypointensity (arrows). (E, F) Follow-up MRI shows resolution of T2w hypointensity, with only a residual juxtacortical gliotic focus: axial T2w with RL phase encoding (E) and FLAIR (F). Images are shown in radiologic view (the right side of the brain is on the left side).

few data are available in the literature regarding postictal MRI abnormalities in such conditions. In the largest case series published, Lee *et al*. reported 11 cases of hyperglycaemia-induced seizures in which postictal subcortical T2 hypointensity could be demonstrated. Even though only five out of 11 showed the typical adjacent cortical swelling, all cases showed a certain amount of gyral and/or leptomeningeal contrast enhancement, both on T1 and FLAIR contrast-enhanced sequences (Lee *et al*., 2016). As the authors suggested, in a postictal context, contrast-enhanced FLAIR sequences may be used to facilitate visualization of cortical/leptomeningeal enhancement, that may be faint or unrecognizable on post-gadolinium T1w sequences, even if no data on contrast-enhanced FLAIR sensitivity in such a context are available (Lee *et al*., 2016).

Our subject presented with hyperglycaemia, while ketonaemia was normal and serum osmolarity was only slightly increased, but still remained within normal range. A signal abnormality similar to those documented in cases with a NKH hyperosmolar state was evident, suggesting that even mild increases in serum osmolarity can lead to an alteration in extracellular water and subsequently T2 signal, and that, collaterally, ketone bodies and hyperosmolarity may not be the only factors in this setting. Restricted diffusion and especially gyral and/or leptomeningeal enhancement were absent in our patient, thus subcortical T2 hypointensity proved to be the only MRI finding which could be considered for correct interpretation.

In certain pathological conditions, such as non-ketotic hyperglycaemia, with or without serum hyperosmolarity, unusual findings may be present on postictal MRI and should be carefully considered in the clinical interpretation and differential diagnosis.

With regards to therapeutic approach, whether antiepileptic treatment should be initiated in cases of hyperglycaemia-related seizures is a matter of debate. In fact, seizure control has been reported in patients upon normalisation of hyperglycaemia and rehydration therapy (Rani *et al*., 2016). In our case, due to seizure recurrence and epileptic discharges on EEG, we decided to initiate treatment with levetiracetam, which is known for its wide spectrum and good safety profile. However, based on the lack of clinical manifestations, as well as EEG epileptic activity at the six-month follow-up examination, the antiepileptic treatment was discontinued. □

Supplementary data.

Summary didactic slides are available on the www.epilepticdisorders.com website.

Disclosures.

None of the authors have any conflict of interest to declare.

References

Cianfoni A, Caulo M, Cerase A, *et al*. Seizure-induced brain lesions: a wide spectrum of variably reversible MRI abnormalities. *Eur J Radiol* 2013; 82: 1964-72.

Hemanth Rao T, Libman RB, Patel M. Seizures and 'disappearing' brain lesions. *Seizure* 1995; 4: 61-5.

Hennis A, Corbin D, Fraser H. Focal seizures and non-ketotic hyperglycaemia. *J Neurol Neurosurg Psychiatry* 1992; 55: 195-7.

Hung WL, Hsieh PF, Lee YC, Chang MH. Occipital lobe seizures related to marked elevation of hemoglobin A1C: report of two cases. *Seizure* 2010; 19: 359-62.

Lee JH, Na DG, Choi KH, *et al*. Subcortical low intensity on MR images of meningitis, viral encephalitis, and leptomeningeal metastasis. *Am J Neuroradiol* 2002; 23: 535-42.

Lee EJ, Kim KK, Lee EK, Lee JE. Characteristic MRI findings in hyperglycaemia-induced seizures: diagnostic value of contrast-enhanced fluid-attenuated inversion recovery imaging. *Clin Radiol* 2016; 71: 1240-7.

Placidi F, Floris R, Bozza A, *et al*. Ketotic hyperglycemia and epilepsia partialis continua. *Neurology* 2001; 57: 534-7.

Putta SL, Weisholtz D, Milligan TA. Occipital seizures and subcortical T2 hypointensity in the setting of hyperglycemia. *Epilepsy & Behav Case Rep* 2014; 2: 96-9.

Raghavendra S, Ashalatha R, Thomas SV, Kesavadas C. Focal neuronal loss, reversible subcortical focal T2 hypointensity in seizures with a nonketotic hyperglycemic hyperosmolar state. *Neuroradiology* 2007; 49: 299-305.

Rani KA, Ahmed MH, Dunphy L, Behnam Y. Complex partial seizure as a manifestation of non-ketotic hyperglycemia: the needle recovered from haystack? *J Clin Med Res* 2016; 8: 478-9.

Seo DW, Na DG, Na DL, Moon SY, Hong SB. Subcortical hypointensity in partial status epilepticus associated with nonketotic hyperglycemia. *J Neuroimaging* 2003; 13: 259-63.

Yaffe K, Ferriero D, Barkovich AJ, Rowley H, Reversible H. MRI abnormalities following seizures. *Neurology* 1995; 45: 104-8.

TEST YOURSELF

(1) What are common findings on postictal MRI?

(2) Is subcortical signal abnormality common postictally?

(3) What can lead to subcortical T2 hypointensity during the postictal state?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".