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ILAE Neuroimaging Task Force highlight: Review MRI scans with semiology in mind

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ABSTRACT – The ILAE Neuroimaging Task Force aims to publish educational case reports highlighting basic aspects related to neuroimaging in epilepsy consistent with the educational mission of the ILAE. It is important to obtain MRI scans early in the clinical course of epilepsy, using an optimized protocol. Furthermore, it is critical that MRI scans are reviewed by experts who have been provided with all the clinical information and results from other investigations. We report a patient with a 21-year history of drug-resistant seizures who was admitted from another centre for presurgical evaluation. She had four previous MRI scans from this centre which were reported as unremarkable. However, a review of the MRI scan obtained on the day of admission, with the patient's ictal semiology in mind, resulted in identification of an epileptogenic lesion which was later confirmed by video-EEG monitoring and interictal PET. This lesion was present on all previous MRI scans and showed no change. The patient underwent lesionectomy, and histopathology of the resected specimen was consistent with a dysembryoplastic neuroepithelial tumour. The patient remains seizure-free, 2.5 years after surgery. This case highlights the importance of obtaining detailed descriptions of seizure semiology and considering them when reviewing MR images.

Key words: ictal semiology, MRI, DNET

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Case presentation

A 37-year-old female with a history of drug-resistant seizures since the age of 16 was admitted for presurgical evaluation from another centre. Her seizures were stereotypical and were characterized by a subjective abnormal spatial perception involving the left visual hemifield, spreading rapidly to the right. Typically, she would perceive people as standing horizontally on a wall knowing that they were, in fact, standing upright. Sometimes she felt stiffness of the left side of her neck. She was fully aware of these symptoms and became anxious and agitated. This was immediately followed by forced deviation and clonic jerking of the head to the left. During this time, her eyes would be open and she would retain awareness, trying to hold onto objects around her, lean on walls, or lie down. In about 5% of the seizures, she would collapse and have possible alteration of awareness. Following her seizures, she was generally briefly confused and tired. These seizures occurred in clusters over the course of a day, with up to 20 seizures, once or twice a week. She has had only three seizures evolving to bilateral tonic-clonic seizures over two weeks at age 18 in the context of medication adjustment.

Her antiseizure drugs included lamotrigine 200 mg bid, controlled-release carbamazepine 200 mg bid, clonazepam 0.25 mg bid, and cannabidiol oil five drops per day. She previously tried divalproex sodium. Her birth and development were normal, and she had no epilepsy risk factors apart from multiple minor sports-related concussions.

Preadmission investigation from another centre included two routine EEGs which were reported as normal as well as an ambulatory EEG that had captured several typical focal aware seizures without a clear EEG correlate. Four MRI scans performed over five years using an appropriate local epilepsy protocol at other centres were reported as unremarkable for epileptogenic lesions. These images were not available for review at the time of admission.

Course in hospital

A repeat MRI scan was performed on the day of admission prior to EEG monitoring. A focused review of the MR images, guided by the patient's semiology, revealed a small <1-cm^3 intracortical T2 hyperintense cystic lesion in the right parasagittal parietal lobe at the vertex, without adjacent FLAIR signal changes or contrast enhancement (*figure 1*). FDG-PET obtained after being seizure-free for >24 hours showed moderate hypometabolism in the same area as the lesion seen on the MRI scan (*figure 2*). Notably, images from previous MRI scans were eventually obtained and also showed this lesion, with no change in appearance or size.

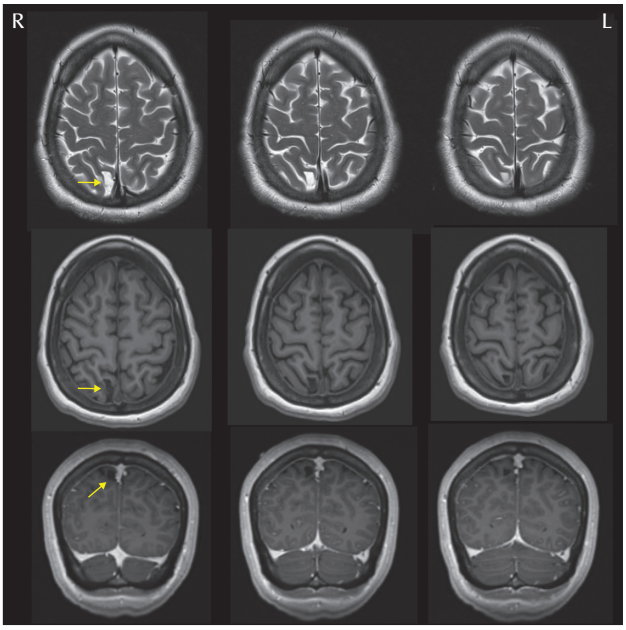

Figure 1. Structural MRI. Arrows show an intracortical cystic lesion that is hyperintense on T2-weighted images (top row, axial) and hypointense on T1-weighted images (middle row, axial), without enhancement (bottom row, coronal).

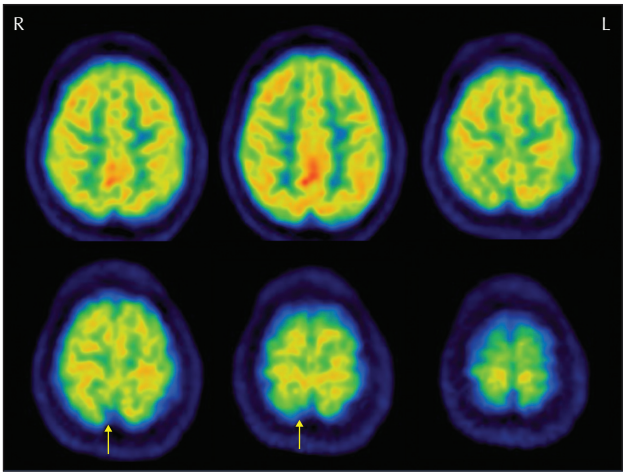

Figure 2. Interictal PET. Arrows show a focal area of moderate hypometabolism in the right posterior mesial parietal convexity.

Scalp video-EEG monitoring was performed over 10 days and interictal EEG showed rare right parasagittal sharp waves, maximal at Cz-C4-P4 (*figure 3*). The patient had three habitual focal aware seizures with motor involvement, with EEG onset in the right parasagittal region, maximum at F4-C4; she also had two habitual focal aware seizures without motor involvement and no associated EEG changes.

The patient underwent a lesionectomy during the same hospital admission. Histopathology of the resected specimen was consistent with a dysembryoplastic neuroepithelial tumour (DNET) WHO Grade

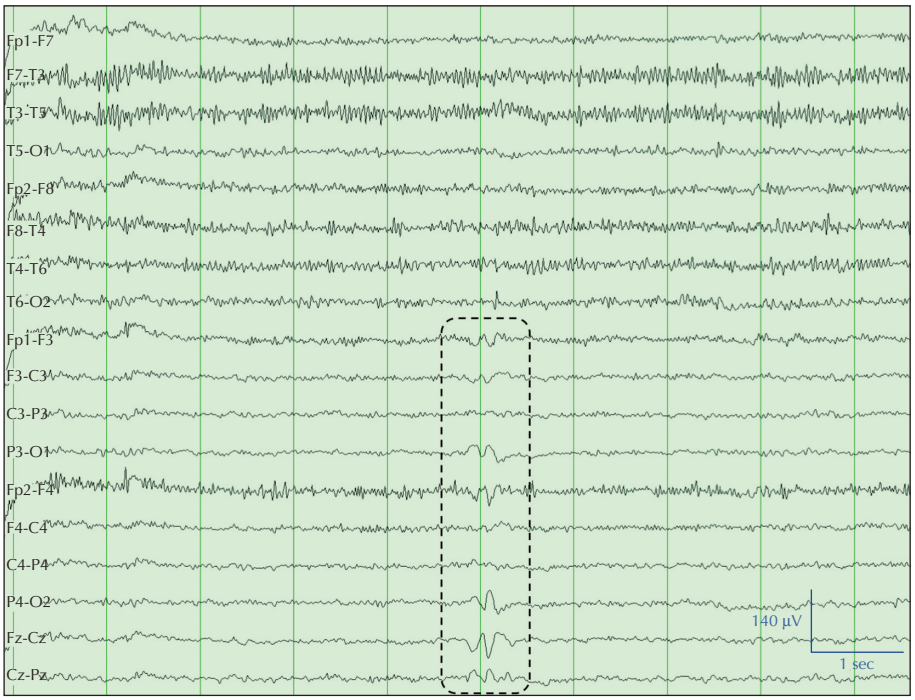

Figure 3. Interictal EEG. Box shows an interictal discharge with maximal negativity at CZ with a broad bilateral parasagittal field (F4-C4-P4 and C3-P3).

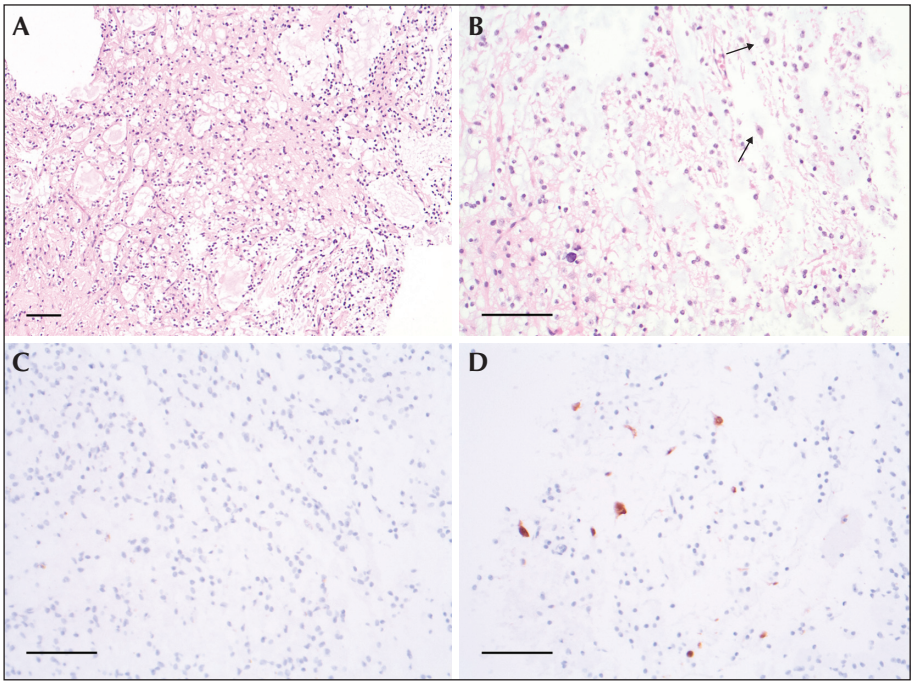

Figure 4. Microscopic features of the resected tumour. (A) Low-power with H&E stain showing a mildly hypercellular neoplasm of bland cells with scattered microcystic areas filled with myxoid material. (B) High-power with H&E stain showing rare floating neurons (arrows) on a background of small oligodendrocyte-like cells. (C) Immunohistochemistry is negative for IDH1 R132H which is frequently present in oligodendrogliomas. (D) Immunohistochemistry is positive for Neu-N in rare neurons. Scale bar = 100 µm.

I (*figure 4*). The specimen was sent for genetic testing and no mutations were detected in the following genes: *BRAF*, *GNA11*, *GNAQ*, *HRAS*, *KIT*, *KRAS*, *NRAS*, *PTEN*, *RAC1*, *RPS27*, *TERT*. Currently, she has remained seizure-free, 2.5 years after surgery with no adverse effects from the procedure.

Discussion

This case highlights the importance of obtaining detailed descriptions of seizure semiology and considering them when reviewing MR images. The clinical symptoms of abnormal spatial perception in the left visual hemifield suggested possible right parietal lobe involvement. Furthermore, forced head deviation to the left with clonic head jerking to the left also strongly suggested right hemispheric involvement, possibly due to seizure spread towards the frontal lobe. The lesion in this case was small and in a location that can be easily overlooked or misinterpreted as normal CSF hyperintensity, illustrating the need for thin MRI sections covering the entire brain, preferably using 3D acquisition (Bernasconi *et al*., 2019; Wang *et al*., 2020). Small lesions on the convexity of the brain, in close proximity to the skull, such as this DNET, often go unnoticed if only thick orthogonal MRI sections are available for analysis. Indeed, the lesion was missed on four previous occasions. However, review of the MRI scans with the ictal semiology in mind resulted in identification of the epileptogenic lesion which was later confirmed by video-EEG monitoring and interictal PET. It is important to obtain MRI scans early in the clinical course, using an optimized protocol (HARNESS-MRI) (Bernasconi *et al*., 2019; Wang *et al*., 2020). Identifying a potentially epileptogenic lesion may have led to earlier epilepsy surgery and improved quality of life in this case. As reported previously (Von Oertzen *et al*., 2002), MRI scans should always be reviewed by trained experts who have been provided with all available clinical information and results of ancillary tests to increase the yield of MRI reading. It is our repeated experience that review of MRI studies in the context of other information and with a directed clinical hypothesis yields superior detection of surgically curable lesions. Furthermore, iterative review of the MRI after obtaining localizing data such as the clinical interpretation of seizure origins, PET, SPECT, cognitive deficits, EEG or others, can lead to identification of lesions that might otherwise be missed. Importantly, the requesting physicians should review MR images themselves, ideally together with a neuroradiologist specialized in epilepsy imaging. □

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

Disclaimer.
This paper was written by experts selected by the International League Against Epilepsy (ILAE) and was approved for publication by the ILAE. Opinions expressed by the authors, however, do not necessarily represent the policy or position of the ILAE.

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

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TEST YOURSELF

(1) A 32-year-old male presents with recurrent seizures characterized by *déjà vu*, followed by an epigastric rising sensation, and an altered level of awareness with oral and bimanual automatisms, without clear lateralization. What is the minimum information that should be included in the MRI requisition form?
A. Seizures NYD
B. 32-year-old male with recurrent seizures.
C. 32-year-old male with recurrent focal impaired awareness seizures, possible temporal lobe onset, side unknown.
D. 32-year-old male with recurrent seizures, possible left temporal onset.
E. 32-year-old male with recurrent seizures, possible right temporal onset.

(2) A 40-year-old female with bilateral tonic-clonic seizures without preceding symptoms or lateralizing features underwent a MRI scan at 3T which was interpreted as normal. The scan was performed using the HARNESS-MRI protocol. The initial EEG was normal, however, a repeat sleep-deprived EEG showed left frontopolar interictal discharges. What should the <u>next</u> step be in terms of MR imagining?

A. Repeat the MRI scan at 3T, using the HARNESS-MRI protocol
B. Obtain a high-field imaging study at 7T.
C. Obtain another MRI scan, adding MR spectroscopy.
D. Review the MRI images yourself along with a neuroradiologist in light of the new EEG findings.
E. All of the above

(3) Typical MR imaging features of dysembryoblastic neuroepithelial tumours include:

A. Typical frontal location
B. Early epilepsy onset
C. Multinodular architecture
D. Mixed signal intensity on FLAIR
E. Frequent calcification

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".