Received: 28 June 2024 | Accepted: 14 October 2024

DOI: 10.1002/epd2.20303

Epileptic Disorders

CLINICAL VIGNETTE

Ictal sign of the cross: A case report and a short literature review

Emilie Drion[1,2] | Cristina Filipescu[1] | Marc Zanello[3,4,5] | Alessandro Moiraghi[3,4,5] | Charles Mellerio[5,6] | Benoît Crépon[1] | Eléonore Guinard[1] | Magali Boutin-Watine[3] | Hajar Selhane[1] | Estelle Pruvost-Robieux[1,4,5] | Grégoire Demoulin[1,4] | Johan Pallud[3,4,5] | Elisabeth Landré[3] | Martine Gavaret[1,4,5]

[1]Neurophysiology and Epileptology Department, GHU Paris Psychiatry and Neurosciences, Sainte-Anne Hospital, Paris, France

[2]Department of Neurology, CHU of Liège, University of Liège, Liège, Belgium

[3]Neurosurgery Department, GHU Paris Psychiatry and Neurosciences, Sainte-Anne Hospital, Paris, France

[4]Paris-Cité University, Paris, France

[5]INSERM UMR 1266, Institute of Psychiatry and Neuroscience of Paris (IPNP), Paris, France

[6]Neuroradiology Department, GHU Paris Psychiatry and Neurosciences, Sainte-Anne Hospital, Paris, France

Correspondence
Emilie Drion, Neurophysiology and Epileptology Department, GHU Paris Psychiatry and Neurosciences, Sainte-Anne Hospital, 1 Rue Cabanis, Paris, France.
Email: edrion@chuliege.be

KEYWORDS
learned automatism, periventricular nodular heterotopia, schizencephaly, stereo-electro-encephalography, temporal lobe epilepsy, etiology: schizencephaly, localization: temporal lobe (left), temporal mesiolateral, phenomenology: automatisms, syndrome: focal non-idiopathic temporal (TLE)

The sign of the cross (SC) is a rarely reported ictal automatism, mainly documented in right temporal lobe epilepsies (TLE). We report the case of a patient with drug-resistant-epilepsy (DRE) related to left complex cortical malformation investigated using stereo-electro-encephalography (SEEG), who presented ictal SC.

A 27-year-old left-handed woman, with right hemiparesis and homonymous lateral hemianopsia, suffered from DRE since 9-month old. She had no familial risk of epilepsy and was a practicing catholic.

Seizures occurred weekly, being characterized by a sensation of chest heat, fear, loss of contact while making the SC with her left hand (Video 1). She presented post-ictal amnesia.

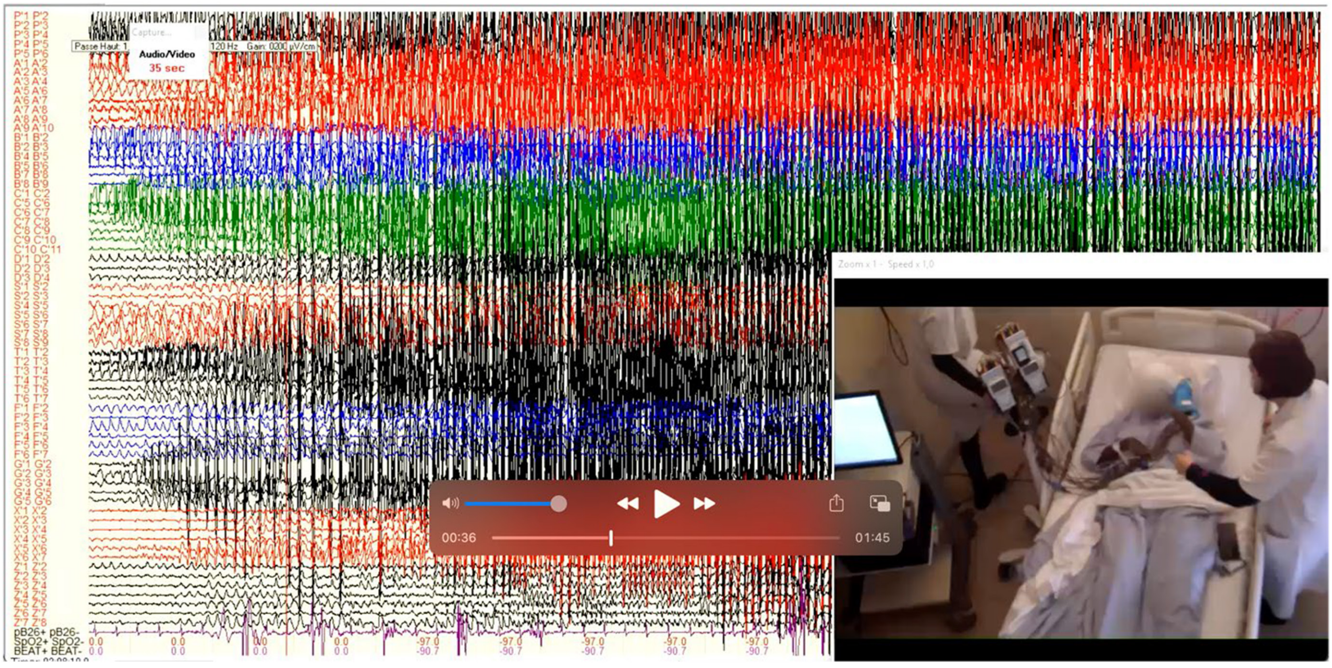
Neurocognitive evaluation showed a global low level with visual memory superior to verbal memory.

The MRI revealed left frontal schizencephaly, extensive left periventricular nodular heterotopia (PNH) and left hippocampal atrophy (Figure 1A). The functional MRI showed right-hemispheric dominance for language. Simultaneous MRI and ^{18}Fluoro-deoxy-glucose positron emission tomography showed left parietal and temporal hypometabolism (Figure 1C).

The video-electro-encephalography showed left temporal slow activity, temporo-parietal interictal spikes, temporal subclinical discharges, and few contralateral slow waves. The main hypothesis was the implication of the schizencephaly inferior and posterior parts. Because of the initial heat sensation, loss of contact and automatisms, we have also explored the left temporal lobe, which was severely hypometabolic (Figure 1C).

SEEG explored the left temporo-peri-sylvian region (Figure 1B). Interictal spikes were recorded in left temporo-mesial structures, PNH, anterior edge of schizencephaly, and middle temporal gyrus.

Abbreviations: DRE, drug-resistant-epilepsy; EZ, epileptogenic zone; MRI, magnetic resonance imaging; MTG, middle temporal gyrus; PNH, periventricular nodular heterotopia; SC, sign of the cross; SEEG, stereo-electro-encephalography; TLE, temporal lobe epilepsy.



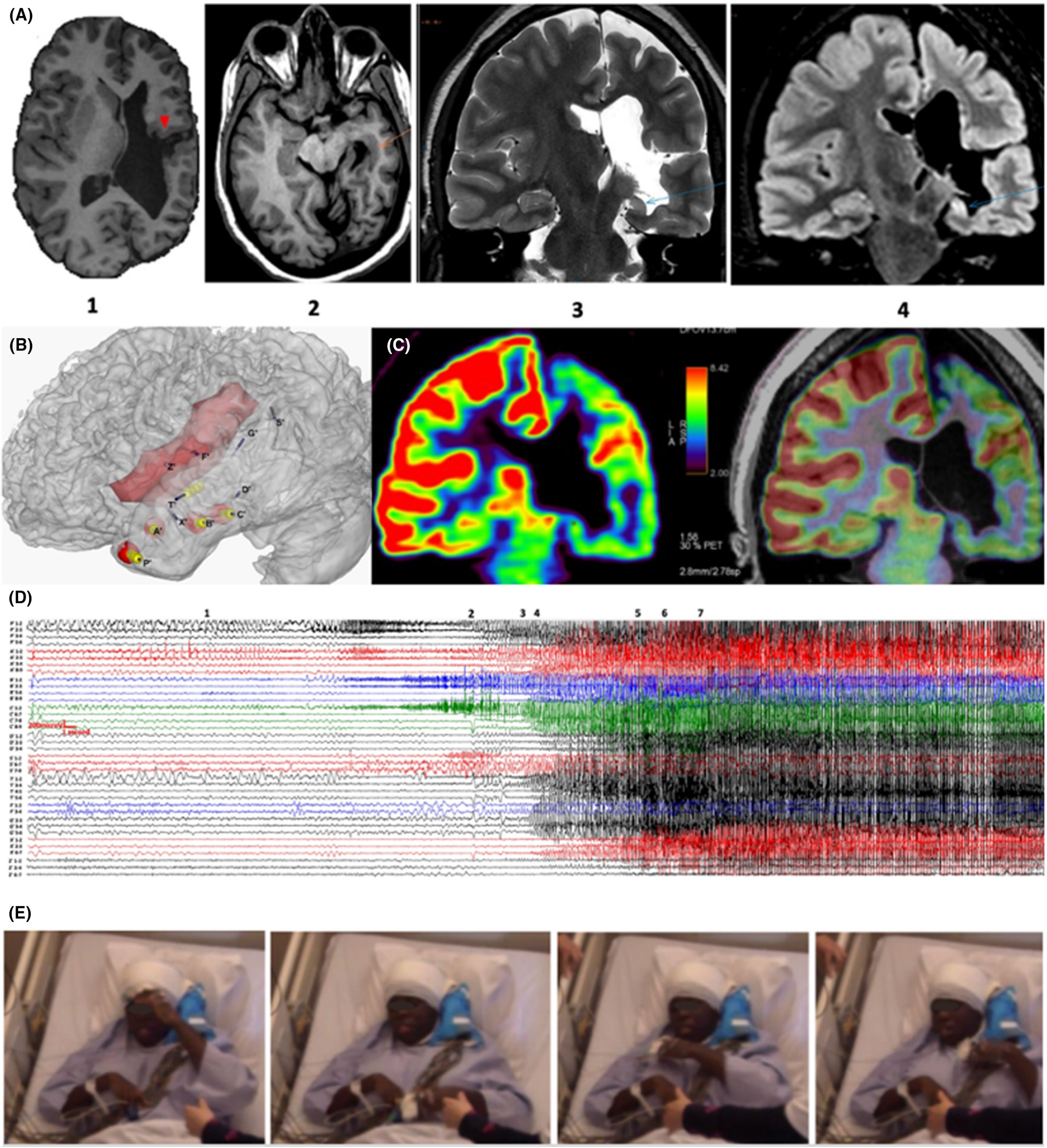
VIDEO 1 Video recording of seizure with repetitive ictal sign of the cross.

Four seizures were recorded. The ictal onset pattern consisted of burst of polyspikes followed by low voltage fast activity involving left temporo-mesial structures (temporal pole internal part, amygdala, hippocampus) and 6 s after seizure onset, the lower, and anterior edge of the schizencephaly, middle temporal gyrus, parietal junction, and PNH (Figure 1D).

The SC occurred during loss of contact, when the discharge involved temporo-mesial structures and spread to lateral temporal cortices, PNH and posterior cingulate, 15 s after seizure onset.

A habitual electro-clinical seizure with the SC was induced by high frequency train stimulation (50 Hz, 1 ms, 5 s, 2 mA) of the heterotopic cortex (C′6–7).

FIGURE 1 (A) (1) MRI, axial plan: Left hemisphere atrophy, left frontal schizencephaly (red dot) and periventricular nodular heterotopia; (2) Axial plan of a 3DT1 gradient echo. Subependymal gray matter heterotopy next to the temporal horn of the left lateral ventricle (orange arrow); (3) Coronal T2: Left hippocampal atrophy with increased signal intensity (blue arrow); (4) Coronal FLAIR: Left hippocampal atrophy with increased signal intensity (blue arrow). (B) Positions of depth electrodes involved by the seizure onset (indicated in red). 3D sagittal view Reconstruction using GARDEL, Medina Villalon S, et al. *J Neurosci Methods*. 2018. PMID: 29605667 DOI: 10.1016/j.jneumeth.2018.03.018. The schizencephaly is represented in light-red. (C) Simultaneous MRI and ^{18}Fluoro-deoxy-glucose positron emission tomography recordings. (D) Ictal SEEG recordings: 11 left intracerebral electrodes were positioned. Electrodes leads and their anatomical localizations: P′ (1–6): Left temporal pole; A′ (1–4): Amygdala; A′ (8, 9): Middle temporal gyrus; B′ (1–3): Left anterior hippocampus; B′ (5, 6): PNH; B′ (8, 9): Middle temporal gyrus; C′ (1, 2): Left posterior hippocampus; C′ (6, 7): PNH; C′ (7–9): Middle temporal gyrus; D′ (1, 2): PNH; D′ (2–4): Lateral malformative temporal cortex; inferior part of the superior temporal gyrus; S′ (1, 2): Posterior cingulate; S′ (6–8): Supramarginal gyrus; T′ (1–4): Schizencephaly (inferior part); T′ (4–6): Superior temporal gyrus; F′ (1–4): PNH, central operculum; G′ (2–6): Posterior superior temporal gyrus; X′ (1–3): Heterotopic cortex, caudal edge of the schizencephaly; X′ (6, 7): Anterior superior temporal gyrus; Z′ (1, 2): Precentral heterotopia, cranial edge of the schizencephaly; Z′ (3–7): Precentral malformative cortex in the frontal operculum. Parameters: High pass filter: 1.6 Hz, low pass filter: 120 Hz. Ictal fast activity occurred at the beginning at the level of the left temporal pole (internal part), amygdala, hippocampus then spread on middle temporal gyri, schizencephaly anterior part, PNH, post cingulate, central operculum. Clinically, the patient had a sensation of chest heat (1), some facial clonus (2), then a loss of contact (3) while she began the SC (4) with her left hand. The SC began 15 s after seizure onset, when the discharge involved mainly medial and lateral parts of this non-dominant temporal lobe. The patient signed the cross five times in succession (total duration 10 s), she did not carry out command (5), then end of the SC (6), her head turned to the right (7), she tried to stand up. She had no other automatism. The seizure lasted 1′50″. Post-ictally, she presented post-ictal amnesia without any other deficit. The main ictal discharge at the time of the sign of the cross was between 5 and 15 Hz. This analysis was performed using AnyWave (Colombet B, et al. AnyWave: A cross-platform and modular software for visualizing and processing electrophysiological signals. *J Neurosci Methods* 2015 Mar 15:242:118–26. doi: 10.1016/j.jneumeth.2015.01.017. Epub 2015 Jan 19). (E) Video snapshots during the SC.



PNH can be associated with other cortical malformations.[1] Both heterotopic and normotopic cortices are potentially involved in the epileptogenic network.[2,3] The epileptogenic network in case of schizencephaly is also complex. Indeed, the abnormal cortex lining schizencephalic cleft, cortices near the cleft and distant areas may be epileptogenic.[4] In this case, despite the complex malformation, the initial ictal discharge was limited to the temporo-mesial structures.

We identified five publications (22 patients) reporting the SC in seizure semiology.[5–9] The SC was reported ictal in 19/22 and post-ictal in only 3/22 cases[5]: 11 patients presented with right TLE, 7 with left TLE, 2 with bi-temporal epilepsy, 1 with right frontal, and 1 with right parietal epilepsy.[5–9]

Language dominance was detailed for only 2/22 patients[5–9]: one patient with left hemisphere language dominance, a bi-temporal epilepsy with the SC occurring only during right temporal seizures[7]; and the second one with bilateral language organization and a left TLE.[9]

Only 2/22 patients underwent intracranial recordings. The first case was explored using foramen ovale electrodes. During the SC, the ictal discharge was visible over the right anterior temporal region on surface EEG, while it ended at foramen ovale.[7] For the second case, characterized by a bi-temporal epilepsy, SEEG highlighted an ictal discharge limited to the left hippocampus while SC occurred.[9] Finally, most reported patients with SC presented with right lateralized epilepsy, mainly temporal.[5–9] Three publications hypothesized the localizing and lateralizing value of SC for the right temporal lobe.[6–8]

The SC may be an ictal automatism, of acquired origin, corresponding to a learned behavioral phenomenon.[5,7,9] New learned behaviors may indeed be included into stereotyped ictal semiology.[8,9] Behavioral motor automatisms are frequent ictal and post-ictal correlates in focal seizures, thought to result mainly from disinhibition of subcortical and brainstem motor centers.[7,10]

The interest of this observation is to document a little-known ictal sign, potentially under-reported and rarely explored using SEEG. This probably acquired automatism of undetermined lateralizing value, seems to occur most frequently in TLE. However, in our observation documented with SEEG and fMRI, the SC occurred when the discharge involved mainly the mesio-lateral cortices of the non-dominant temporal lobe.

ACKNOWLEDGMENTS

The author thank Vincent Guesnery and Florence Pattenotte, Communication department of the GHU Paris Psychiatry and Neurosciences, for anonymizing the video; and all the nurses and EEG technicians of the neurophysiology and epileptology department.

ORCID

Emilie Drion https://orcid.org/0000-0002-1495-8178
Cristina Filipescu https://orcid.org/0000-0001-6951-506X
Estelle Pruvost-Robieux https://orcid.org/0000-0002-6107-0964

REFERENCES

1. Severino M, Geraldo AF, Utz N, Tortora D, Pogledic I, Klonowski W, et al. Definitions and classification of malformations of cortical development: practical guidelines. Brain. 2020;143:2874–94.
2. Pizzo F, Roehri N, Catenoix H, Medina S, McGonigal A, Giusiano B, et al. Epileptogenic networks in nodular heterotopia: a stereoelectroencephalography study. Epilepsia. 2017;58(12):2112–23.
3. Filipescu C, Landré E, Gavaret M, Zanello M, Pallud J. Bilateral periventricular nodular heterotopia: can SEEG-guided radiofrequency thermocoagulations cure the epilepsy? Epileptic Disord. 2024;26(1):158–60.
4. Choi HY, Koh EJ. Long-term outcome of surgical treatment of patients with intractable epilepsy associated with schizencephaly. Acta Neurochir. 2013;155(9):1717–24.
5. Arango-Jaramillo E, Lozano-García L, Benjumea-Cuartas V, Andrade-Machado R. Periictal sign of the cross or Signum Crucis as a lateralizing sign in focal epilepsies: not only a right temporal lobe epilepsy feature. Epilepsy Behav. 2018;78:52–6.
6. Lin K, Marx C, Caboclo LOSF, Centeno RS, Sakamoto AC, Yacubian EMT. Sign of the cross (Signum Crucis): observation of an uncommon ictal manifestation of mesial temporal lobe epilepsy. Epilepsy Behav. 2009;14(2):400–3.
7. Wennberg R, McAndrews MP, Zumsteg D, Velazquez JLP. The sign of the cross as a learned ictal automatism? Epilepsy Behav. 2009;15:394–8.
8. Nooraine J, Jayaraman A, Reddy S, Iyer RB, Raghavendra S. Ictal sign of cross-does it have any religious annotations at all? Seizure. 2013;22(7):584–5.
9. Fernández-Cabrera A, López-González FJ, García-De Soto J, Pardellas-Santiago E, Lara-Lezama LB, Rodríguez-Osorio X. The sign of the cross: a very rare automatism in temporal lobe epilepsy. Two case reports. Rev Neurol. 2023;77(4):105–8.
10. Gloor P. Neurobiological substrates of ictal behavioral changes. Adv Neurol. 1991;55:1–34.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Drion E, Filipescu C, Zanello M, Moiraghi A, Mellerio C, Crépon B, et al. Ictal sign of the cross: A case report and a short literature review. Epileptic Disord. 2024;00:1–5. https://doi.org/10.1002/epd2.20303

Test yourself

1. The sign of the cross is an ictal sign found mainly in parietal lobe epilepsy: true or false?
2. The lateralizing value of the sign of the cross is well determined for the dominant temporal lobe: true or false?
3. The sign of the cross can be ictal or post-ictal: true or false?

Answers may be found in the Supporting information.