JOURNAL OF NEUROSURGERY:
Case Lessons

J Neurosurg Case Lessons 3(17): CASE22106, 2022
DOI: 10.3171/CASE22106

Stereo-electroencephalography evidence of an eccentrically located seizure-onset zone around a polymorphous low-grade neuroepithelial tumor of the young: illustrative case

Koichi Hagiwara, MD, PhD,[1] Takashi Kamada, MD, PhD,[1] Satoshi O. Suzuki, MD, PhD,[2] Ayako Miyoshi, MD,[1] Hideaki Tanaka, MD, PhD,[3] Hiroshi Shigeto, MD, PhD,[1,4] Shinji Ohara, MD, PhD,[1,3] and Naoki Akamatsu, MD, PhD[1]

[1]Epilepsy and Sleep Center and [3]Department of Neurosurgery, Fukuoka Sanno Hospital, Fukuoka, Japan; [2]Department of Psychiatry, Shourai Hospital, Saga, Japan; and [4]Division of Medical Technology, Department of Health Sciences, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

BACKGROUND Polymorphous low-grade neuroepithelial tumor of the young (PLNTY) is a newly identified low-grade brain tumor with frequent epileptic presentation. Despite the facilitated use of invasive electroencephalography owing to the growing availability of stereo-electroencephalography (SEEG), intracranial features of tumor-related seizures are still scarcely described. This report provides the first description of SEEG-recorded seizures in PLNTY to provide an insight into its surgical strategy.

OBSERVATIONS Spontaneous clinical seizures were recorded with SEEG in a young adult patient with drug-resistant epilepsy associated with a PLNTY in the left lateral temporal cortex. The seizure onset was characterized by low-voltage fast activity (LVFA) and showed eccentric localization with respect to the tumor: LVFA was localized in the anterior portion of the tumor and spread toward the adjacent polar cortex. The language risks associated with the resection of the posterior temporal cortex could thus be minimized.

LESSONS PLNTY can show a focal and eccentric seizure-onset zone around the tumor. The present findings serve to improve the functional and seizure outcomes using the staged invasive approach in PLNTY.

https://thejns.org/doi/abs/10.3171/CASE22106

KEYWORDS epileptogenic zone; long-term epilepsy-associated brain tumor; low-voltage fast activity; polymorphous low-grade neuroepithelial tumor; resection; stereo-electroencephalography

Polymorphous low-grade neuroepithelial tumor of the young (PLNTY) is a recently identified rare entity of epilepsy-associated neuroepithelial tumor.[1] PLNTY has distinctive histological and genetic features that consist of oligodendroglioma-like cellular infiltrates, components with variable morphological polymorphism, intense aberrant expression of CD34, and gene mutations involving the constituents of the mitogen-activated protein kinase pathway such as BRAF V600E or fibroblast growth factor receptors.[1,2] As with other long-term epilepsy-associated brain tumors (LEATs),[3] seizures are usually the first and the only symptom of patients with PLNTY and begin to occur during childhood or early adulthood. On imaging, PLNTY often shows cystic components or calcification,[1,4] and the temporal lobe appears to be the most common location.[1,4,5] PLNTY has recently been accepted into the 2021 World Health Organization classification of central nervous system tumors.[6]

While previous reports of PLNTY described the aforementioned clinical, imaging, and histopathological features,[1,2,4,5] none has described intracranial EEG features. Here we report a case investigated with stereo-electroencephalography (SEEG) to help understand the relationship between the tumor and epileptogenic zone in this new entity of LEAT and thereby to provide an insight into its surgical strategy.

ABBREVIATIONS EEG = electroencephalography; LEAT = long-term epilepsy-associated brain tumor; LVFA = low-voltage fast activity; MRI = magnetic resonance imaging; PLNTY = polymorphous low-grade neuroepithelial tumor of the young; SEEG = stereo-electroencephalography.

INCLUDE WHEN CITING Published April 25, 2022; DOI: 10.3171/CASE22106.
SUBMITTED March 3, 2022. **ACCEPTED** March 9, 2022.
© 2022 The authors, CC BY-NC-ND 4.0 (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Illustrative Case

A 23-year-old right-handed woman had no prior medical conditions or family history of epilepsy other than her epilepsy. She initially presented with bilateral tonic-clonic seizures at the age of 18 years. They were suppressed after initiation of an antiseizure medication (lamotrigine) by a referral neurologist, but she continued to have aphasic seizures, which brought her to our epilepsy center. Scalp EEG showed focal interictal spikes in the left anterior temporal region with inversion of phase at F7 or T1. Her ictal symptoms were characterized by the lack of verbal comprehension, with or without being followed by impaired awareness and distal-dominant automatisms slightly preceding on the left. Postictal aphasia lasted several minutes. Ictal EEG showed a left temporal leading spike and then generalized background suppression with left temporal predominance for 5 to 6 seconds. This initial phase was followed by a low-amplitude alpha rhythm predominantly over the left temporal region, which then evolved into bihemispheric delta discharges. Her brain magnetic resonance imaging (MRI) revealed no structural or signal abnormalities in the hippocampi but a cystic cortical lesion that lay across the left superior and middle temporal gyri (Fig. 1A). There was neither calcification (Fig. 1B) nor contrast enhancement within or around the lesion (Fig. 1C and D). A [^{18}F]-fluorodeoxyglucose positron emission tomography showed a focal left lateral temporal hypometabolism corresponding to the lesion (Fig. 1E). Her neuropsychological assessment showed preserved verbal as well as visual memory performance. LEAT was a possibility, but she pursued medical treatment until she continued to have seizures several times a month (up to six per month) despite trials of several antiseizure medications (lamotrigine 400 mg, levetiracetam 1,000 mg, and lacosamide 200 mg). Then she decided to receive an invasive EEG investigation. SEEG was performed to assess (1) whether the hippocampus is spared from ictal-onset discharges, (2) the extent of potentially MRI-negative epileptogenic zone/network, and (3) its relationship with the language area (see Fig. 2 for the SEEG implantation scheme). Interictal spikes were centered around the anterior portion of the cystic cortical lesion (Fig. 3A). Similarly, ictal low-voltage fast activity (LVFA) was localized anteriorly around the lesion and spread toward the polar region (Fig. 3B; see also Fig. 2 for the anatomo-electrical relationship). The posterior portion of the lesion as well as more posterior temporal cortex did not show LVFA but only brief fast activity without background suppression. The hippocampus was involved only in prolonged seizures (>15 seconds) with subsequent evolution into a focal-to-bilateral tonic-clonic seizure. Unlike focal cortical dysplasia,[7] the lesion appeared to have a high epileptogenic threshold because electrical cortical stimulation (50 Hz, 1–5 mA) did not induce after-discharges or seizures.

The patient received extended resection that consisted of left anterolateral temporal corticectomy (complete resection of the lesion at the posterior limit) combined with polectomy. The histological examination showed

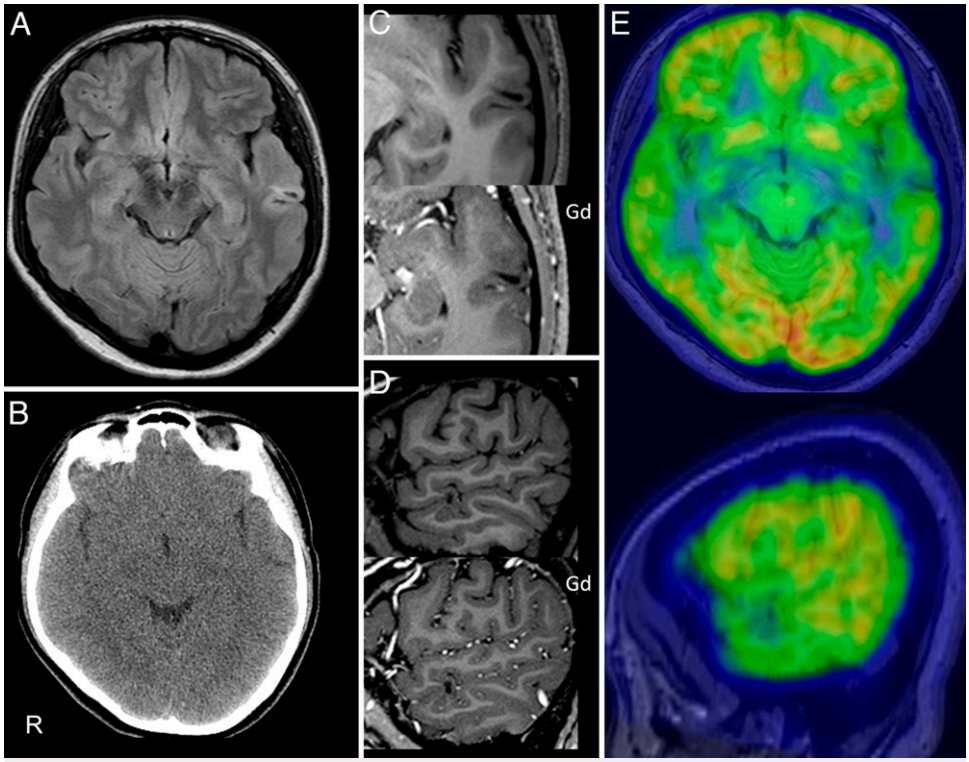

FIG. 1. A: Fluid-attenuated inversion recovery image demonstrating a cystic cortical lesion in the left temporal lobe. A small hyperintensity was observed in the subcortex. **B:** Computed tomography scan showing no calcification within the lesion. **C:** Axial T1-weighted images before and after gadolinium (Gd) administration demonstrating no contrast enhancement within or around the lesion. **D:** Sagittal T1-weighted views of the lesion before and after Gd administration. No contrast enhancement was present, as in the axial view. **E:** An [^{18}F]-fluorodeoxyglucose positron emission tomography scan showing a hypometabolism corresponding to the cystic lesion.

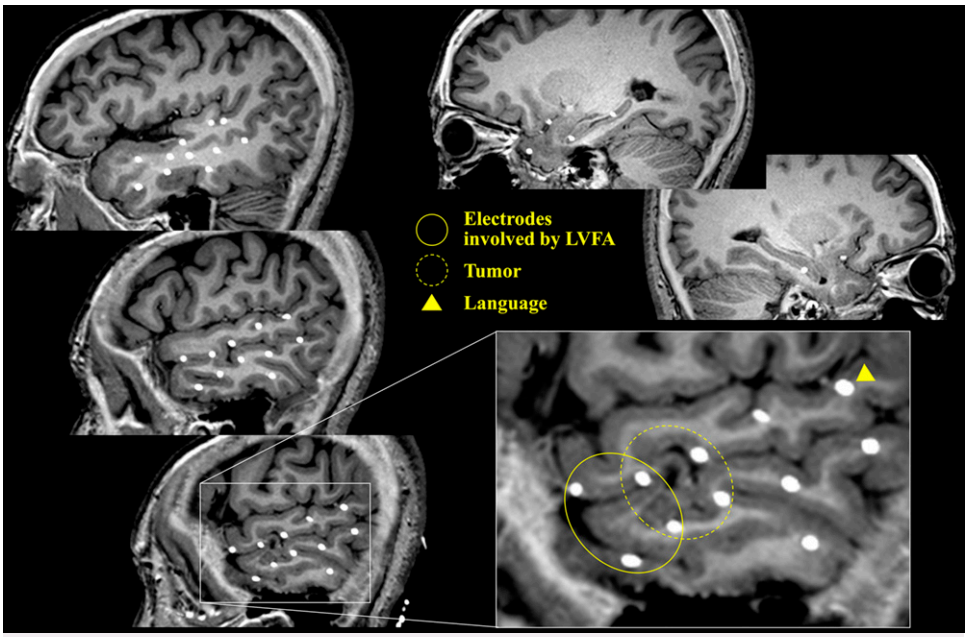

FIG. 2. SEEG electrode positions in the patient. The electrodes involved by LVFA (*circle*; also see Fig. 3 for SEEG findings) were located anterior to the tumoral lesion (*dotted circle*). A language symptom (speech arrest) was induced by electrical cortical stimulation in the posterior superior temporal gyrus (*yellow arrowhead*).

sharply demarcated, infiltrative growth of oligodendrocyte-like tumor cells with intense CD34-immunopositivity in the cortex and subcortex (see Fig. 4 for the key histopathological findings). Tumor cells with pleomorphic, atypical nuclei were focally observed. They were also positive for the glial markers, including glial fibrillary acidic protein (GFAP) and oligodendrocyte transcription factor 2 (OLIG2), whereas no neuronal staining such as for synaptophysin, neuronal nuclear antigen (Neu-N), and neurofilament was observed. Nuclear expression of α-thalassemia mental retardation X-linked (ATRX) was retained, and only a few cells expressed p53 ($<$10%). The MIB-1/Ki-67 labeling index was very low ($<$1%), with virtually no mitosis, supporting the diagnosis of a low-grade tumor. Molecular analysis revealed a BRAF V600E mutation. Based on these morphological, immunohistochemical, and molecular features, a diagnosis of PLNTY was concluded. The depth electrodes were adjacent to but not within the core region with dense cellular infiltrates of the tumor, and histological differences among the electrode positions were not discernible. There was no associated cortical dysplasia, and complete resection of the tumor was confirmed both histologically and on postoperative MRI. At her last follow-up visit 1 year after the surgery, she remained free of seizures and showed no cognitive impairment.

Discussion

Observations

SEEG disclosed an eccentric seizure-onset zone relative to the tumoral lesion. LVFA representing the seizure-onset zone was limited to the anterior portion of the tumor and the adjacent polar region. By contrast, the posterior portion of the tumor as well as more posterior temporal cortex were spared from LVFA. Accordingly, complete tumor resection with extension to the pole was carried out without language complications and achieved complete seizure freedom. The histopathological examination confirmed the diagnosis of PLNTY, a new entity of LEAT whose anatomo-electrical relationships of seizures have yet to be reported.

Invasive EEG recordings of spontaneous clinical seizures are not frequently performed in tumor-related epilepsy: it has been estimated that only 10% of patients receiving resection for tumor-related epilepsy are monitored with chronic intracranial electrode implantation.[8] This is due largely to the high seizure-free rate after gross total resection alone, which was as high as 79% in a systematic literature review.[9] However, this finding indicates the fact that $>$20% of cases continue to have seizures postoperatively, and therefore there is still room for improvement in the surgical strategy. Accurate delineation of the seizure-onset zone using invasive EEG monitoring has the potential to improve seizure outcomes in patients with tumor-related epilepsy.[10] To date, however, only a single study has explicitly assessed the impact of the two-stage surgery approach with invasive EEG monitoring.[10] Despite the limited variety of tumors in that study, it was suggested that excellent seizure outcomes can be achieved after complete resection of the seizure-onset zone, which can be widespread and eccentric to the tumoral lesion. To our knowledge, the current report is the first to demonstrate intracranially recorded seizures in PLNTY. Their onset was characterized by LVFA and showed eccentric localization with respect to the tumor. The latter finding is of particular importance when using SEEG as an invasive EEG tool in PLNTY because undersampling in the peritumoral region can result in failure to detect ictal-onset activity (LVFA) and thus an inability to delineate the seizure-onset zone to be resected. Indeed, the peritumoral spatial sampling in the present case allowed accurate definition of the seizure-onset zone, thereby maximizing the chance of seizure freedom. This also led to minimizing the language risk because the posterior temporal cortex was spared from LVFA. Considering the better patient

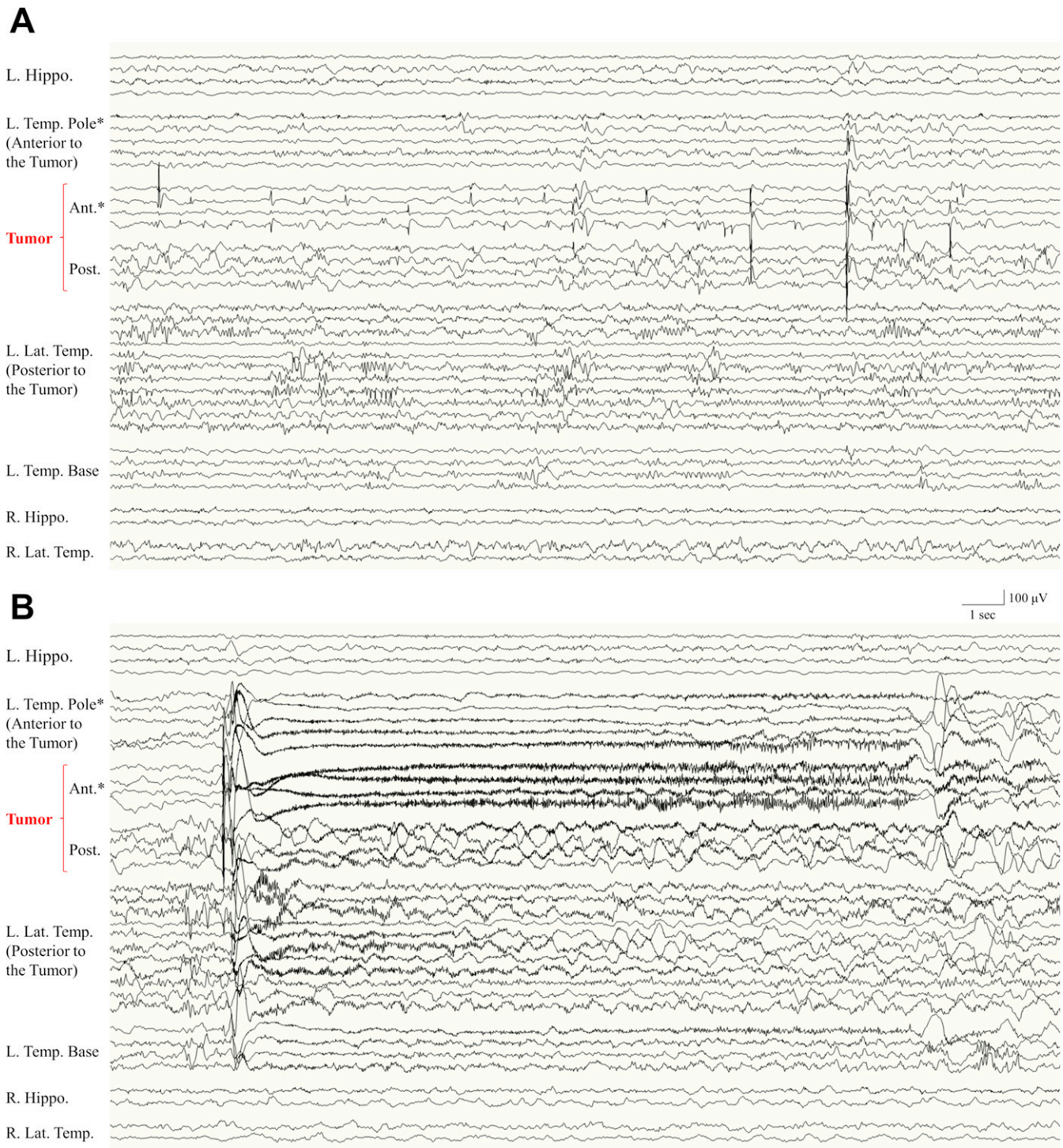

FIG. 3. SEEG findings. Interictal spikes (**A**) and ictal LVFA (**B**) were localized to the anterior portion of the tumoral lesion and propagated toward the adjacent polar cortex (*asterisks*).

experience and lower procedural complication risks with SEEG than with subdural grids,[11] there may be a greater opportunity to perform tailored resections using SEEG-recorded seizures in LEAT. Our findings would help refine the SEEG implantation scheme in future cases suspected of having PLNTY to better predict and optimize their surgical outcomes.

We were unable to find a specific correlation between the localization of seizure-onset and histopathological findings. This is a limitation that remains to be addressed in future studies

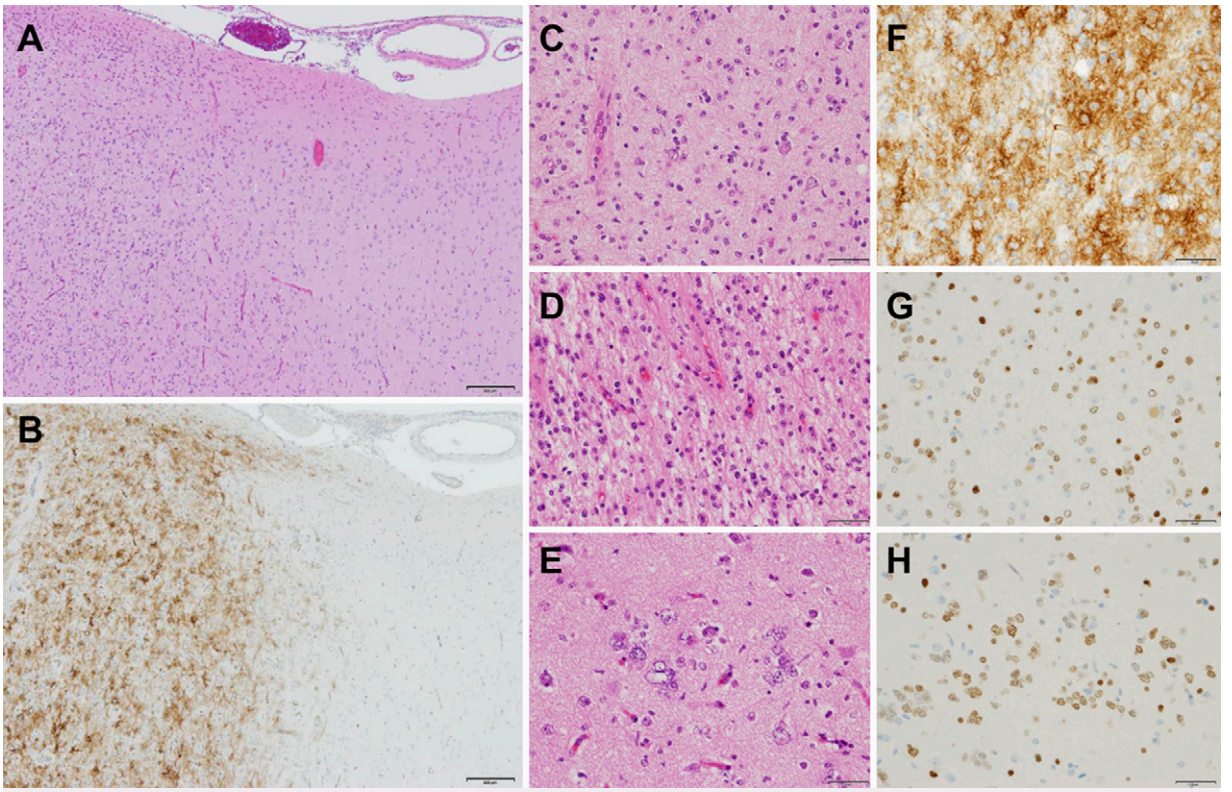

FIG. 4. Histopathological findings of the tumor. Low-power-field views showed a sharply bordered, dense, and diffuse proliferation of the tumor cells with strong CD34 immunopositivity within the cerebral cortex (left half of each section; **A,** hematoxylin and eosin staining; **B,** CD34 immunostaining). High-power-field views showed the tumor cells with oligodendrocyte-like morphology (**C and D,** in cortex and subcortex, respectively). A few subcortical tumor cells showed prominent nuclear atypia (**E**). Strong expression of CD34 was observed in the tumor cells shown in panel C (**F**). Oligodendrocyte transcription factor 2 (OLIG2) expression was confirmed in both the oligodendrocyte-like cells and atypical cells (**G and H,** for cortex and subcortex, respectively). Bar = 200 μm (A and B), 20 μm (C–H).

using a large number of patients with sufficient peritumoral electrode coverage.

Lessons

PLNTY showed a focal seizure onset with LVFA that was eccentrically located around the tumor. When exploring it with SEEG, adequate spatial sampling in the peritumoral region is essential to successfully identify the seizure-onset zone and optimize the functional as well as seizure outcomes. The lessons learned from the present case will serve to improve the surgical strategy using the two-staged approach in PLNTY and potentially in other types of LEATs.

Acknowledgments

We would like to thank EEG technicians at Epilepsy and Sleep Center, Fukuoka Sanno Hospital, Fukuoka, Japan, for their help in acquiring the electrophysiological data of the patients.

References

1. Huse JT, Snuderl M, Jones DT, et al. Polymorphous low-grade neuroepithelial tumor of the young (PLNTY): an epileptogenic neoplasm with oligodendroglioma-like components, aberrant CD34 expression, and genetic alterations involving the MAP kinase pathway. *Acta Neuropathol.* 2017;133(3):417–429.
2. Gupta VR, Giller C, Kolhe R, Forseen SE, Sharma S. Polymorphous low-grade neuroepithelial tumor of the young: a case report with genomic findings. *World Neurosurg.* 2019;132:347–355.
3. Blümcke I, Aronica E, Becker A, et al. Low-grade epilepsy-associated neuroepithelial tumours: the 2016 WHO classification. *Nat Rev Neurol.* 2016;12(12):732–740.
4. Johnson DR, Giannini C, Jenkins RB, Kim DK, Kaufmann TJ. Plenty of calcification: imaging characterization of polymorphous low-grade neuroepithelial tumor of the young. *Neuroradiology.* 2019;61(11):1327–1332.
5. Broggi G, Certo F, Altieri R, Caltabiano R, Gessi M, Barbagallo GMV. A "polymorphous low-grade neuroepithelial tumor of the young (PLNTY)" diagnosed in an adult. Report of a case and review of the literature. *Surg Neurol Int.* 2021;12:470.
6. WHO Classification of Tumours Editorial Board. *World Health Organization Classification of Tumours of the Central Nervous System.* 5th ed. International Agency for Research on Cancer; 2021.
7. Chassoux F, Devaux B, Landré E, et al. Stereoelectroencephalography in focal cortical dysplasia: a 3D approach to delineating the dysplastic cortex. *Brain.* 2000;123(Pt 8):1733–1751.
8. Rosenow F, Menzler K. Invasive EEG studies in tumor-related epilepsy: when are they indicated and with what kind of electrodes? *Epilepsia.* 2013;54(suppl 9):61–65.
9. Englot DJ, Han SJ, Berger MS, Barbaro NM, Chang EF. Extent of surgical resection predicts seizure freedom in low-grade temporal lobe brain tumors. *Neurosurgery.* 2012;70(4):921–928.

10. Mittal S, Barkmeier D, Hua J, et al. Intracranial EEG analysis in tumor-related epilepsy: evidence of distant epileptic abnormalities. *Clin Neurophysiol.* 2016;127(1):238–244.
11. Tandon N, Tong BA, Friedman ER, et al. Analysis of morbidity and outcomes associated with use of subdural grids vs stereoelectroencephalography in patients with intractable epilepsy. *JAMA Neurol.* 2019;76(6):672–681.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Hagiwara, Kamada, Suzuki, Shigeto, Ohara, Akamatsu. Acquisition of data: Hagiwara, Kamada, Suzuki, Miyoshi, Tanaka, Shigeto, Ohara. Analysis and interpretation of data: Hagiwara, Suzuki, Tanaka, Shigeto, Ohara. Drafting the article: Hagiwara, Shigeto. Critically revising the article: Hagiwara, Suzuki, Ohara, Akamatsu. Reviewed submitted version of manuscript: Hagiwara, Suzuki, Miyoshi, Shigeto, Ohara, Akamatsu. Approved the final version of the manuscript on behalf of all authors: Hagiwara. Administrative/technical/material support: Hagiwara, Tanaka, Akamatsu. Study supervision: Hagiwara, Shigeto, Akamatsu.

Correspondence

Koichi Hagiwara: Epilepsy and Sleep Center, Fukuoka Sanno Hospital, Fukuoka, Japan. hagiwara-kyu@umin.ac.jp.