

Case report

Serial assessment of multimodality imaging in anti-leucine-rich glioma-inactivated 1 antibody encephalitis: A case report

Takafumi Wada, Hitoshi Mori, Katsuro Shindo *

Department of Neurology, Kurashiki Central Hospital, 1-1-1 Miwa, Kurashiki/Okayama, 710-8602, Japan

ARTICLE INFO

Keywords:

Anti-LGI1 encephalitis
ASL
SPECT
¹⁸F-FDG-PET

ABSTRACT

In autoimmune encephalitis, abnormalities of diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR), arterial spin labeling (ASL) in magnetic resonance imaging (MRI), single-photon emission computed tomography (SPECT) and ¹⁸F-fluorodeoxyglucose-positron emission tomography (¹⁸F-FDG-PET) have been reported. However, there are few studies of long-term follow-up of imaging. We report a case of anti-leucine-rich glioma-inactivated 1 antibody encephalitis whose MRI (DWI, FLAIR and ASL), ^{99m}TcHMPAO SPECT (PAO-SPECT) and ¹⁸F-FDG-PET were evaluated through the clinical course. ASL, PAO-SPECT and ¹⁸F-FDG-PET consistently showed abnormalities in almost the same area. Serial assessment of these imaging modalities is useful in evaluating disease activity and efficacy of treatment.

1. Introduction

Anti-leucine-rich glioma-inactivated 1 antibody encephalitis (anti-LGI1 encephalitis) is the autoimmune encephalitis characterized by acute progressive cognitive dysfunction, psychiatric symptoms, epilepsy, faciobrachial dystonic seizures and hyponatremia. Moreover, diffusion-weighted imaging (DWI) and fluid-attenuated inversion recovery (FLAIR) show high intensity in the temporal lobe in magnetic resonance imaging (MRI), and abnormalities in cerebrospinal fluid (CSF) are often detected; however, some cases lack these abnormalities. In autoimmune limbic encephalitis, there have been reports of abnormal findings in single-photon emission computed tomography (SPECT) and ¹⁸F-fluorodeoxyglucose-positron emission tomography (¹⁸F-FDG-PET). Recently, MRI arterial spin labeling (ASL) has also been reported to show abnormalities in limbic encephalitis. ASL is a non-invasive imaging of cerebral blood flow that does not require contrast enhancement or radiation, but uses magnetic labeling of proton spins in arterial blood as a tracer [1]. ASL has been used to evaluate the pathophysiology of autoimmune encephalitis [2]. Previous studies suggest that ASL is useful in epilepsy follow-up as it also reflects cerebral perfusion changes during epileptic seizures [3]. Although there have been reports that ASL is useful in assessing the state of anti-LGI1 encephalitis [8,9], few cases have been reported in which ASL was followed up with other imaging studies to assess cerebral perfusion and metabolism. Herein, we report a case of anti-LGI1 encephalitis evaluated by MRI (DWI, FLAIR and ASL),

SPECT, and ¹⁸F-FDG-PET.

2. Case report

A 42-year-old female without any past history presented with numbness and pain in her right upper extremity and both lower extremities from 3 months before admission. Her appetite and activity had decreased 2 months before admission, and she began to feel anxiety 1 month before admission. She also presented with memory impairment.

On admission, her body temperature was 37.6 °C. Neurological examination revealed no cranial nerve impairment, paralysis, or abnormalities in reflexes. Moreover, she didn't show involuntary movement. Blood testing was negative for auto-antibodies including anti-nuclear, anti-neutrophil cytoplasmic, anti-GAD, anti SS-A and anti-SS-B antibodies. Cerebrospinal fluid (CSF) analysis revealed cell count of 1 /μL, protein of 39 mg/dL, and IgG index of 0.63. Whole-body CT showed no lymphadenopathy or malignant lesions. Electroencephalography (EEG) showed intermittent rhythmic delta activities in the left frontotemporal region, and sharp waves that started in the left frontotemporal region with expansion to the right. MRI revealed faint high intensity in the left mesial temporal lobe on DWI. FLAIR revealed high intensity and ASL revealed increased cerebral blood flow in the same region. ^{99m}TcHMPAO SPECT (PAO-SPECT) showed increased cerebral blood flow in the left mesial temporal lobe. ¹⁸F-FDG-PET showed hypermetabolism that coincided with the region of increased cerebral blood flow in the ASL

* Corresponding author.

E-mail address: shindo@kchnet.or.jp (K. Shindo).<https://doi.org/10.1016/j.ensci.2022.100426>

Received 13 June 2022; Received in revised form 29 July 2022; Accepted 10 September 2022

Available online 14 September 2022

2405-6502/© 2022 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

(Fig. 1).

After admission, serum anti-LGI1 antibody was positive; thus, she was diagnosed as anti-LGI1 encephalitis. The patient's memory impairment continued to worsen, and intravenous methylprednisolone was administered. There was no clear improvement in her symptoms, so plasma exchange and intravenous immunoglobulin (IVIg) were added. After these treatments, her anxiety and sensory disturbance disappeared, but her memory impairment remained.

On MRI 3 days after administration of IVIg, DWI showed a reduction of high intensity in the left temporal lobe. FLAIR also showed a reduction of high intensity in the left temporal lobe, but it revealed faint high signal in the right temporal lobe. ASL showed a reduction of hyper cerebral blood flow in the left temporal lobe, but it also newly revealed increased cerebral blood flow in the right temporal lobe. PAO-SPECT 2 days after administration of IVIg also showed reduced hyper blood flow in the left temporal lobe and increased blood flow in the right temporal lobe (Fig. 2).

Intravenous cyclophosphamide (IVCY) was administered for residual memory impairment, and the symptoms, such as disorientation, improved. On MRI 9 days after IVCY, DWI revealed that high intensity in the left temporal lobe almost completely disappeared and high intensity appeared in the right temporal lobe; however, FLAIR showed residual high intensity in the left temporal lobe and enhanced high intensity in the right temporal lobe. ASL showed increased cerebral blood flow in the right temporal lobe but not in the left temporal lobe. PAO-SPECT 10 days after IVCY showed increased blood flow in the right temporal lobe and the increased blood flow in the temporal lobe almost completely disappeared. ^{18}F -FDG-PET 22 days after IVCY showed hyper metabolism that coincided with ASL (Fig. 3). EEG one month after IVCY showed intermittent rhythmic delta activities in the bilateral temporal regions. The evolutionary pattern noted on EEG before administration of intravenous methylprednisolone disappeared. She discharged home on day 51.

3. Discussion

We evaluated MRI (DWI, FLAIR and ASL), PAO-SPECT, and ^{18}F -FDG-PET before treatment, after first-line immunotherapy, and after second-

line immunotherapy in a case of anti-LGI1 encephalitis with rapid progressive anxiety, memory impairment, and abnormal sensation.

ASL and PAO-SPECT imaging before treatment showed increased blood flow in the DWI and FLAIR high-intensity area, and ^{18}F -FDG-PET also showed increased metabolism in the same area. The images after first-line immunotherapy showed a faint high-signal area in the right temporal lobe in FLAIR, which was not apparent in DWI. On the other hand, the images after second-line immunotherapy showed high intensity in the right mesial temporal lobe in DWI and FLAIR, increased cerebral blood flow in the same region in ASL and SPECT, and increased hypermetabolism in ^{18}F -FDG-PET. In the present case, EEG was also followed before and after treatment. EEG before treatment suggested dysfunction of the left frontotemporal region and seizures starting from the left frontotemporal region. EEG after IVCY showed disappearance of ictal patterns with the reduction of imaging abnormalities in the left temporal lobe. It showed intermittent rhythmic delta activities in the bilateral temporal regions, suggesting that functional abnormalities appeared in the right hemisphere, reflecting the imaging abnormalities that appeared in the right temporal lobe.

^{18}F -FDG-PET is useful in the diagnosis of autoimmune encephalitis and is recommended when MRI cannot be performed [4]. It is also useful in evaluating the disease severity [5]. Imaging evaluation of autoimmune encephalitis has also been performed with other modalities, such as in cases of anti-N-methyl-D-aspartate (NMDA) receptor antibody encephalitis. ASL and SPECT have been reported to show increased cerebral blood flow [6,7]. In cases of anti-LGI1 encephalitis, ASL and ^{18}F -FDG-PET have been used to evaluate the state of disease. Significantly, in a case of anti-LGI-1 encephalitis with status epilepticus, increased cerebral blood flow in the ASL and hyper metabolism in ^{18}F -FDG-PET showed similar improvement before and after treatment [8], and in a case of anti-LGI1 antibody encephalitis without status epilepticus, ASL and ^{18}F -FDG-PET showed abnormalities in the same region [9]. These findings suggest that in the acute phase of anti-LGI1 encephalitis, increased blood flow in ASL and hyper metabolism in ^{18}F -FDG-PET may reflect epileptic seizures and inflammation.

A case of NMDA receptor antibody encephalitis whose ASL and ^{18}F -FDG-PET were followed-up for comparison has been reported. In the acute phase, ASL showed bilateral occipito-parietal hypoperfusion co-

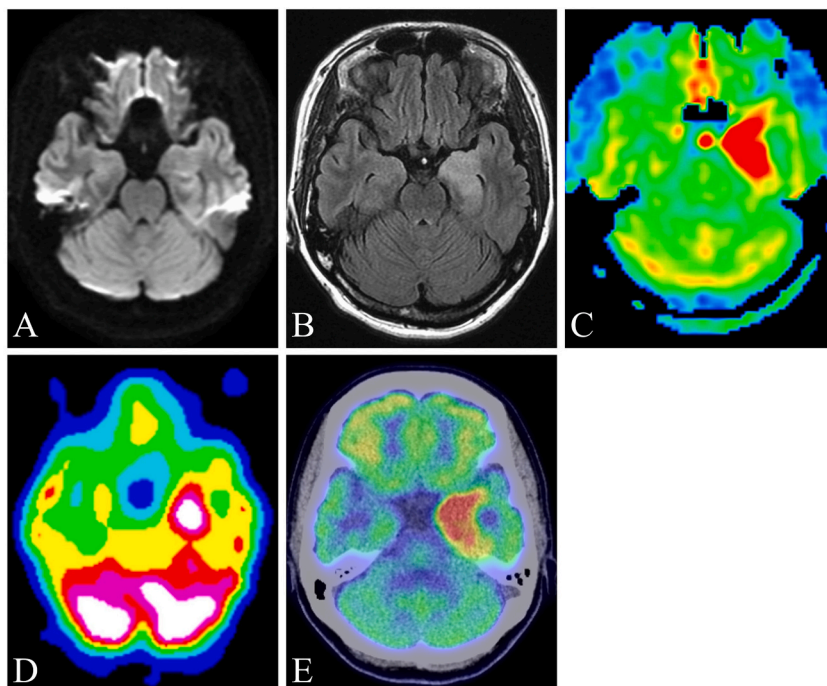


Fig. 1. Images on admission.

The MRI machine was PHILIPS Ingenia 3.0 T, using dS Head 32ch 3.0 T coil. A) DWI. There is slightly high intensity in the left mesial temporal lobe. B) FLAIR. The left mesial temporal lobe shows hyper intensity. C) ASL. There is increased cerebral blood flow in the left mesial temporal lobe. Post labeling delay was 2500 ms. D) PAO-SPECT. It shows increased cerebral blood flow in the left mesial temporal lobe. SPECT was performed using the following protocol: 1110 MBq of $^{99\text{m}}\text{Tc}$ -HMPAO was administered, and imaging was performed on a Dual-head SPECT scanner: Symbia T2 (Siemens Japan) starting about 5 min later. E) ^{18}F -FDG-PET. There is hyper metabolism in the left mesial temporal lobe, which is coinciding with the region of increased cerebral blood flow in ASL. It was performed using the following protocol: 60 min after administration of 288.2 MBq ^{18}F -FDG, CT was performed, followed by PET from the parietal to the thighs. Abbreviations; MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; FLAIR; fluid-attenuated inversion recovery; ASL, arterial spin labeling; PAO-SPECT, $^{99\text{m}}\text{Tc}$ HMPAO single-photon emission computed tomography; ^{18}F -FDG-PET, ^{18}F -fluorodeoxyglucose-positron emission tomography; CT, computed tomography.

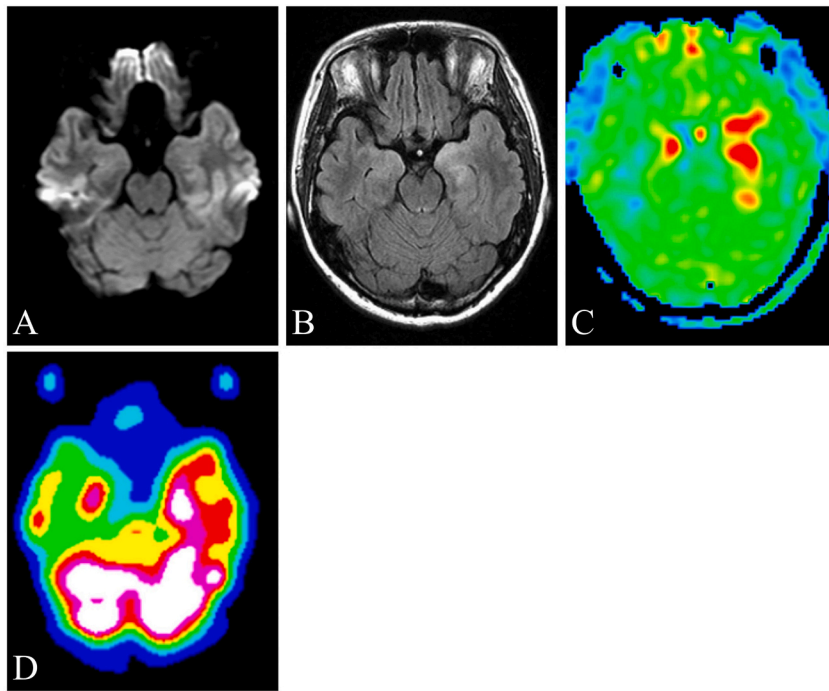


Fig. 2. Images after the treatment of intravenous methylprednisolone, plasma exchange, and IVIg. All imaging protocols are the same as Fig. 1. A) DWI. High intensity in the left temporal lobe was reduced. High intensity in the right temporal lobe is not apparent. B) FLAIR. High intensity in the left temporal lobe is reduced, but faint high intensity in the right temporal lobe appeared. C) ASL. The hyperperfusion area in the left temporal lobe is reduced. On the other hand, increased cerebral blood flow is newly detected in the right mesial temporal lobe. D) PAO-SPECT. Similar to ASL, there is an area of increased blood flow in the right mesial temporal lobe. Abbreviations; IVIg, intravenous immunoglobulin; DWI, diffusion-weighted imaging; FLAIR; fluid-attenuated inversion recovery; ASL, arterial spin labeling; PAO-SPECT, ^{99m}Tc HMPAO single-photon emission computed tomography.

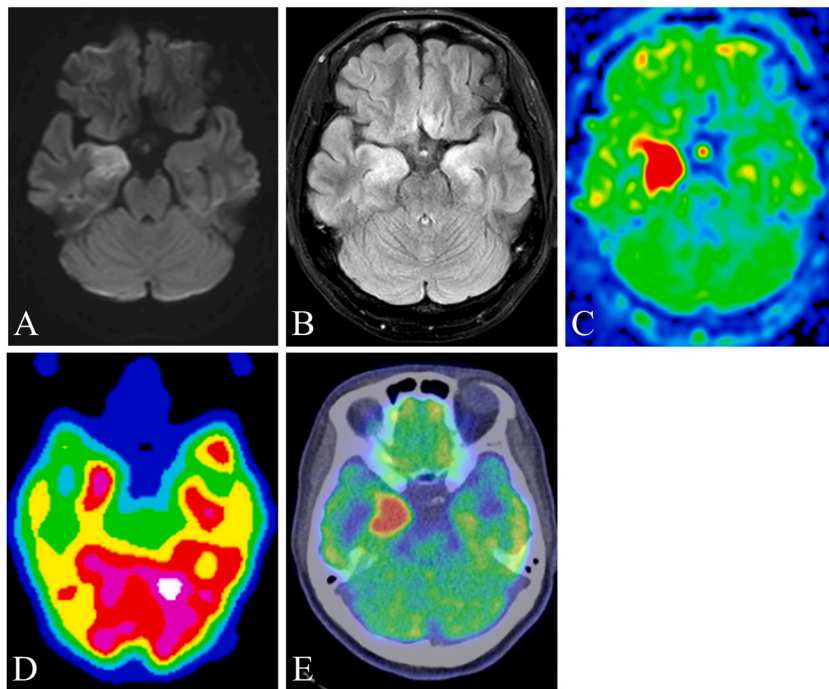


Fig. 3. Images after intravenous cyclophosphamide. All imaging protocols were same as Fig. 1 and Fig. 2. A) DWI. High intensity in the right mesial temporal lobe is apparent. B) FLAIR. High intensity in the right mesial temporal lobe is enhanced. On the other hand, there is a residual high signal in the left temporal lobe. C) ASL. Increased cerebral blood flow in the right mesial temporal lobe is evident. The hyperperfusion area in the left temporal lobe disappears. D) PAO-SPECT. There is increased cerebral blood flow in the right mesial temporal lobe. The hyperperfusion area in the left temporal lobe is reduced. E) ^{18}F -FDG-PET. Hypermetabolism is observed in the right mesial temporal lobe, which is almost coincident with the hyperperfusion area of ASL. Hypermetabolism in the left temporal lobe disappears. Abbreviations; DWI, diffusion-weighted imaging; FLAIR; fluid-attenuated inversion recovery; ASL, arterial spin labeling; PAO-SPECT, ^{99m}Tc HMPAO single-photon emission computed tomography; ^{18}F -FDG-PET, ^{18}F -fluorodeoxyglucose-positron emission tomography.

localized with ^{18}F -FDG-PET hypometabolism, and both lesions were recovered after treatment [11]; however, there has been no report of anti-LGI1 encephalitis whose MRI (DWI, FLAIR and ASL), ^{18}F -FDG-PET, and SPECT were followed-up for comparison. The results of the present case suggest that ASL, ^{18}F -FDG-PET, and SPECT in anti-LGI1 encephalitis almost equally reflects the activity of disease.

In the present case, there was no abnormalities in CSF cell count or protein levels; therefore, CSF analysis could not be used to evaluate the state of disease. It has been reported that as many as 62% of patients with autoimmune encephalitis have CSF abnormalities [10]; thus, CSF

analysis is not necessarily useful for determining the disease activity or efficacy of treatment. In such cases, follow-up of DWI and FLAIR as well as ASL, ^{18}F -FDG-PET, and SPECT findings may help to assess disease activity and the efficacy of treatment.

4. Conclusion

In anti-LGI1 encephalitis, ASL, ^{18}F -FDG-PET and SPECT may be useful to evaluate the pathogenesis in addition to DWI and FLAIR. Moreover, serial assessment of these imaging modalities may be useful

in determining disease activity and efficacy of treatment.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

None.

Acknowledgement

None.

References

- [1] J.A. Detre, J.S. Leigh, D.S. Williams, A.P. Koretsky, Perfusion imaging, *Magn. Reson. Med.* 23 (1992) 37–45, <https://doi.org/10.1002/mrm.1910230106>.
- [2] R. Li, S. Jin, Y. Wang, J.-F. Li, H.-F. Xiao, Y.-L. Wang, L. Ma, Brain perfusion alterations on 3D pseudocontinuous arterial spin-labeling MR imaging in patients with autoimmune encephalitis: a case series and literature review, *AJNR Am. J. Neuroradiol.* 43 (2022) 701–706, <https://doi.org/10.3174/ajnr.A7478>.
- [3] I.B. Galazzo, S.F. Storti, A.D. Felice, F.B. Pizzini, C. Arcaro, E. Formaggio, R. Mai, M. Chappel, A. Beltramello, P. Manganotti, Patient-specific detection of cerebral blood flow alterations as assessed by arterial spin labeling in drug-resistant epileptic patients, *PLoS One* 10 (2015), e0123975, <https://doi.org/10.1371/journal.pone.0123975>.
- [4] F. Graus, M.J. Titulaer, R. Balu, S. Benseler, C.G. Bien, T. Cellucci, I. Cortese, R. C. Dale, J.M. Gelfand, M. Geschwind, C.A. Glaser, J. Honnorat, R. Höftberger, T. Iizuka, S.R. Irani, E. Lancaster, F. Leypoldt, H. Prüss, A. Rae-Grant, M. Reindl, M. R. Rosenfeld, K. Rostásy, A. Saiz, A. Venkatesan, A. Vincent, K.-P. Wandinger, P. Waters, J. Dalmau, A clinical approach to diagnosis of autoimmune encephalitis, *Lancet Neurol.* 15 (2016) 391–404, [https://doi.org/10.1016/S1474-4422\(15\)00401-9](https://doi.org/10.1016/S1474-4422(15)00401-9).
- [5] F. Leypoldt, R. Buchert, I. Kleiter, J. Marienhagen, M. Gelderblom, T. Magnus, J. Dalmau, C. Gerloff, J. Lewerenz, Fluorodeoxyglucose positron emission tomography in anti-N-methyl-d-aspartate receptor encephalitis: distinct pattern of disease, *J. Neurol. Neurosurg. Psychiatry* 83 (2012) 681–686, <https://doi.org/10.1136/jnnp-2011-301969>.
- [6] A. Miao, Q. Liu, Z. Li, W. Liu, W.L. Wang, J. Ge, C. Yu, Y. Wang, S. Huang, Y. Yu, Q. Shi, J. Sun, X. Wang, Altered cerebral blood flow in patients with anti-NMDAR encephalitis, *J. Neurol.* 267 (2020) 1760–1773, <https://doi.org/10.1007/s00415-020-09747-x>.
- [7] V. Llorens, I. Gabilondo, J.C. Gómez-Esteban, M. Agundez, M. Mendibe, J. C. Bergara, R. Ciordia, A. Saiz, J.J. Zarranz, Abnormal multifocal cerebral blood flow on Tc-99m HMPAO SPECT in a patient with anti-NMDA-receptor encephalitis, *J. Neurol.* 257 (2010) 1568–1569, <https://doi.org/10.1007/s00415-010-5546-z>.
- [8] C. Espinosa-Jovel, R. Toledano, I. García-Morales, J. Álvarez-Linera, A. Gil-Nagel, Serial arterial spin labeling MRI in autonomic status epilepticus due to anti-LGI1 encephalitis, *Neurology* 87 (2016) 443–444, <https://doi.org/10.1212/WNL.0000000000002903>.
- [9] A. Dinoto, M. Cheli, M. Ajčević, F. Dore, C. Crisafulli, M. Ukmar, A. Sartori, P. Manganotti, ASL MRI and 18F-FDG-PET in autoimmune limbic encephalitis: clues from two paradigmatic cases, *Neurol. Sci.* 42 (2021) 3423–3425, <https://doi.org/10.1007/s10072-021-05207-0>.
- [10] J.C. Probasco, L. Solnes, A. Nalluri, J. Cohen, K.M. Jones, E. Zan, M.S. Javadi, A. Venkatesan, Abnormal brain metabolism on FDG-PET/CT is a common early finding in autoimmune encephalitis, *Neurol. Neuroimmunol. Neuroinflamm.* 4 (2017), e352, <https://doi.org/10.1212/NXI.0000000000000352>.
- [11] C. Lapucci, G. Boffa, F. Massa, D. Franciotta, L. Castelletti, A. Uccelli, S. Morbelli, F. Nobili, L. Benedetti, L. Roccatagliata, Could arterial spin labelling perfusion imaging uncover the invisible in N-methyl-d-aspartate receptor encephalitis? *Eur. J. Neurol.* 26 (2019) e86–e87, <https://doi.org/10.1111/ene.13977>.