American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2019; 20: 1883-1887
DOI: 10.12659/AJCR.919938

Received: 2019.09.06
Accepted: 2019.10.13
Published: 2019.12.16

Arterial Spin Labeling Magnetic Resonance Imaging in the Assessment of Non-Convulsive Status Epilepticus in Alzheimer's Disease: A Report of Two Cases

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

BDEFG 1 Tatsushi Mutoh
BDEF 2 Kaoru Eguchi
BD 1,2 Shuzo Yamamoto
B 2 Nobuyuki Yasui
DE 1 Yasuyuki Taki

1 Department of Nuclear Medicine and Radiology, Institute of Development, Aging, and Cancer, Tohoku University, Sendai, Miyagi, Japan
2 Sendai East Neurosurgical Hospital, Sendai, Miyagi, Japan

Corresponding Author: Tatsushi Mutoh, e-mail: tmutoh@tohoku.ac.jp
Conflict of interest: None declared

Case series

Patients: Female, 69-year-old • Male, 70-year-old

Final Diagnosis: Nonconvulsive status epilepticus

Symptoms: Altered mental status • cognitive impairment

Medication: —

Clinical Procedure: ASL perfusion MRI

Specialty: Neurology

Objective: Challenging differential diagnosis

Background: The diagnosis of early non-convulsant status epilepticus (NCSE) can be challenging and can overlap with other critical conditions. Two patients with Alzheimer's disease are reported with clinically suspected NCSE presenting in the emergency setting who were diagnosed using arterial spin-labeling magnetic resonance imaging (ASL-MRI) sequences.

Case Reports: In Case 1, a 69-year-old woman with mild Alzheimer's disease and diabetes presented with acute worsening of cognitive status and fluctuating level of consciousness. In Case 2, a 70-year-old man with mild cognitive impairment due to Alzheimer's disease and hypertension presented with acute loss of consciousness and left hemiparesis, without evidence of hypoglycemia or a hypertensive crisis. In both cases, ASL-MRI perfusion images showed focal cerebral hyperperfusion in the posterior cingulate and parietal associative cortex, which involved neurodegenerative areas associated with epilepsy in early Alzheimer's disease. In both cases, the patients developed generalized tonic-clonic epileptic seizures that lasted for 5 minutes or more, which indicated the emergence of status epilepticus that developed from the initial presentation of NCSE. In both cases, electroencephalogram (EEG) findings confirmed that the seizures were controlled by intravenous administration of antiepileptic drugs. Both patients discharged home from the hospital without recurrence of seizures, between 10–12 days after the onset of symptoms.

Conclusions: These two cases have demonstrated that ASL-MRI is feasible as an emergency diagnostic tool in clinically suspected NCSE in patients with Alzheimer's disease.

MeSH Keywords: Dementia • Magnetic Resonance Imaging • Regional Blood Flow • Status Epilepticus

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/919938

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

In elderly patients with dementia, transient events, including syncope and confusion, are the most common neurological emergencies [1]. In such cases, the differential diagnoses should include status epilepticus, which is a potentially treatable cause of altered consciousness in the elderly [3]. Although the diagnosis of convulsive status epilepticus is based on the clinical presentation [2], assessment of non-convulsive status epilepticus (NCSE) is usually challenging in patients with dementia. Difficulty in the early diagnosis of NCSE is due to the lack of significant motor phenomena and the presence of symptoms and signs that overlap with those of other critical conditions, such as transient ischemic attack (TIA), stroke, hypoglycemia, and metabolic encephalopathy [3].

In the ictal phase, electroencephalography (EEG) is required to confirm the diagnosis of NCSE [4]. However, the use of emergency or continuous EEG recordings are limited in general emergency units that are not part of specialized epilepsy centers. Recently, arterial spin-labeling (ASL) perfusion magnetic resonance imaging (MRI) has become a more commonly used imaging tool for the early clinical diagnosis of disorders such as stroke, tumors, status epilepticus, and dementia [5–7].

Therefore, as an alternative approach for the diagnosis of NCSE, particularly in cases that require the exclusion of acute stroke or causes of dementia, ASL is an important diagnostic approach to consider. Two patients with Alzheimer's disease are reported with clinically suspected NCSE presenting in the emergency setting who were diagnosed using the ASL-MRI sequences.

Case Reports

Case 1

A 69-year-old woman arrived by ambulance to our neurological emergency room with acute and worsening cognitive status and fluctuating level of consciousness. Several years previously, she had been diagnosed with mild Alzheimer's disease, according to the revised diagnostic criteria of the National Institute on Aging-Alzheimer's Association (NIA-AA) [8], She was also treated for diabetes and hypertension with oral medication. However, she occasionally experienced episodes of hypoglycemia, characterized by pallor and a reduced level of consciousness or transient seizures, but usually recovered with oral intake of carbohydrates. The use of a portable glucose meter indicated a blood sugar concentration of 9.4 mmol/L (170 mg/dl).

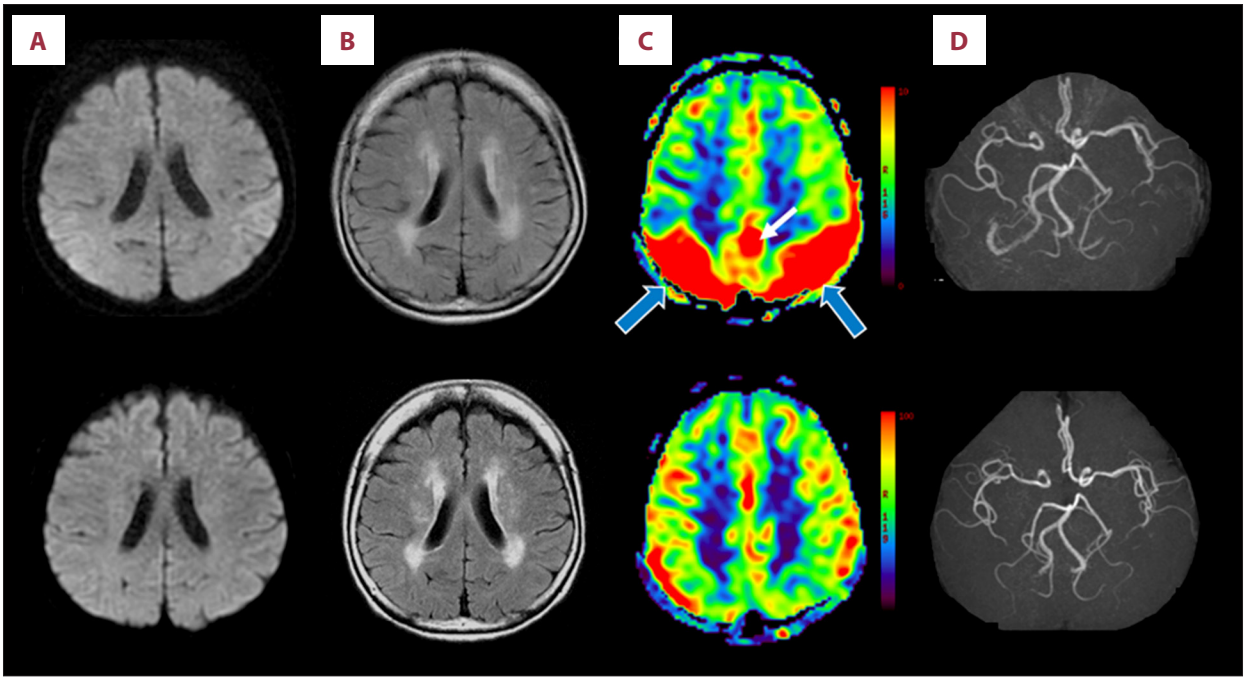

Figure 1. Case 1: A 69-year-old woman with Alzheimer's disease who presented with acute worsening of cognitive status and fluctuating level of consciousness. The upper and lower rows include MRI findings. (**A**). The diffusion-weighted images. (**B**) The fluid-attenuated inversion recovery images. (**C**) The ASL-MRI perfusion images. (**D**) Magnetic resonance angiography images obtained on admission and hospital day 2, respectively. Axial brain slices at the level of the lateral ventricles are shown (**A–C**). ASL shows focal areas of increased signal intensity, indicating hyperperfusion in the bilateral parietal lobes (thick blue arrows) and the precuneus area of the superior parietal lobe (thick white arrow).

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

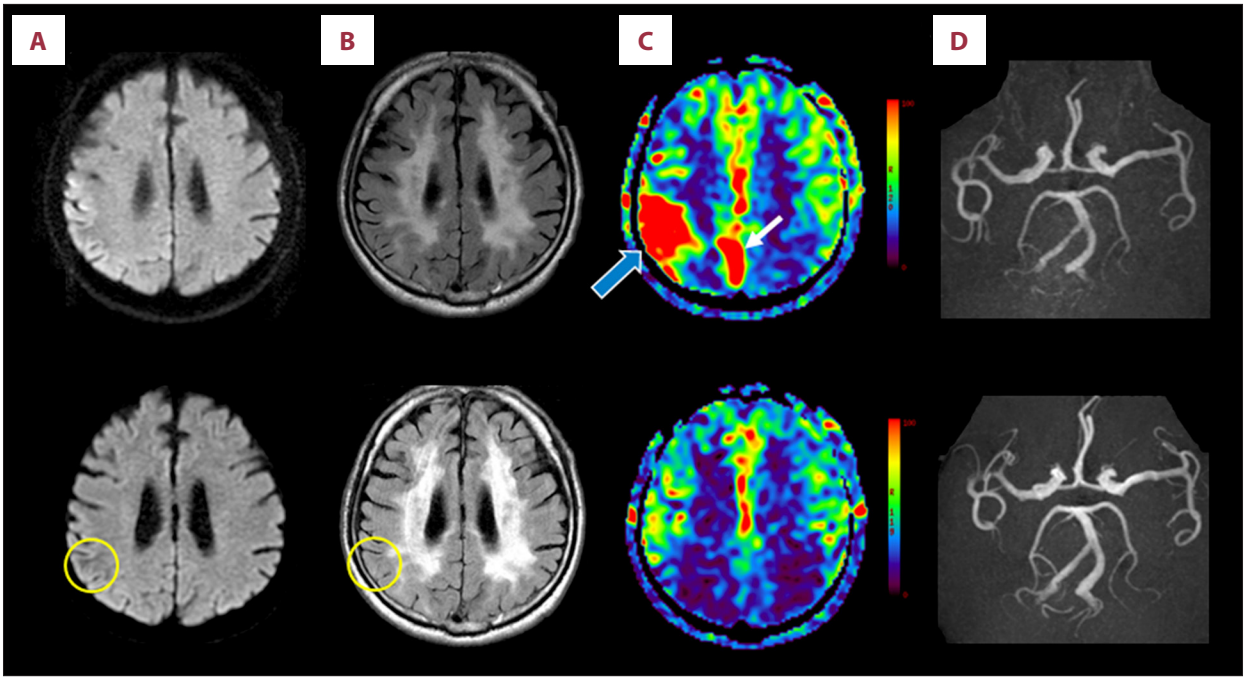

Figure 2. Case 2: A 70-year-old man with hypertension and early Alzheimer's disease who presented with loss of consciousness and left hemiparesis. The upper and lower rows show the MRI findings. (**A**) The diffusion-weighted images. (**B**) The fluid-attenuated inversion recovery images. (**C**) The ASL-MRI perfusion images. (**D**) The magnetic resonance angiography images obtained on hospital admission and hospital day 2, respectively. Axial brain slices at the level of the lateral ventricles (**A–C**) are shown. ASL shows hyperperfusion in the right inferior parietal lobe (thick blue arrows) and the precuneus area of the superior parietal lobe (thick white arrow). The yellow circles indicate chronic cortical infarction of the right parietal lobe.

On admission to the emergency department, she was found to have impaired verbal responses, although she remained functional with no apparent seizures.

Emergency brain MRI using a 1.5T SIGNA™ MRI scanner (GE Healthcare Life Sciences, Logan, UT, USA) showed slightly increased signal intensity in the parietal lobes bilaterally on diffusion-weighted imaging (DWI) (Figure 1A, 1B). ASL-MRI sequences were acquired using pseudo-continuous arterial spin labeling (pCASL) perfusion, with 3D ASL, HDxtVer 23, and a post-labeling delay of 1525–2025 ms [5], showed focal cortical hyperperfusion in the superior and inferior parietal lobes bilaterally (Figure 1C). The ASL findings involved neurodegenerative areas affected by early Alzheimer's disease, including the posterior cingulate and parietal cortex [9], which are associated with an increased risk of epilepsy [10]. Magnetic resonance angiography (MRA) showed no apparent vascular lesions (Figure 1D). Subsequently, she experienced a generalized tonic-clonic seizure that began on the left side of the face and lasted for 5 minutes or more. The seizure was controlled by an intravenous bolus injection of diazepam (5 mg), followed by infusion with fosphenytoin (22.5 mg/kg). No epileptiform activity could be detected on EEG performed the next day, and cerebral ASL-MRI showed normal perfusion. The patient was discharged from the hospital 12 days after the onset of her symptoms.

Case 2

A 70-year-old man was admitted to the hospital as an emergency with loss of consciousness, left hemiparesis, and mild cognitive impairment. He had a known history of Alzheimer's disease, which was previously diagnosed according to the criteria of the Japanese Alzheimer's Disease Neuroimaging Initiative (J-ADNI) [11]. DWI showed slightly increased abnormal signal intensity around the right parietal cortex (Figure 2A, 2B). ASL showed hyperperfusion in the right inferior parietal lobe and precuneus area of the superior parietal lobe (Figure 2C, upper panel), which correlated well with hypoperfused brain areas associated with degenerative changes in Alzheimer's disease [10], and cortical involvement by a small ischemic lesion as a cause of post-stroke epilepsy [12]. No remarkable findings were demonstrated by MRA (Figure 2D). While waiting for admission to a hospital bed, he experienced a generalized tonic-clonic seizure that started in the left hand, and which was controlled by infusion of intravenous diazepam (10 mg), and levetiracetam (500 mg), followed by an injection of propofol (2 mg/kg), after approximately 30 minutes. ASL-MRI performed on the following

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

day showed normalization of the right lateral area of parietal hyperperfusion, and the hypoperfusion in the bilateral parietal lobes (Figure 2C, lower panel). The EEG showed no apparent epileptogenic discharges. The patient was discharged from the hospital 10 days after the onset of his symptoms.

Discussion

Alzheimer's disease, and mixed forms of dementia, including vascular dementia, are associated with between a 5-fold and 10-fold increased risk of developing epilepsy when compared with age-matched controls, which account for between 10–20% of cases of new-onset epilepsy [3]. Several factors may contribute to the development of secondary epilepsy, including the deposition of β-amyloid, neuronal loss, and gliosis involving the cerebral cortex, as well as dementia-related comorbidities associated with hypertension and diabetes [3].

Recent functional neuroimaging studies, using positron emission tomography (PET), have shown that posterior cerebral hypometabolism involving the posterior cingulate cortex and parietal lobes may contribute to the occurrence of epileptic seizures in Alzheimer's disease [13,14]. It has been proposed that epileptic activity deactivates default mode networks, including the posterior cingulate cortex, leading to an altered level of consciousness and cognitive function during seizures [15]. The two cases presented in this report showed hyperperfusion in these posterior cerebral areas during ictal phase, followed by relative hypoperfusion after treatment. These findings supporting a higher incidence of NCSE in the brain areas most vulnerable to the increased production of proteins associated with Alzheimer's disease and with neurodegeneration [16]. Also, the involvement of previous cerebral ischemic infarction in Case 2 may have accelerated epileptogenic activities [12], although the relationship with Alzheimer's disease-associated parietal areas remains unclear.

In both cases presented in this report, emergency imaging using the ASL-MRI sequences showed hyperperfusion compatible with the clinical diagnosis of NCSE. The use of this novel imaging technique to detect NCSE requires comparative studies with current gold-standard diagnostic methods, including ictal EEG, using the Salzburg Consensus Criteria [4]. However, there exists a time-delay between the onset of NCSE and the initial findings on EEG, with an average interval of 73 hours reported in real-world emergency settings and acute ischemic stroke [7,17]. Furthermore, the presence of a close association with pathophysiological processes that sustain cognitive impairment in dementia may also complicate the diagnosis. Also, in patients with suspected hypoglycemia, we may not know whether the patient had a diagnosis of NCSE, as hypoglycemia can also lead to bilateral hyperperfusion [18]. In the two cases presented in this report, a definitive diagnosis of NCSE was not possible because of the negative EEG findings following the treatment of their clinical symptoms. Although the clinical application of ASL perfusion MRI in the diagnosis of NCSE is proposed, recent reports have shown that perfusion abnormalities on ASL can identify 40% of elderly patients with status epilepticus [7]. Also, the use of ASL combined with DWI and MRI to assist early assessment of NCSE has also been validated by the use of ictal EEG [5,19].

Conclusions

To the best of our knowledge, this is the first report to demonstrate the feasibility of perfusion-based MRI using ASL sequences as an emergency tool that may help to diagnose clinically suspected NCSE in patients with Alzheimer's disease.

Acknowledgments

The authors are grateful to Dr. Noriaki Watabe for the clinical management of the two patients described in this report.

Conflict of interest

None.

References:

1. Matuchansky C: Diagnosis of reversible causes of coma. Lancet, 2015; 385: 1179
2. Trinka E, Cock H, Hesdorffer D et al: A definition and classification of status epilepticus-report of the ilae task force on classification of status epilepticus. Epilepsia, 2015; 56: 1515–23
3. Liu S, Yu W, Lu Y: The causes of new-onset epilepsy and seizures in the elderly. Neuropsychiatr Dis Treat, 2016; 12: 1425–34
4. Leitinger M, Beniczky S, Rohracher A et al: Salzburg consensus criteria for non-convulsive status epilepticus – approach to clinical application. Epilepsy Behav, 2015; 49: 158–63
5. Yamamoto S, Mutoh T, Tatewaki Y et al: Identification of non-convulsive status epilepticus with bradylalia using arterial spin-labeling magnetic resonance imaging. Acute Med Surg, 2019; 6: 73–77
6. Haller S, Zaharchuk G, Thomas DL et al: Arterial spin labeling perfusion of the brain: Emerging clinical applications. Radiology, 2016; 281: 337–56
7. Ueno T, Kimura T, Funamizu Y et al: Evaluation of cerebral blood flow in older patients with status epilepticus using arterial spin labeling. eNeurologicalSci, 2019; 14: 56–59
8. McKhann GM, Knopman DS, Chertkow H et al: The diagnosis of dementia due to alzheimer's disease: Recommendations from the National Institute On Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement, 2011; 7: 263–69
9. Miners JS, Schulz I, Love S: Differing associations between abeta accumulation, hypoperfusion, blood-brain barrier dysfunction and loss of pdgfrb pericyte marker in the precuneus and parietal white matter in Azheimer's disease. J Cereb Blood Flow Metab, 2018; 38: 103–15

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

10. Horvath A, Kiss M, Szucs A et al: Precuneus-dominant degeneration of parietal lobe is at risk of epilepsy in mild Alzheimer's disease. Front Neurol, 2019; 10: 878.
11. Yagi T, Kanekiyo M, Ito J et al: Identification of prognostic factors to predict cognitive decline of patients with early Alzheimer's disease in the japanese Alzheimer's disease neuroimaging initiative study. Alzheimers Dement, 2019; 5: 364–73
12. Arabi M, Dirani M, Hourani R et al: Frequency and stratification of epileptogenic lesions in elderly with new onset seizures. Front Neurol, 2018; 9: 995
13. Picco A, Archetti S, Ferrara M et al: Seizures can precede cognitive symptoms in late-onset Alzheimer's disease. J Alzheimers Dis, 2011; 27: 737–42
14. Cretin B, Di Bitonto L, Blanc F et al: Left temporal lobe epilepsy revealing left posterior cortical atrophy due to Alzheimer's disease. J Alzheimers Dis, 2015; 45: 521–26
15. Danielson NB, Guo JN, Blumenfeld H: The default mode network and altered consciousness in epilepsy. Behav Neurol, 2011; 24: 55–65
16. Kisler K, Nelson AR, Montagne A et al: Cerebral blood flow regulation and neurovascular dysfunction in Alzheimer disease. Nat Rev Neurosci, 2017; 18: 419–34
17. Varelas PN, Spanaki MV, Hacein-Bey L et al: Emergent EEG: Indications and diagnostic yield. Neurology, 2003; 61: 702–4
18. Terakawa Y, Tsuyuguchi N, Yamamura A et al: The influence of hypoglycemia on cerebral blood flow in cases of hypoglycemic coma. Neurol India, 2009; 57: 69–72
19. Shimogawa T, Morioka T, Sayama T et al: The initial use of arterial spin labeling perfusion and diffusion-weighted magnetic resonance images in the diagnosis of nonconvulsive partial status epileptics. Epilepsy Res, 2017; 129: 162–73

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]