3D ASL Perfusion: Biomarker of Activity in Japanese Encephalitis

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Introduction

Japanese encephalitis (JE) is mosquito-borne flaviviral endemic encephalitis that is still a major health problem in some countries of the Far East and Southeast Asia. Most patients with JE present with flu-like symptoms, anorexia, nausea, vomiting, neck rigidity, hemiparesis, convulsions, and/or altered mentality. Children under 15 years of age are principally affected in endemic areas. The most consistent and characteristic MR imaging findings in JE are bilateral symmetric T2 hyperintensities in both thalami, with or without hemorrhage.

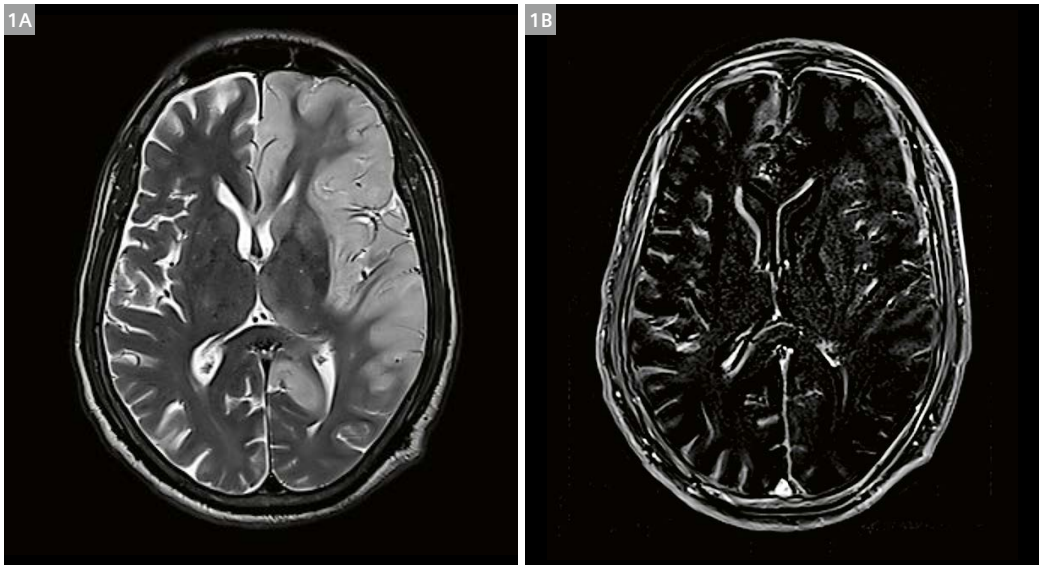
Case report

A 62-year-old male patient who had previously been healthy was admitted to the emergency department at Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai, India. He was in a disoriented state and had been suffering from recurrent new onset seizures and fever for one day. On examination, the patient was initially restless but then became drowsy and stopped responding to oral commands. After admission, he suffered no seizures or fever episodes.

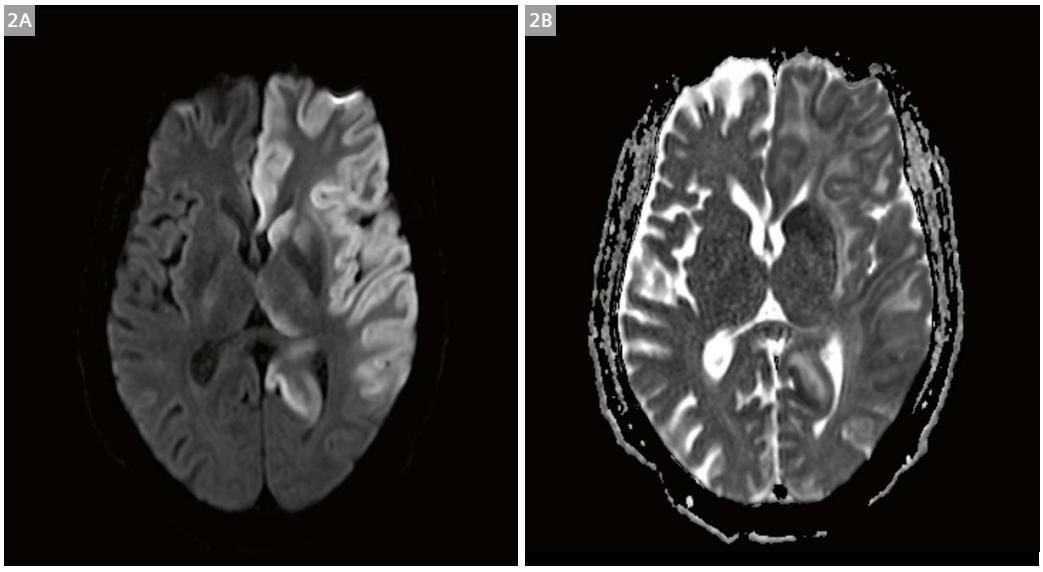
The patient was referred to the 3T MRI Centre at the Barnard Institute of Radiology for MRI of the brain. MR imaging was performed on a 3T MAGNETOM Skyra (Siemens Healthcare, Erlangen, Germany) on the second day of hospital admission. A standard institutional brain protocol (T1w sagittal, T2w axial, FLAIR coronal, DWI, MR angiogram) was performed, along with a contrast study and 3D ASL perfusion using PASL with a FAIR Q2TIPS method.

Radiological differential diagnosis for unilateral gyral edema with diffusion restriction and increased perfusion in ASL includes:

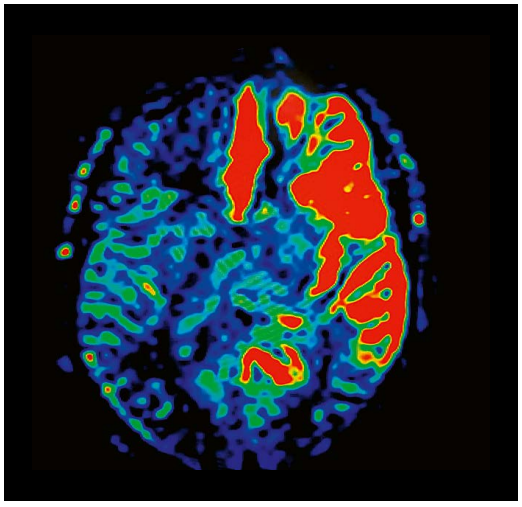
1. Encephalitis
2. Infarct



1 **(1A)** T2w shows significant gyral edema in the left frontoparieto-temporal region and hyperintensity in the left caudate, putamen, and thalamus.
(1B) T1 contrast subtracted image shows no abnormal enhancing areas in the brain parenchyma.



2 **(2A)** DWI; **(2B)** ADC shows diffusion restriction in the left fronto-parietotemporal region and left deep grey matter.



3 ASL image shows increased cerebral blood flow in the left frontoparietotemporal region

Age	Sex	No.	Hospital	Sample	Receiving date	Investigation	Result
62	Male	MS-5787	RGGGH	Blood & CSF	29.12.2016	HSV	negative
						CMV	negative
						VZV	equivocal
						HBSAg	negative
						EBV	negative
						JE serum	positive
						JE CSF	positive

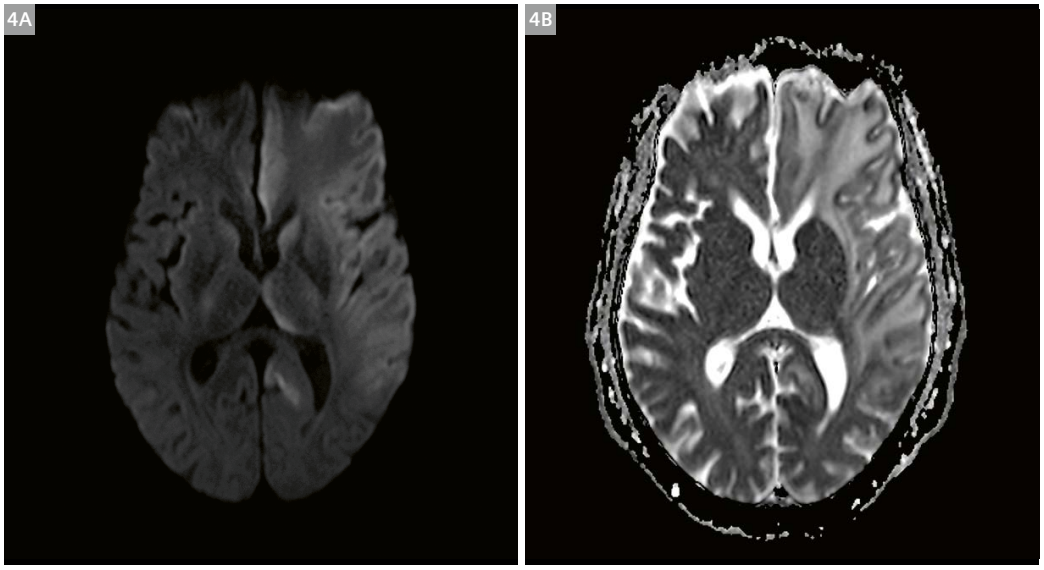
Table 1: Serology report

Follow-up MRI

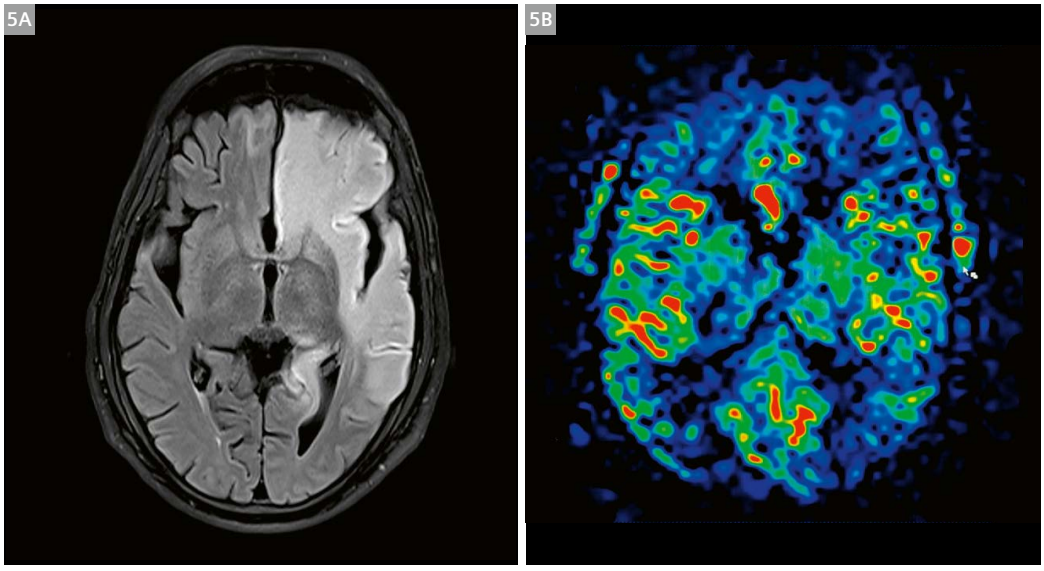
After treatment with empirical antibiotics, anticonvulsants, and anti-edema measures, the patient clinically improved and became conscious, oriented, and ambulant. Follow-up MRI was performed after three weeks.

Discussion

Although the present case concerns a 62-year-old man, JE is mostly found in children and young adults. Patients with JE are often asymptomatic in the beginning. After a few days, they typically present with non-specific febrile illness, coryza, diarrhea, and rigors. If patients progress to



4 **(4A)** DWI; **(4B)** ADC shows normalization of ADC values with facilitated diffusion in the left fronto-parietotemporal region and deep grey matter.



5 **(5A)** Axial FLAIR image shows persistent gyral edema. **(5B)** ASL image shows normalization of perfusion with decreased cerebral blood flow in the left fronto-parietotemporal region and deep grey matter.

meningoencephalitis, symptoms such as neck rigidity, cachexia, and convulsions occur. If they survive, there is gradual recovery with or without persistent symptoms of neurologic injuries.

The diagnosis of JE is based on essential and supportive criteria [1]. According to the essential criteria, patients must present with acute encephalitic syndrome, which is defined as a person of any age, at any time of year, having acute onset of fever and a change in mental status and/or new onset of seizures. Supportive criteria include the following:

1. Patient comes from a known JE-endemic area
2. JE-virus-specific IgM are detected in serum and cerebrospinal fluid using MAC ELISA
3. Thalamic lesions appear on CT or MRI scans with an appropriate clinical and epidemiological background

For confirmation of the disease, patients must fulfill the essential criteria and any two of the three supportive criteria [1].

Pathologic changes in the brains of acute JE patients are characterized by glial nodules and circumscribed necrolytic foci mainly in the bilateral thalami, substantia nigra, basal ganglia, brain stem, cerebellum, cerebral cortex, and white matter [2]. The MR imaging findings reflect the pathologic changes in those areas [3, 4]. The characteristic finding most consistently present in JE is the bilateral involvement of both thalamic lesions with or without hemorrhage on MR imaging [4]. Reports of unilateral lesion in JE are extremely rare [2, 5].

Our case displays unilateral involvement of the left frontoparietotemporal gyrus and the left deep grey matter (caudate nucleus, putamen, and thalamus) showing T2 hyperintensity with diffusion restriction and increased perfusion in ASL.

In terms of whether this could be an infarct: Despite such massive hemispherical involvement with diffusion restriction, no neurological deficit is present. In addition, an infarct usually involves decreased perfusion. Our case has increased perfusion with no neurological deficit, so it is less likely to be an infarct.

Follow-up imaging revealed persistent signal changes in T2w and FLAIR sequences. However, decreased cerebral blood flow with ASL perfusion as well as facilitated diffusion was observed.

Temporal lobe involvement is much more common in herpes simplex encephalitis (HSE) than in JE. This may cause problems in differentiating JE from HSE. A typical MR imaging finding in HSE is bilateral asymmetric T2 hyperintensity in the limbic systems, such as the medial temporal lobes, insular cortices, and inferolateral frontal lobes, regardless of hemorrhage and contrast enhancement. Unilateral temporal lobe involvement is not uncommon in HSE, but it typically spares deep gray matter such as the thalamus, basal ganglia, and substantia nigra. Therefore, the concurrent involvement of the temporal lobe, thalamus, substantia nigra, and basal ganglia in our case indicate that this is more likely to be JE than HSE.

Conclusion

We reported a rare case of JE with unilateral involvement of the thalamus, caudate nucleus, putamen, and frontoparietotemporal lobe. ASL perfusion can be a useful biomarker to assess disease activity in these patients. To our knowledge, no reports of using ASL perfusion to follow up on Japanese encephalitis patients exist.

Acknowledgment

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