



Clinical letter

Culpable brain lesion causing complex partial status in Wilson's disease: Deduction by arterial spin labeled perfusion MRI



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1. Introduction

Seizures are an uncommon presentation of Wilson's disease. We report the use of Arterial Spin Labeled Magnetic Resonance Imaging (ASL MRI) in demonstrating the hyperperfused epileptogenic zone in a patient with Wilson's disease who presented with complex partial status and was imaged in the peri-ictal period. The clinical history and electroencephalogram (EEG) findings are correlated.

2. Case presentation

A 16-year-old girl presented with a history of new onset seizures. Her semiology favored complex partial seizures of right frontal origin characterized by facial deviation and head aversion to the left followed by tonic posturing of the left upper limb. Seizure duration was approximately one minute with no post ictal confusion and recurred every ten minutes throughout the night. She presented to us 12 hours after her first seizure. Her clinical history was positive for Wilson's disease diagnosed five years ago when she had presented with dystonia and tremors of her right hand, followed by dystonia of the trunk and left upper limb. She had low serum Ceruloplasmin levels and a positive Kayser-Fleischer (KF) ring at that time and had been on d-Pencillamine treatment for the past five years. On current admission she was on d-Pencillamine 500 mg/day, trihexyphenydyl and pyridoxine and

had normal copper levels and almost complete improvement in dystonia and tremors.

Clinical examination revealed normal sensorium and orientation. She had bilateral KF rings visible to the unaided eye, vertical gaze paresis and subtle incoordination of the upper limbs. Seizures abated with intravenous fosphenytoin. Ultrasound of the abdomen showed evidence of chronic liver disease. Hematological and metabolic parameters were within normal limits (Serum total copper 12 µg/dl, ceruloplasmin 4 mg/dl, serum free copper was nil, 24 hour urinary copper 22.2 µg/dl).

EEG did not reveal any epileptiform abnormalities with only non-specific intermittent low amplitude polymorphic slow waves over both hemispheres, maximally over the right frontal region.

Peri-ictal MRI of the brain (3T GE Discover 750w, GE Healthcare, Milwaukee, USA) showed asymmetric bilateral fluid attenuated inversion recovery (FLAIR) hyperintense gliotic changes with subtle local volume loss in both frontal regions particularly the superior frontal gyri, predominantly on the right side. A non-enhancing well-defined cystic lesion in the right superior frontal gyrus, appearing T1 hypointense, T2 hyperintense with suppression on FLAIR suggested progression to a focal cystic encephalomalacic change (Fig. 1a–c). ASL MR perfusion showed elevated cerebral blood flow surrounding the cystic lesion in the right superior and middle frontal and precentral gyri (Fig. 1d,e). Other more classic findings of bilateral putaminal atrophy and abnormal mineralization (Fig. 1f) with diffuse midbrain FLAIR hyperintensity with formation of a "face of the giant panda" sign (Fig. 1g) characteristic of Wilson's disease were also present.

3. Discussion

Seizures are uncommon in Wilson's disease occurring in about 4–8.3% of patients [1]. Patients who develop seizures typically

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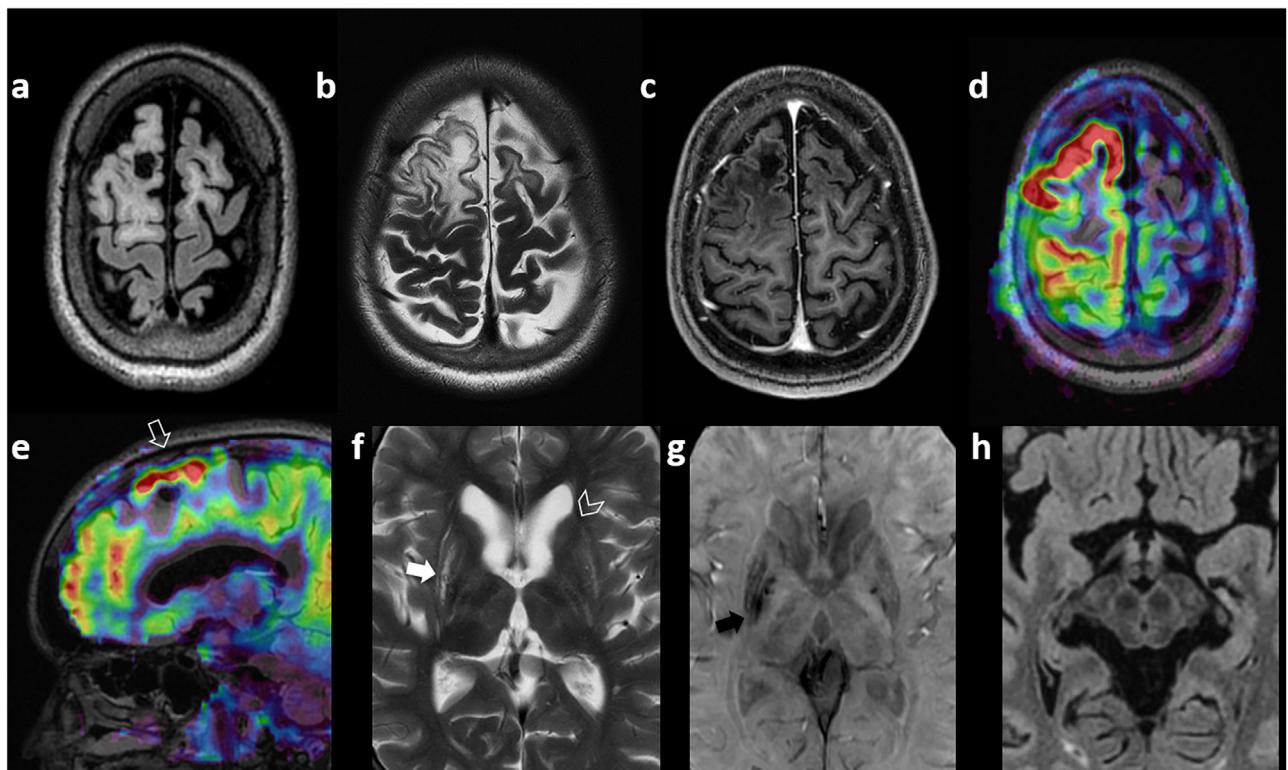


Fig. 1. Fluid attenuated inversion recovery (FLAIR) (a), T2 (b) & contrast enhanced T1 axial (c) magnetic resonance (MR) images show a non-enhancing T2 hyperintense cystic lesion that completely suppresses on FLAIR with perilesional T2 and FLAIR hyperintensities. Similar T2 and FLAIR hyperintensities are seen to a lesser extent over the contra lateral left superior frontal gyri where volume loss is also apparent. Arterial Spin Labeled (ASL) fusion images (axial –d and right parasagittal – e) show hyperperfusion (highlighted in red) surrounding the subcortical cavitation. Axial T2 (f) shows the corpus striatal atrophy and hyperintensity (arrows) with exaggerated mineralization (black arrow) of the putamina on susceptibility weighted (SW) images (g). Axial FLAIR (h) at the level of the brainstem shows subtle hyperintensity of the midbrain resulting in a face of the giant panda sign. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

present in the second decade, often after initiation of de-coppering therapy in a majority of patients (46.3%), and rarely as the presenting feature before chelation in up to a fifth of this subset. Generalized tonic clonic seizures are the most common followed by simple and complex partial seizures. Status epilepticus as in our patient, has been reported in approximately 1% of Wilson's disease patients [1].

Uncontrolled seizures in Wilson's are found to be commonly associated with white matter cavitatory lesions although the reverse is not true. The incidence of white matter lesions has been reported to be 10% in case series of Wilson's. The frontal lobe is most commonly affected followed by the temporal, occipital and parietal lobes [1]. Histopathological studies of the cortical-subcortical lesions in Wilson's disease have been well described in an autopsy case series. They describe a pattern of status spongiosis with vacuolation of nervous tissue characterized by coalescent spongiotic foci of liquefactive necrosis involving the U fibres, involvement of the deeper layers of the cortex with striking neovascularization, Alzheimer type 1 astrocytic cells and loss of oligodendrocytes in necrotic areas. Variable inflammation with Opalski cells of macrophagic lineage were also present [2].

The most likely explanation for these white matter lesions is the toxicity caused by free copper accumulation with a good correlation being found between brain copper content and their incidence. Also consistent with the distribution of these lesions was the presence of the higher copper content in the frontal regions even more than in the basal ganglia [2].

White matter gliosis and cavitation result in partial deafferentiation of the cortex from afferent thalamic inputs, which may

promote synchronization of neuronal activity and hence become epileptogenic in patients with Wilson's disease [3].

ASL MRI is a non-contrast perfusion technique that yields parametric maps of absolute values of cerebral blood flow (CBF). It uses radiofrequency pulses at the upper level of neck to label flowing blood which acts as a magnetically tagged endogenous tracer. Images of the brain are then acquired as the tagged blood enters the cerebral microcirculation. We used a 3D pseudocontinuous ASL sequence (PLD 2025 ms).

ASL has been well documented to show peri-ictal hyperperfusion and interictal hypoperfusion in the evaluation of a range of localization related epilepsies. While PET detects epileptogenic lesions on the basis of their metabolism, the presence of an intact neurovascular coupling in the epileptogenic zone forms the basis of using ASL to detect alterations of local blood flow in epileptogenic lesions [4].

In our case, the patient presented with complex partial seizures with a semiology that was clearly of right hemispheric onset. However, despite the relatively superficial white matter changes on the structural MRI, EEG was unable to provide definitive evidence of ictal abnormalities. Peri-ictal ASL succeeded in localizing and demonstrating the full extent of the hyperperfused epileptogenic zone involving the right frontal gyri surrounding a subcortical cavitatory lesion as well as the irritative zone extending over much of the frontoparietal regions correlating well with the seizure semiology.

4. Conclusion

While the association of white matter cavitatory changes and epilepsy in Wilson's disease has been previously described, to our knowledge this is the first case report of MRI findings that allow direct attribution of epileptogenicity to these lesions using the ASL technique. ASL may play a valuable role in delineating the epileptogenic zone in symptomatic epilepsy.

Conflict of Interest

None.

References

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