Vessel Wall Enhancement in Unilateral Primary Angiitis of the Central Nervous System

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A 20-year-old man presented with seizures. Brain magnetic resonance imaging (MRI) showed multiple left-hemispheric T2-weighted-fluid-attentuated inversion recovery (T2-FLAIR)-hyperintense/gadolinium-enhancing lesions. He was prescribed natalizumab and then fingolimod for presumed multiple sclerosis (MS), which resulted in years-long clinico-radiographic stability.

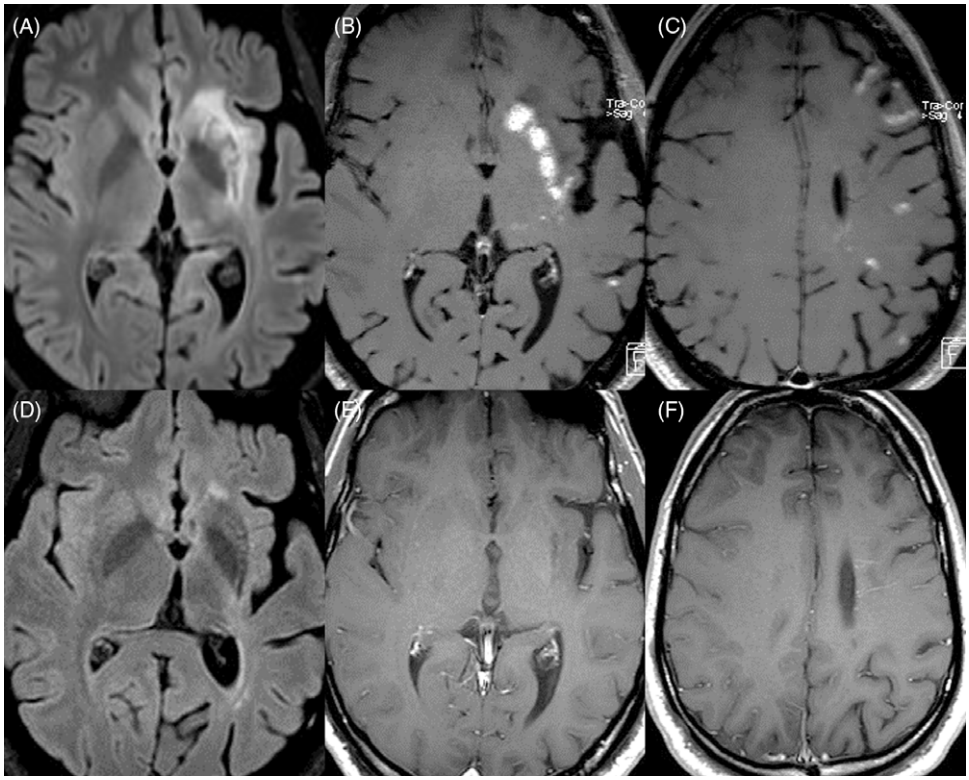

Figure 1: *Neuroimaging improvement after immunotherapy for unilateral relapsing primary angiitis of the CNS. Brain MRI shows left-sided striatal T2-FLAIR-hyperintensity (A) and gadolinium enhancement (B); left-sided gadolinium-enhancing cortical/juxta-cortical lesions are also seen (C). Mild left-hemispheric atrophy is present (A–C). Follow-up MRI 11 months post-immunotherapy shows marked improvement of T2-FLAIR-hyperintensity (D) and enhancement (E, F).*

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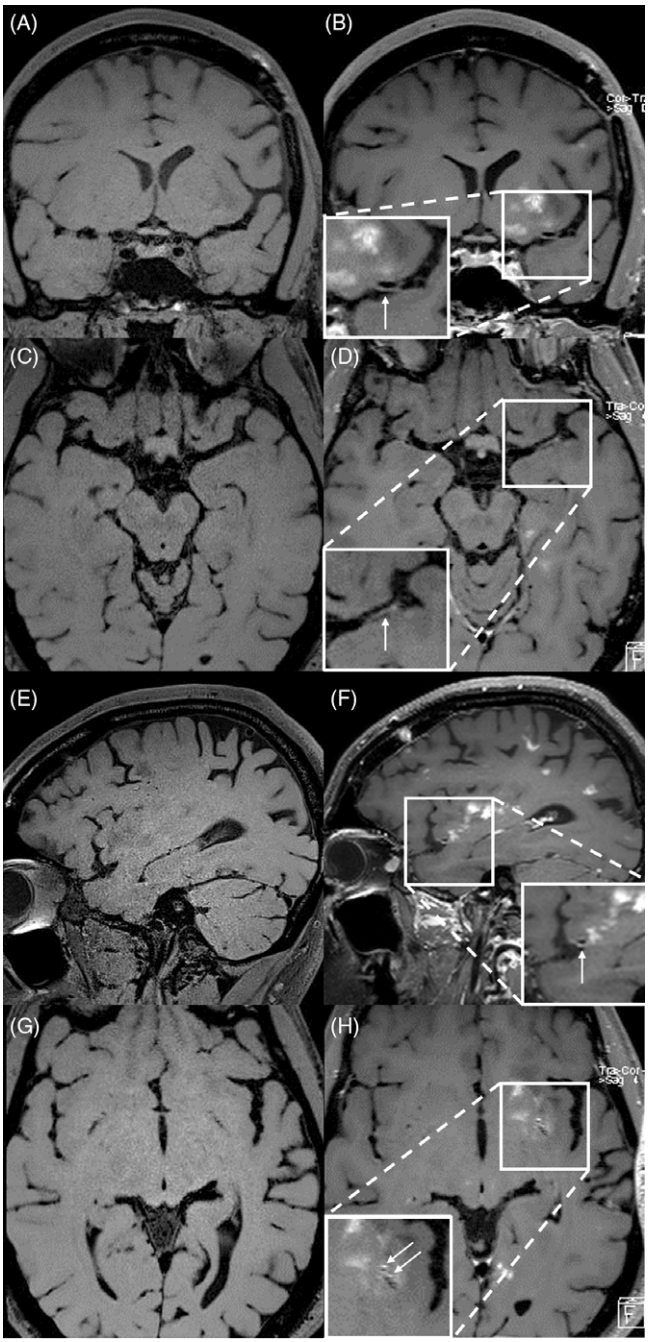

Figure 2: *Vessel wall enhancement in unilateral relapsing primary angiitis of the CNS. Compared to pre-gadolinium imaging (A, C, E, G), VW-MRI shows left-sided middle cerebral artery M1 segment (B, D, F, arrows) and lenticulostriate (H, arrows) vessel wall enhancement post-gadolinium.*

At the age of 31 years, fingolimod was substituted with ocrelizumab due to recurrent infections. Subsequently, he developed right-sided weakness/numbness. Repeat brain MRI revealed new left-hemispheric T2-FLAIR-hyperintense/gadolinium-enhancing lesions and mild left-hemisphere atrophy (Figure 1, A–C). On follow-up imaging, persistent (>6 months) enhancement of lesions was noted. Cervical spine MRI showed no cord abnormality. Cerebrospinal fluid (CSF)-specific oligoclonal bands were absent. Extensive testing for infectious and malignant etiologies, including CSF John Cunningham virus PCR and cytology, were negative. Comprehensive serum and CSF neural antibody testing, including serum testing for myelin oligodendrocyte glycoprotein (MOG)-IgG was negative. Selective involvement of one hemisphere, persistent lesion enhancement, and absence of CSF-specific oligoclonal bands were atypical for MS. His presentation was, however, compatible with unilateral primary angiitis of the central nervous system, which has been termed unilateral relapsing primary angiitis of the central nervous system (UR-PACNS) due to its potential for relapse.[1] Conventional angiogram was non-diagnostic, and brain biopsy revealed only perivascular inflammation without transmural inflammation. Vessel wall MRI (VW-MRI) performed 5 months after brain biopsy revealed enhancement of the left middle cerebral artery M1 segment and lenticulostriate arteries (Figure 2), supporting a diagnosis of UR-PACNS. Corticosteroids and cyclophosphamide resulted in excellent clinico-radiographic response (Figure 1, D–F).

UR-PACNS is a rare, recently characterized neuro-inflammatory syndrome.[1] It has been defined as biopsy-proven PACNS with clinical and radiographic disease confined to one hemisphere, with or without hemi-atrophy.[1] Unique clinical features of UR-PACNS include presentation with seizures rather than ischemic stroke or hemorrhage, as well as chronic disease course.[1] The differential diagnosis of uni-hemispheric lesions with seizures includes Rasmussen's encephalitis, unilateral cortical FLAIR-hyperintense Lesions in Anti-MOG-associated Encephalitis with Seizures (FLAMES), and gliomatosis cerebri.[1–4] Onset in adulthood, persistent lesion enhancement, undetectable serum MOG-IgG, and chronic (>10 years) disease course all favor UR-PACNS over these competing diagnoses in our case.[1–4] Conventional angiogram is typically non-diagnostic in UR-PACNS and diagnosis is usually made by brain biopsy, which shows lymphocytic vasculitis of small- and medium-sized vessels.[1] Although brain biopsy is the gold standard for PACNS diagnosis, it has a clinical sensitivity of only 53%–63%, as exemplified by the non-diagnostic biopsy results in our case.[5] Clinicians may be appropriately hesitant to prescribe intensive immunosuppressive therapy in the absence of a positive biopsy indicating PACNS, due to potential risks of empiric treatment.[6] VW-MRI has been used to demonstrate intracranial vessel wall inflammation and can support a diagnosis of PACNS in cases with a non-diagnostic brain biopsy.[7] Our case highlights that VW-MRI can help diagnose UR-PACNS even when brain biopsy is non-diagnostic, resulting in appropriate initiation of intensive immunosuppressive therapy.

Disclosures

B.G. Weinshenker reports no disclosures relevant to the manuscript but reports personal fees from Novartis, personal fees from Horizon Therapeutics, personal fees from Alexion, personal fees from UCB Biosciences, personal fees from Mitsubishi Tanabe, personal fees from Genentech, and personal fees from Roche, outside the submitted work. In addition, B.G. Weinshenker has a patent NMO-IgG for diagnosis of neuromyelitis optica with royalties paid to RSR Ltd.; Oxford University;

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Statement of Authorship

AB designed and conceptualized the study; drafted the manuscript; analyzed and interpreted the data; and composed the figures. SSS, CPW, MAL, and KS interpreted the data and revised the manuscript for intellectual content. BGW designed and conceptualized the study; analyzed and interpreted the data; revised the manuscript for intellectual content; and supervised the study.

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