LETTER TO THE EDITOR

To The Editor

Utility of Vessel Wall Imaging in Suspected CNS Vasculitis with Normal Routine Workup

Keywords: Stroke, Vessel wall imaging, Brainstem

A 55-year-old man presented with an episode of vertigo that lasted for 3 h. This was associated with balance difficulty which did not fully resolve until 3 weeks after the event. His past history was unremarkable except for a new-onset headache which started a month prior. It was holocephalic, dull aching, persistent throughout the day with no other associated neurological symptoms and gradually improved over few weeks. At the time of his headache, clinical evaluation, C-reactive protein (CRP), and an MRI of the brain were normal.

He presented 3 months after with a sudden right-sided weakness and dysarthria. On examination, he had hypermetric saccades with right gaze and right pyramidal weakness. Brain MRI showed an acute left paramedian pontine infarct and a chronic infarction of the superior right paramedian pons which was not present on his previous MRI (Figure 1A–B). Vascular imaging with CT angiography and MRA did not show any vascular abnormality. The patient denied a catheter angiogram. However, due to high suspicion for a focal arteriopathy of the basilar artery (BA), he underwent an enhanced MRI with vessel wall imaging (VWI) (Figure 1C–E). This showed thickening and asymmetric circumferential enhancement in the wall of the mid and distal BA and minimal enhancement of the intracranial segments of both vertebral arteries. CRP was minimally elevated at 8.7 (upper limit: 8). He denied symptoms of autoimmune connective tissue disorders. Cerebral spinal fluid (CSF) analysis showed normal protein and cell count. CSF infection panel was negative, including Herpes Simplex Virus (HSV), Varicella Zoster Virus (VZV), and tuberculosis. Serum anti-nuclear antibodies, extractable nuclear antigen, anti-double-stranded DNA antibodies, and complement levels were normal. Lyme disease testing and HIV serology were negative. Body Positron Emission Tomography (PET)/Computed Tomography (CT) did not reveal any abnormal uptake.

He was initially started on dual antiplatelet therapy and prednisone (1 mg/kg). Aspirin was continued, and methotrexate was added with gradual tapering of steroids over the next 3 months as the follow-up MRI showed improvement (Figure 1F). However, there was a residual enhancement of the BA, without new clinical symptoms. He was started on cyclophosphamide infusions with an increasing dose of steroids and a subsequent MRI after 3 months showed near-complete resolution of vessel wall enhancement.

This case vignette describes a middle-aged gentleman with no vascular risk factors and recurrent posterior circulation strokes over 3 months. This was associated with a normal routine workup for cardio-embolic etiology and the absence of any evident large or small vessel pathology. The use of VWI suggested an inflammatory etiology despite the absence of vascular pathology on conventional imaging.

Posterior circulation strokes account for one-fifth of all ischemic strokes.[1] Mechanisms of recurrent ischemia include large artery atherosclerosis, small vessel disease, cardio-embolism, in-situ thrombosis, and branch occlusive disease (BOD). Less common causes are dissections, infections, dolichoectasias, fibromuscular dysplasia, and central nervous system (CNS) vasculitis (primary or secondary). Investigations include a basic lab workup, CT with angiography (head and neck), echocardiography (bubble study for a patent foramen ovale), and prolonged cardiac rhythm monitoring for atrial fibrillation/flutter. Second-tier investigations include detailed autoimmune workup, erythrocyte sedimentation rate, CRP, VWI, and lumbar puncture.

The major differential diagnoses here were CNS infections or vasculitis. This patient had a negative workup for infections and VWI was an important imaging sequence in establishing a focal arteriopathy. The VWI changes, in this case, are not typical for BOD. BOD presents with perforator infarcts, commonly seen in the posterior circulation with plaque occluding the perforator ostia. Typical VWI changes associated with BOD include an eccentric pattern of enhancement with a plaque along the lateral vessel wall. Mossa-Basha et al retrospectively reviewed patients with intracranial vasculopathy and showed that the presence of T2 juxtaluminal hyperintense band along with eccentric vessel wall involvement favors intracranial atherosclerotic disease, whereas diffuse circumferential wall enhancement, as seen in this case, is more supportive of vasculitis.[2]

A high index of suspicion is needed for the diagnosis of primary or secondary CNS vasculitis. Secondary causes include Anti-Neutrophilic Cytoplasmic antibodies (ANCA)-associated vasculitis (microscopic polyangiitis, granulomatosis with polyangiitis (GPA), eosinophilic GPA), polyarteritis nodosa, systemic autoimmune diseases (lupus, Sjogren's syndrome, rheumatoid arthritis, Bechet's syndrome), cryoglobulinemic vasculitis, and giant cell arteritis. Mimics of CNS vasculitis include drug-induced vasculopathy (such as cocaine) and radiation-induced vasculopathy.[1] Focal isolated CNS vasculitis is uncommon but can occur in settings of infection or as a part of primary angiitis of the CNS (PACNS).[3,4] PACNS is one of the great masqueraders and can present with a myriad of manifestations. Clinical features like multifocal strokes, ataxia, seizures, cognitive dysfunction, intracranial hemorrhages with non-specific symptoms like fever, headache, weight loss, malaise along with supportive findings on catheter angiography/MRI-VWI hint toward this diagnosis. PET/CT has been used to detect large and medium vessel vasculitis (sensitivity 75%–90% and specificity 85%–100%)[5]; however, its use in PACNS is evolving. A biopsy from the affected cortex and meninges remains the gold standard despite its invasive nature.[6] The imaging changes in our patient were in high-risk structures, thus he denied a brain biopsy. This highlights the role of imaging and serology in establishing the diagnosis.

Treatment recommendations for PACNS are mostly extrapolated from other forms of vasculitis. Corticosteroids with immunosuppressants are the mainstay therapies, with rituximab as an emerging therapy. The usual regimen is to start prednisone and

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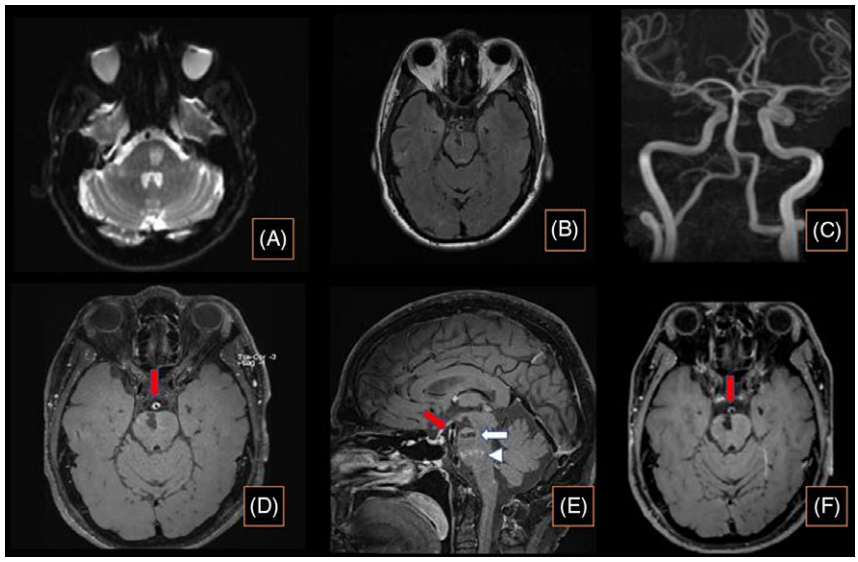

Figure 1. *MRI and Vessel wall imaging for the patient. A) Diffusion-weighted MRI showing acute left paramedian pontine infarct. B) FLAIR MRI from the same study in A showing chronic superior right paramedian pontine infarct. C) Circle of Willis Time of Flight MRA showing patent Basilar artery.D & E) Enhanced vessel wall imaging-MRI axial sections showing concentric enhancement of the Basilar artery (red arrow) as well as the old (white arrow) and new (arrowhead) pontine infarcts. F) Follow-up images showing improvement in the basilar artery enhancement (red arrow) following immunosuppressive therapy.*

cyclophosphamide (induction phase) if there are severe symptoms or an insufficient response to steroids. After an induction phase achieves remission, transitioning to a lower dose of steroids and less toxic agents like azathioprine is considered.[6] Since thrombosis is often associated with vasculitis, the use of antiplatelet therapy is thought to be beneficial. However, there are conflicting data for antiplatelets use in this setting.[7] While antiplatelet therapy reduces the risk of thrombosis, it carries a risk of bleeding. Thus, antiplatelet use has been decided on an individualized case-based approach. Serial enhanced MRIs, starting a month of initiating treatment, then every 3–4 months for the first year have been used to monitor the response to treatment.[8] We used a similar approach to assess the treatment response.

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Disclosures

The authors have no conflicts of interest to disclose.

Statement of Authorship

AW conceived of the presented idea. AW wrote the initial draft and discussed with CH, AFM, and MA who added further details. All authors discussed the results and contributed to the final manuscript.

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