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Case Report

Diagnostic dilemma in CNS vasculitis: a case of primary angiitis of central nervous system mimicking anti-neutrophilic cytoplasmic antibody-associated vasculitis

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ABSTRACT

Authors present a diagnostically challenging case of Central Nervous System (CNS) vasculitis presenting with aphasia, confusion, and right-sided weakness due to cerebral vascular accident, initially suspected to be Anti-Neutrophilic Cytoplasmic Antibody (ANCA)-associated vasculitis due to elevated PR3 ANCA titers. The work up for lupus and anti-phospholipid antibodies was negative. Magnetic Resonance Imaging of brain demonstrated abnormal T2 FLAIR and diffusion-weighted imaging with patchy, enhancing lesions, progression of middle cerebral artery involvement, and subacute infarcts in the left parietal and occipital lobes. He responded to Intravenous methylprednisolone followed by oral prednisone and Rituximab infusions every 6 months. Inspite of this, his disease progressed as he developed recurrent headaches, transient ischemic attacks, seizures, paranoia, altered mental status, and agitation. His repeat ANCA test came back negative. Due to the absence of systemic features and subsequent negative ANCA result, his diagnosis was revised to Primary Angiitis of the CNS (PACNS). Treatment with daily oral cyclophosphamide in a dose of 2 mg per kg body weight resulted in disease stabilization and clinical improvement.

Keywords: CNS vasculitis, ANCA associated Vasculitis, PACNS, Cyclophosphamide

INTRODUCTION

ANCA-associated CNS vasculitis and PACN are both rare entities with overlapping clinical presentations and neurological manifestations.[1] They also share similarities in laboratory findings, radiological features, and histopathological patterns, making differentiation challenging-especially when ANCA titers are negative or only mildly elevated.[1] Moreover, treatment protocols for both conditions are largely similar.[1] Authors report a diagnostically complex case of CNS vasculitis initially suspected to be PR3 ANCA-associated due to elevated ANCA titers. He was treated with glucocorticoids and rituximab infusions every 6 months with good response to this regimen. Later, he developed frequent headaches, seizures, agitation, paranoia and transient ischemic attacks. Then, his diagnosis was revised to PACNS as he did not develop any systemic features of ANCA associated vasculitis and repeat ANCA levels were also negative. The patient was treated with daily oral cyclophosphamide, resulting in disease stabilization. Additionally, we review existing literature on ANCA associated CNS vasculitis and PACNS.[1,4,5-7,9]

CASE REPORT

A 48-year-old Caucasian male presented in September 2021 with aphasia, confusion, and right-sided weakness. His blood pressure was elevated to 207/108 mmHg. Brain MRI revealed an acute left middle cerebral artery infarct and a chronic infarct in the left middle cerebral peduncle. His medical history included primary hypertension, hyperlipidemia, type 2 diabetes mellitus with neuropathy, bilateral knee osteoarthritis, lumbar spine degenerative

arthritis, and prior COVID-19 infection. Transthoracic echocardiography showed severe left ventricular hypertrophy with an ejection fraction of 55% and moderate left atrial dilation. In October 2021, he was readmitted with worsening aphasia and headache. Repeat MRI of brain demonstrated abnormal T2 FLAIR and diffusion-weighted imaging with patchy, enhancing lesions, progression of middle cerebral artery involvement, and subacute infarcts in the left parietal and occipital lobes.

Initial treatment with acyclovir was discontinued after negative HSV studies. He subsequently developed acute psychosis with agitation and combative behavior that was managed with quetiapine. Laboratory evaluation revealed mildly elevated PR3 ANCA (5.6; normal: 0.0–3.5), ESR of 26 mm/hour, HbA1c of 9.9%, and mild proteinuria. Autoimmune and infectious workup was negative. CSF analysis showed elevated protein (104 mg/dl), WBC count of 2, and RBC count of 5387. Carotid ultrasound revealed <50% bilateral stenosis. Chest CT showed no hilar lymphadenopathy or pulmonary nodules. EEG demonstrated diffuse symmetric low voltage.

Digital subtraction angiography revealed multifocal moderate to severe stenosis of the posterior cerebellar arteries (left >right), focal narrowing of the distal left anterior cerebral artery, and mild smooth narrowing of MCA and ACA branches-findings consistent with vasculitis and were unlikely due to atherosclerosis. The patient was treated with intravenous methylprednisolone 1000 mg daily for 3 days followed by oral prednisone (60 mg/day), resulting in symptomatic improvement. A leptomeningeal biopsy was recommended but declined by the family.

Proteinuria was attributed to diabetic nephropathy, and kidney biopsy was not pursued. A diagnosis of ANCA-associated isolated CNS vasculitis was made, and rituximab infusions were administered every 6 months over 2.5 years. Despite treatment, he experienced recurrent headaches, transient ischemic attacks, and seizures. Rituximab was discontinued in October 2024. In July 2025, he presented with new-onset paranoia, altered mental status, and agitation. Examination revealed aphasia and disorientation. MRI showed stable encephalomalacia in the left posterior temporal, parietal, and occipital lobes, with no new parenchymal changes. ANCA testing was negative. Given the absence of systemic features and persistently negative ANCA titers, the diagnosis was revised to PACNS. He received daily oral cyclophosphamide in a dose of 2 mg per kg body weight and TMP/SMX prophylaxis. Prednisone was discontinued due to uncontrolled hyperglycemia. His mental status returned to baseline, and he remains clinically stable on daily oral cyclophosphamide without any adverse effects.

DISCUSSION

ANCA-associated isolated CNS vasculitis and PACNS are rare inflammatory disorders involving small to medium-sized vessels. The etiology of both conditions remains unknown.[1] Clinical manifestations may include ischemic infarction, intracranial hemorrhage, cognitive decline, encephalopathy, and headaches. Notably, pituitary gland involvement is more commonly seen in ANCA-associated vasculitis (AAV) of the CNS, presenting with hypopituitarism, diabetes insipidus, or visual disturbances due to optic chiasm compression.[2] Chronic hypertrophic pachymeningitis is another frequent feature of AAV, often presenting with headaches and cranial nerve palsies.[3] Radiological findings in AAV may include cerebral infarcts, extensive white matter lesions on T2 FLAIR imaging, subarachnoid and subdural hemorrhages, pituitary enlargement, and alternating vessel narrowing and dilation.[1]

PACNS has an estimated annual incidence of 2 cases per million person-years, with a median age of 50,4 and a male predominance of 2:1.[4,5] Clinical features were nonspecific, with headache being the most common symptom, followed by aphasia, hemiparesis, ataxia, numbness, cognitive dysfunction, seizures, and visual disturbances.[4,5] CSF abnormalities are present in approximately 75% of cases, although ESR and CRP levels may remain normal.[6,7] Conventional angiography may reveal alternating segments of stenosis and dilation, as well as arterial occlusions.[8]

CNS biopsy typically shows small to medium vessel vasculitis affecting parenchymal and leptomeningeal arteries, with granulomatous, necrotizing, or lymphocytic patterns. Treatment for PACNS generally includes glucocorticoids and cyclophosphamide for 12 to 18 months.[9] Rituximab, an anti-CD20 monoclonal antibody, is increasingly used for induction and maintenance therapy.[10] Other agents such as mycophenolate mofetil, methotrexate, and azathioprine may be employed for maintenance of remission.[11] Treatment response can be measured by assessing for any improvement in neurologic symptoms and neuroimaging abnormalities. Follow-up noninvasive imaging, such as MRI, is preferred over invasive angiography. The absence of new lesions on imaging can be a reliable way to assess disease progression.

CONCLUSION

This case highlights the diagnostic complexity of isolated CNS vasculitis, initially presumed to be ANCA-associated due to elevated PR3 ANCA titers. Despite initial improvement with glucocorticoids and rituximab, the patient experienced persistent neurological symptoms including aphasia, paranoia, and altered mental status. Subsequent negative ANCA titers and absence of systemic features prompted a revised diagnosis of primary angiitis of the central nervous system (PACNS). Treatment with oral cyclophosphamide led to symptom control and disease stabilization without adverse effects. This case underscores the importance of reevaluating diagnoses in

refractory CNS vasculitis and the need for individualized treatment strategies.

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