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Case Report

C-Anca Associated Cns Vasculitis - A Rare Presentation

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Abstract

Antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV) is a necrotizing small-vessel vasculitis with infrequent central nervous system (CNS) involvement. CNS manifestations may occur through contiguous granulomatous spread, de novo intracranial granuloma formation, or primary vasculitic involvement of cerebral vessels [1], but are reported in only about 15% of patients with AAV [2]. Isolated CNS involvement without systemic features is particularly rare and poses significant diagnostic challenges.

We report a 20-year-old female with subacute progressive cerebellar symptoms over six months. Brain MRI demonstrated multiple T2/FLAIR hyperintense lesions involving deep gray matter and brainstem structures, with branching linear and nodular perivascular enhancement along Virchow–Robin spaces, without leptomeningeal enhancement. Cerebrospinal fluid analysis was non-inflammatory, infectious and granulomatous etiologies were excluded, and c-ANCA was positive. Based on clinicoradiological correlation and exclusion of alternative diagnoses, a diagnosis of probable c-ANCA–associated CNS vasculitis was made. Treatment with high-dose corticosteroids followed by rituximab resulted in significant clinical improvement.

Keywords: Antineutrophil Cytoplasmic Antibody (ANCA); Vasculitis; AAV; Small Vessels; CNS; Rituximab

Introduction

Anti-neutrophil cytoplasmic antibody (ANCA)–associated vasculitides (AAV) are pauci-immune small-vessel vasculitides characterized by autoantibodies directed against proteinase-3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA). The major clinicopathological subtypes include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) [3]. Although neurological involvement is common during the course of systemic AAV, central nervous system (CNS) involvement is relatively uncommon, occurring in less than 15% of patients, yet contributing disproportionately to morbidity [4].

CNS manifestations in AAV most often occur in the setting of established systemic disease and include hypertrophic pachymeningitis, pituitary involvement, ischemic or haemorrhagic stroke, and, less frequently, inflammatory parenchymal lesions [5]. Pathogenetically, CNS involvement may arise from small-vessel vasculitis affecting intracranial vessels, contiguous spread of granulomatous inflammation from adjacent structures, or de novo granulomatous or vasculitic lesions within the brain parenchyma [6,7]. Clinical presentations are heterogeneous and depend on the anatomical structures involved, often posing significant diagnostic challenges.

Isolated CNS involvement without systemic features is particularly rare and diagnostically problematic, as it can mimic infectious, granulomatous, and infiltrative disorders such as neurosarcoidosis, CLIPPERS, lymphoma, or chronic meningitis. Neuroimaging findings are variable and non-specific, and cerebrospinal fluid analysis may be normal, further complicating diagnostic certainty. While

tissue biopsy remains the gold standard, it is frequently impractical in deep or multifocal CNS lesions, necessitating a clinicoradiological diagnosis supported by serology and exclusion of alternative etiologies.

We report a young woman with a subacute progressive cerebellar and brainstem syndrome caused by isolated c-ANCA–associated CNS vasculitis, characterized by distinctive perivascular MRI enhancement and a non-inflammatory CSF profile, who showed marked clinical improvement following immunotherapy with high-dose corticosteroids and rituximab.

Case Presentation

A 20-year-old woman with no prior medical comorbidities presented with a 6-month history of progressively worsening tremor and imbalance. The illness began with tremulousness of the left hand while performing goal-directed movements such as reaching to hold a cup. Over the next month, similar tremulousness developed in the right hand, leading to difficulty in writing, with progressive deterioration in handwriting legibility. Over subsequent months, fine motor tasks including drinking, writing, and buttoning clothes became increasingly impaired.

During the month preceding presentation, her symptoms progressed to involve gait imbalance, characterized by swaying to both sides, a broad-based gait, and inability to walk in a straight line. She also developed slurring of speech, head nodding, and generalized tremulousness.

Two weeks prior to presentation, she experienced frequent falls and became unable to write due to severe upper limb tremor.

There was no history of seizures, altered consciousness, abnormal posturing, headache, fever, vomiting, visual symptoms, dysphagia, sensory loss, urinary incontinence, behavioral change, or cognitive decline. There were no constitutional or systemic symptoms such as joint pain, skin rash, weight loss, anorexia, or cough. Family history was non-contributory.

On general examination, she was hemodynamically stable, with no rash, joint swelling, or systemic signs of vasculitis.

Neurological examination revealed normal higher mental functions. Speech was dysarthric. Ocular examination showed right-beating nystagmus with slow saccades and mild left-sided ptosis; pupils were equal and reactive, and extraocular movements were full. There was prominent cerebellar intention tremor, more marked on the right, along with titubation. Muscle tone and power were normal in all limbs. Cerebellar testing revealed bilateral finger–nose ataxia, impaired heel–shin testing, and dysdiadochokinesia. Gait was ataxic with a broad base, and tandem walking was impaired.

Neuroanatomical localisation

The combination of intention tremor, limb and truncal ataxia, dysarthria, and titubation localized the pathology to the cerebellar hemispheres and vermis, with involvement of cerebellar outflow pathways. Associated nystagmus, slow saccades, and ptosis suggested concomitant brainstem (midbrain) involvement. The absence of pyramidal signs, sensory deficits, cortical features, or encephalopathy argued against a diffuse cortical or metabolic process.

Neuroimaging

MRI brain demonstrated multiple well-defined hyperintense lesions on FLAIR sequences involving the bilateral caudate nuclei, basal ganglia, thalami, and midbrain. Several lesions showed a perivascular distribution along the Virchow–Robin spaces. Post-contrast T1-weighted images revealed branching linear and nodular perivascular enhancement along penetrating vessels. There was no associated mass effect or surrounding edema. Diffusion-weighted imaging showed no restricted diffusion, and susceptibility-weighted imaging revealed no microbleeds or hemorrhage. There was no leptomeningeal or pachymeningeal enhancement.

Based on this pattern, differential diagnoses considered included chronic infectious meningitis, neurosarcoidosis, CLIPPERS, infiltrative lymphoma, and inflammatory vasculitis.

Laboratory and cerebrospinal fluid evaluation

Routine laboratory investigations were within normal limits. Serological testing for HIV and VDRL was negative.

Cerebrospinal fluid analysis revealed 3 cells/mm^3 with normal protein (34 mg/dL) and glucose (60 mg/dL), indicating a non-in-

flammatory profile. The absence of pleocytosis, elevated protein, or hypoglycorrhachia argued against chronic infectious meningitis, neurosarcoidosis, and leptomeningeal lymphoma. Serum and CSF cryptococcal antigen tests were negative.

Serum angiotensin-converting enzyme levels were normal, and ANA blot testing was negative.

p-ANCA was negative, while c-ANCA was positive. Although c-ANCA positivity can be seen in infections, connective tissue diseases, and malignancies, no clinical, laboratory, or radiological evidence supporting these secondary causes was identified.

Diagnosis and treatment

Based on the subacute progressive clinical course, localisation to cerebellar and brainstem structures, characteristic MRI findings with perivascular enhancement, positive c-ANCA serology, and exclusion of alternative etiologies, a diagnosis of probable c-ANCA–associated isolated CNS vasculitis was made. It was noted that normal CSF findings do not exclude CNS vasculitis, particularly in cases of isolated parenchymal involvement [10].

The patient was treated with intravenous methylprednisolone 1 g daily for 5 days, followed by induction therapy with rituximab administered as two doses of 1 g given two weeks apart. Rituximab was preferred over cyclophosphamide in view of the patient's young age, isolated CNS involvement, and concerns regarding long-term toxicity.

Follow-up

At one-month follow-up, there was marked clinical improvement with resolution of dysarthria and titubation, complete resolution of left upper limb tremor, and improvement in right-sided coordination. At three months, the patient demonstrated near-complete neurological recovery, with normalization of speech and gait and significant improvement in right upper limb coordination, regaining independence in activities of daily living and ambulation.

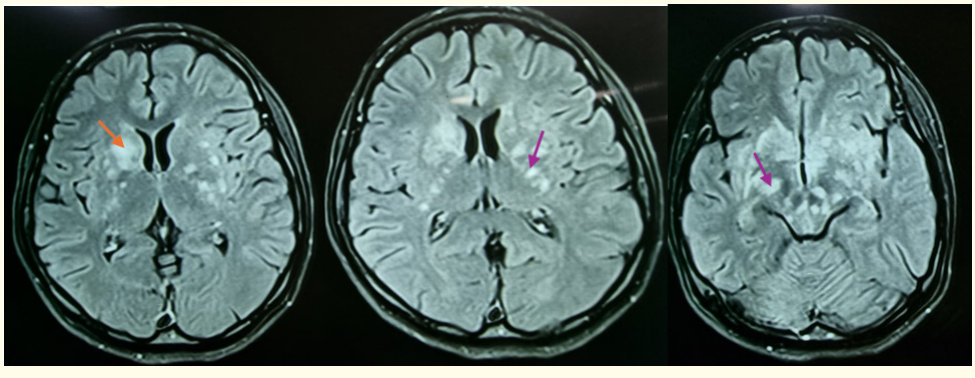

Image 1: Well defined FLAIR hyperintensities in right caudate nucleus(orange arrow) and along virchow robin spaces(purple arrow).

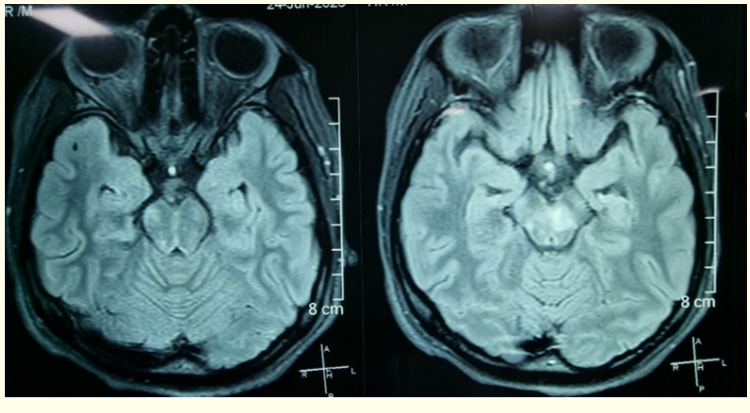

Image 2: FLAIR hyperintensities in midbrain too.

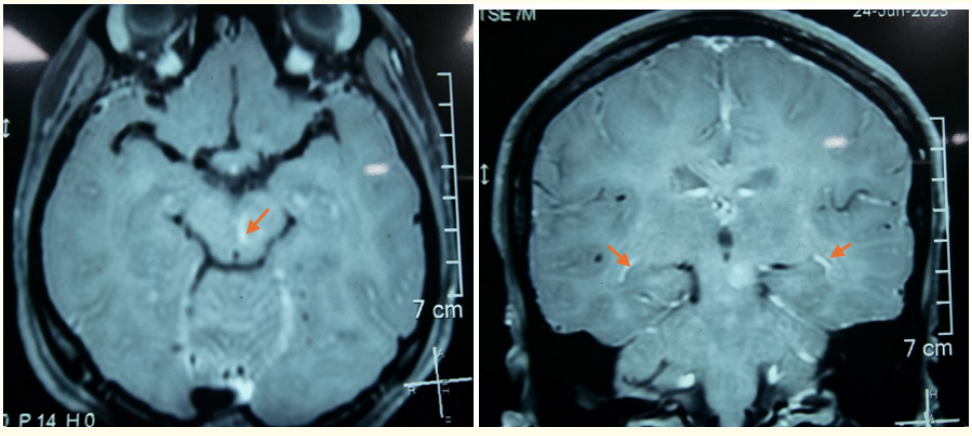

Image 3: Patchy contrast enhancement in some lesions- branching and linear enhancements.

Discussion

ANCA-associated vasculitis (AAV) is a necrotizing pauci-immune small-vessel vasculitis characterized by myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA) antibodies [8]. The major clinicopathological variants include granulomatosis with polyangiitis, microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis, and single-organ–limited forms such as renal-limited AAV. Although AAV is a multisystem disorder, central nervous system (CNS) involvement is relatively uncommon and typically occurs in the context of established systemic disease, most often in middle-aged patients.

Three pathogenic mechanisms of CNS involvement in AAV have been described: contiguous granulomatous spread from adjacent structures causing meningeal, cranial nerve, or pituitary involvement; de novo intracerebral granulomatous lesions; and small-vessel vasculitis leading to ischemic or haemorrhagic complications [9]. The present case is unusual in that CNS involvement occurred in isolation, without systemic manifestations, and presented as a progressive cerebellar–brainstem syndrome in a young patient.

The neuroimaging pattern in this case was atypical for CNS vasculitis, as it was non-ischemic and parenchymal, with multifocal deep gray matter and brainstem lesions showing branching perivascular enhancement along the Virchow–Robin spaces. This pattern necessitated careful exclusion of alternative diagnoses. Chronic infectious meningitis and granulomatous disorders were considered unlikely due to a non-inflammatory cerebrospinal fluid profile, negative serum and CSF cryptococcal antigen testing, and normal serum angiotensin-converting enzyme levels. Neurosarcoidosis and leptomeningeal malignancy were further argued against by the absence of leptomeningeal enhancement. CLIPPERS was excluded due to lesion distribution beyond the pons and cerebellum, and primary CNS lymphoma was considered unlikely given the absence of diffusion restriction, susceptibility changes, or mass-like enhancement.

Although cerebrospinal fluid abnormalities are frequently reported in CNS vasculitis, normal CSF findings do not exclude the diagnosis and have been described in cases of isolated parenchymal involvement. In the present case, the diagnosis of probable isolated CNS AAV was supported by a converging clinico-radiological phenotype, exclusion of competing diagnoses, and positive c-ANCA serology.

The possibility of secondary ANCA positivity was also considered, as ANCA reactivity has been reported in infections, connective tissue diseases, and malignancies. However, no clinical, laboratory, or radiological evidence supporting these conditions was identified, supporting a pathogenic role for c-ANCA in this patient.

Regarding treatment, cyclophosphamide has traditionally been used for induction therapy in severe AAV. However, recognition of the central role of B cells in AAV pathogenesis has led to the use of rituximab as an effective alternative. Randomized trials have demonstrated that rituximab is comparable to cyclophosphamide for

induction of remission and may be superior in relapsing disease [11]. In this young patient with isolated CNS involvement, rituximab was preferred to minimize long-term toxicity while achieving effective disease control, resulting in marked clinical recovery.

Conclusion

ANCA-associated vasculitis is an uncommon but important cause of inflammatory central nervous system disease. Although CNS involvement typically occurs in the context of established systemic disease, this case highlights that AAV can rarely present as isolated CNS vasculitis, even in young patients and in the absence of systemic manifestations. A progressive cerebellar–brainstem syndrome with multifocal parenchymal lesions and perivascular enhancement should prompt consideration of CNS vasculitis, even when cerebrospinal fluid findings are non-inflammatory.

Positive ANCA serology, when interpreted in the appropriate clinical and radiological context and after exclusion of secondary causes, can provide critical diagnostic support when tissue biopsy is not feasible. Early recognition and timely initiation of immunotherapy are essential to prevent neurological disability. This case underscores the importance of a clinicoradiological approach to diagnosis and demonstrates that rituximab-based therapy can be an effective and well-tolerated induction strategy in isolated CNS AAV.

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