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Ayisha Farooq Khan
Aga Khan University Karachi,Pakistan

Lubna Jafri
Aga Khan University Karachi,Pakistan

Saad Shafqat
Aga Khan University Karachi,Pakistan

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PRIMARY ANGIITIS OF THE CENTRAL NERVOUS SYSTEM PRESENTING AS SUDDEN VISION LOSS IN A YOUNG PATIENT

Ayisha Farooq Khan[1], Lubna Jafri[1], Saad Shafqat[1]
[1]Aga Khan University Hospital, Karachi

Correspondence Author: Ayisha Farooq Khan *Aga Khan University Hospital, Karachi* ***Email:*** *ayisha.farooq@aku.edu*

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ABSTRACT
Primary angiitis of the central nervous system is a rare disorder that primarily affects the cerebral vessels and can prove to be a diagnostic challenge to the clinicians. It can present with a variety of clinical manifestations and lacks the evidence of any systemic disease. Digital subtraction angiography is often necessary to confirm the diagnosis of cerebral vasculitis but in cases where it may fail to do so, brain biopsy is eventually required. Obliviousness to this condition may lead to false management strategies and hence it is imperative to make an accurate diagnosis to facilitate proper treatment that mainly includes a combination of steroids and immunosuppressive agents. We report a case of a 27-year-old male with sudden bilateral vision loss who underwent extensive workup and was ultimately diagnosed with primary angiitis of the central nervous system. He was treated with steroids and responded well to it.

Keywords: Primary angiitis; cerebral vessels; steroids

INTRODUCTION
Vasculitis of the central nervous system (CNS) is rare disorder that either occurs due to the primary disease of the blood vessels of the CNS or as part of a systemic disorder. Primary angiitis of the central nervous system (PACNS) accounts for 1.2% of the CNS vasculitis and mainly involves the small and medium sized vessels. It is more frequent in males and usually occurs in the fifth decade.[1] The diagnosis is particularly challenging as there is a myriad of clinical manifestations and the imaging findings might not always be specific. Extensive workup is needed to rule out the differentials and mimics. Timely diagnosis is crucial in initiation of treatment with glucocorticoids and/or immunosuppressant agents.

We describe a case of a young gentleman with sudden bilateral loss of vision. He was diagnosed with CNS vasculitis based on digital subtraction angiography and treated accordingly. This report further aims to discuss the diagnostic challenges and the treatment options pertaining to PANCS.

CASE PRESENTATION
A 27-year-old male, functionally independent at home, presented to Aga Khan University Hospital with bilateral vision loss for one hour. This vision loss had a sudden onset, was painless and there was no history of similar complains in the past. There was no associated headache, fever, blurring of vision, diplopia, eye redness, photophobia, or altered mental status. His past medical history and drug history was not significant.

On examination, his higher mental functions were intact, and he was cooperative throughout. The general physical examination was unremarkable. On neurological examination, the speech was normal, and pupils were equal and reactive to light and accommodation. His vision was limited to light perception and hand movements bilaterally. The extra ocular eye movements were intact and fundoscopic examination was normal. The rest of the cranial nerves, motor exam, and sensory exam were unremarkable. Cerebellar and gait examination were limited due to visual impairment.

The initial baseline blood work-up was unremarkable. MRI Brain with contrast was done that showed multiple areas of acute infarction involving bilateral cortical watershed territory, bilateral occipital lobes and bilateral cerebellar hemispheres (Figure 1). There was no post contrast enhancement.

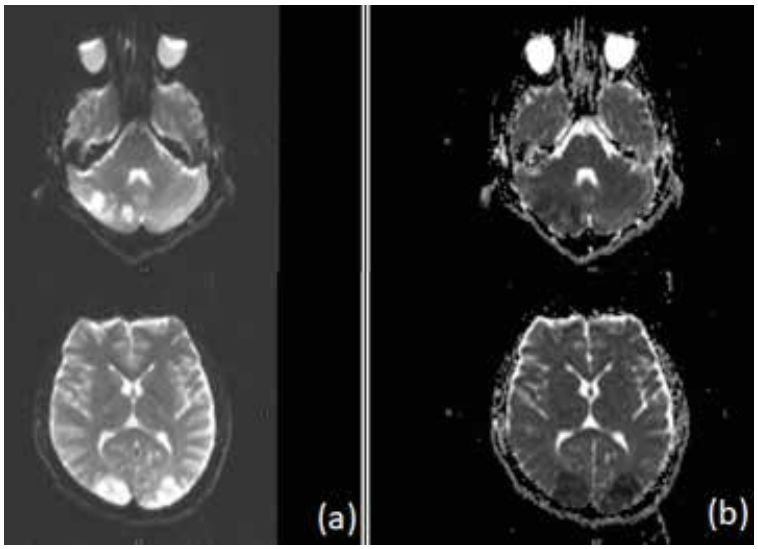

Figure 1: (a) MRI brain diffusion-weighted imaging (DWI) sequence demonstrating multiple hyper intense signals in right cerebellar hemisphere and bilateral occipital lobes. (b) Apparent diffusion coefficient (ADC) sequence with corresponding area of low intensity consistent with an acute infarct.

A CT angiogram (CTA) was ordered for intracranial arteries which showed mild narrowing of the bilateral vertebral arteries with beaded appearance (Figure 2) and raised the suspicion of vasculitis. There was no evidence of intracranial aneurysm or AV malformation on the CTA.

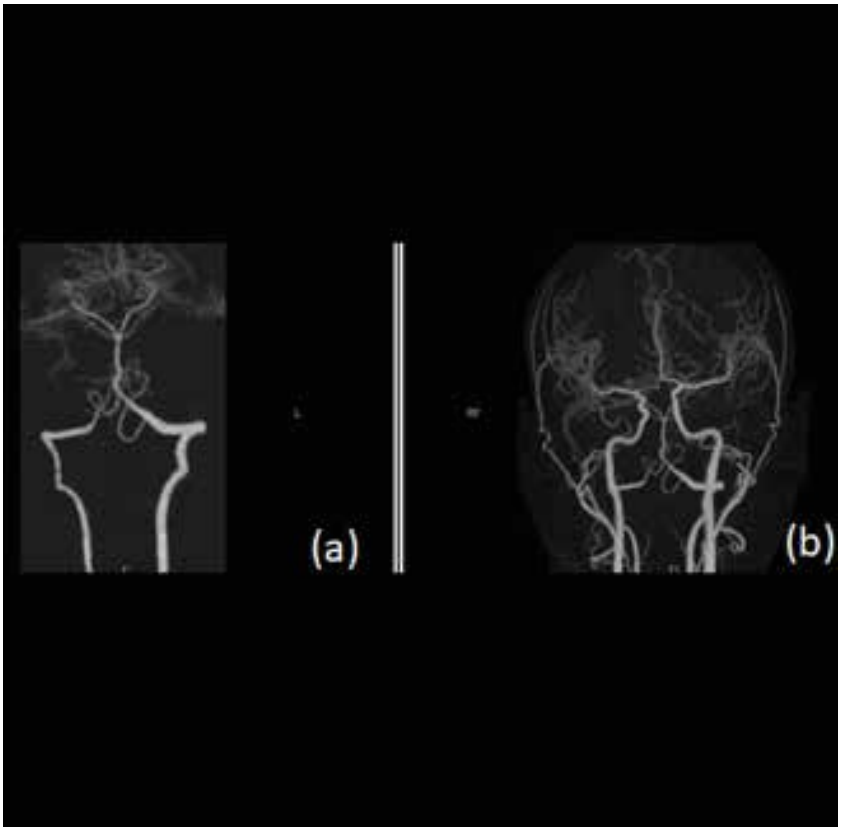

Figure 2: CT angiogram showing mild narrowing of bilateral vertebral arteries more on the right side (a) and a patent anterior circulation with normal caliber of both internal carotids, anterior and middle cerebral arteries (b).

Four-vessel angiogram was also done to confirm the diagnosis of vasculitis. It showed multifocal intimal thickening and focal dissections involving bilateral internal carotid and vertebral arteries, more prominent in the distal vertebral arteries (Figure 3).

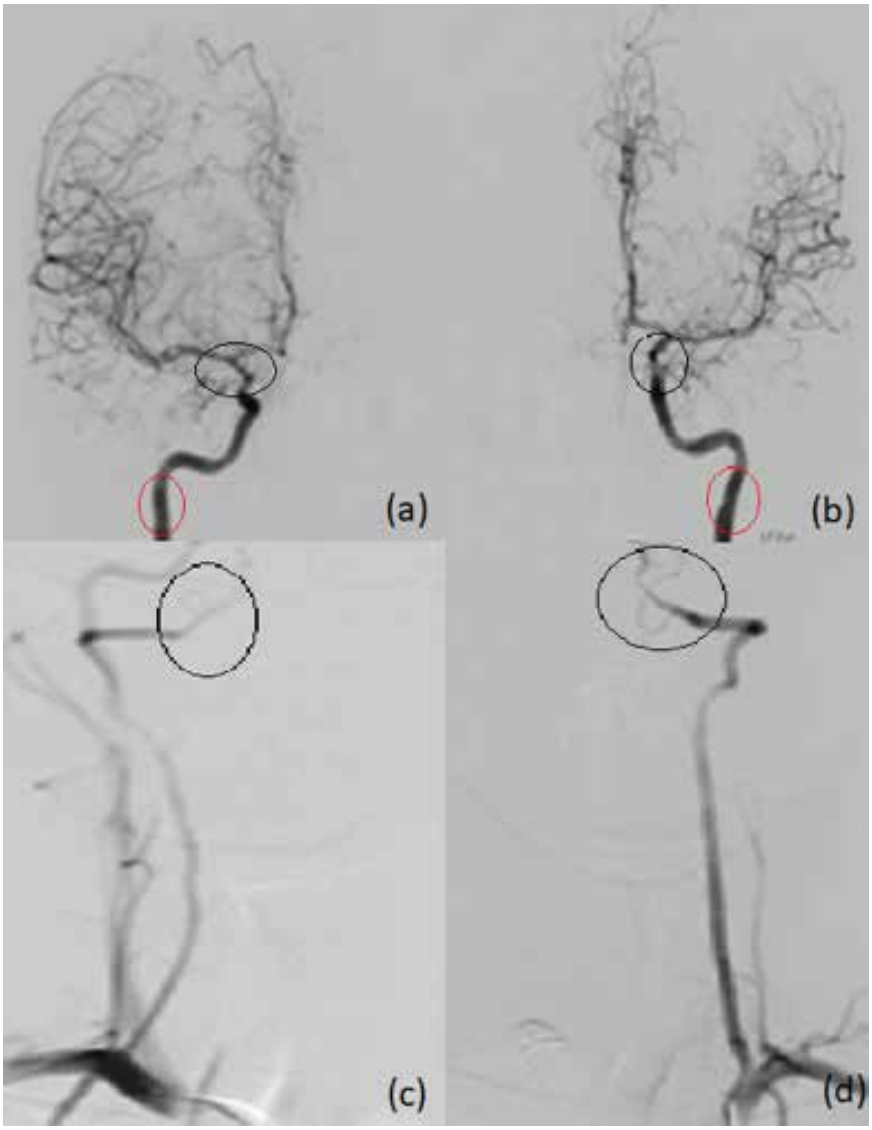

Figure 3: Diagnostic cerebral angiogram showing multifocal intimal thickening in the right internal carotid artery (image a- black circle) and focal dissection (image a- red circle) along with thickening of the left internal carotid artery (image b- black circle) and dissection (image b- red circle). Irregularity, narrowing and a beaded appearance of the right vertebral artery (image c) and the left vertebral artery (image d) can also be seen (Right >Left).

Irregularity, beaded appearances and focal dissection were also noted in bilateral P1 segments of the posterior cerebral arteries, along with diffuse narrowing of the right anterior cerebral artery. These features were suggestive of primary angiitis of the central nervous system (CNS) manifestation in systemic vasculitis.

Cerebrospinal fluid (CSF) studies showed glucose of 119 mg/dl (normal 40-70 mg/dl) while serum glucose was 200 mg/dL. CSF protein was 43 mg/dL (normal: 15-40 mg/dL) and white cell count of 2 uL (normal <5 uL). CSF Gene expert and AFB smear were negative. Other lab workup, which was ordered included Factor V Leiden, Protein S, protein C, Anti thrombin III, ANCA, ANA, anti dsDNA, ESR, B12, Hepatitis B surface antigen, hepatitis A IgM, Anti HCV, Hepatitis E IgM. All this workup came out to be negative. Serum homocysteine level, however, was slightly elevated at

19.3 umol/L (normal: 5-12). His EKG, transthoracic echocardiogram, lipid profile and blood sugars were within normal.

Based on the afore-mentioned findings, the patient was started on intravenous injection of methylprednisolone 1g/day for a total of five days. By day 5 of methylprednisolone, there was a slight improvement in the patient's vision bilaterally and he could count fingers in addition to light perception and hand movement. He was sent home on tablet aspirin, statin, and tablet prednisolone 30 mg/day with the plan to taper it off on a weekly basis. He was seen in clinic regularly after discharge and his symptoms improved significantly. On his recent follow-up six months after the initial presentation, he stated that 70% of his vision was restored. He was able to carry out most of his daily activities independently except driving his motorcycle.

DISCUSSION

Primary angiitis of the central nervous system (PACNS), also known as CNS vasculitis or idiopathic angiitis of the CNS, typically presents with an insidious onset and subacute symptoms such as headache or cognitive impairment. Focal symptoms, including hemiparesis, aphasia, transient ischemic attack, ataxia, seizures, dysarthria and visual impairment, may appear late.[2]

Differentiating PACNS from its mimics, such as reversible cerebral vasoconstriction syndromes and secondary cerebral vasculitis, is crucial. Although the exact pathophysiology remains unclear, it is believed that inflammatory cells infiltrating the vessel walls within the CNS can cause swelling and thickening of the vessel wall, resulting in luminal narrowing and compromised CNS perfusion. PACNS commonly present as ischemic stroke as a focal manifestation, while intracranial hemorrhage may rarely occur if a weakened and inflamed vessel wall ruptures.[3]

Diagnosing PACNS can be challenging and requires a comprehensive workup, which should be tailored to the individual patient's needs, especially in a young stroke patient. Typically, the blood work-up such as erythrocyte sedimentation rate, C-reactive protein, and ferritin is usually normal. In addition, liver enzymes, renal function tests, serum electrolytes, viral markers, angiotensin converting enzyme, coagulation profile (anticardiolipin antibodies, lupus anticoagulant, etc.) and immunologic workup (ANCA, ANA, Anti Ro, Anti La, etc.) must be done to rule out secondary causes of CNS vasculitis.[4]

Cerebrospinal fluid analysis may be normal in some cases, while in others, it may show mildly elevated proteins and non-specific lymphocyte findings. MRI Brain with contrast is often abnormal, with up to 90% of cases showing some form of abnormality. About 50% of cases show ischemic infarcts that typically affect multiple vessel tributaries and involve both the cortex and subcortical areas in a bilateral fashion. Additionally, one-third of cases may show contrast enhancement.[5]

To diagnose PACNS, conventional cerebral angiography is more specific than MRA. A systemic review of 55 studies on 907 patients found that the middle cerebral artery was the most involved vessel in 59 % of the cases, followed by the posterior cerebral artery (34%) and anterior cerebral artery (33%). Internal carotid artery, vertebral and the basilar arteries were the least commonly affected.[6] However, in our patient's case, both vertebral arteries and both internal carotid arteries were involved bilaterally. Recent trends show that angiographic diagnosis without tissue confirmation is increasingly relied upon, as in our case.[7] Nevertheless, biopsy is still considered the gold standard for diagnosis and can help exclude mimics.

In order to standardize the diagnostic approach, Calabrese et al. proposed a set of criteria which includes the following: a) the presence of an unexplained neurologic deficit following a comprehensive clinical and laboratory evaluation; b) documentation by cerebral angiography and/or tissue examination of an arteritic process within the central nervous system; and c) no indication of a systemic vasculitis or any other condition that could explain the angiographic or pathologic features.[8] Our patient met all the three criteria.

Acute attacks of PACNS are treated mainly with IV or oral corticosteroids. Intravenous high dose steroids at 1 g/day for 3-5 days is used but data has also shown lower doses to be beneficial.[9] Immunosuppressive agents like azathioprine, methotrexate and mycophenolate may be used as maintenance therapy, with the latter appearing to be the least effective of the three.[10] Our patient was given IV methylprednisolone 1g/day for five days followed by a tapered regimen of oral steroids to which he showed significant improvement, as explained earlier. The outcome is favorable when treated with a combination of steroids and cyclophosphamide.

CONCLUSION

PACNS is a rare but serious condition that requires timely diagnosis with cerebral angiography and biopsy. Physicians should be aware of comprehensive diagnostic approach for young patients who present

with stroke symptoms without typical risk factors to distinguish it from other mimickers. Early recognition and treatment with corticosteroids and immunosuppressive agents can be life-saving and improve outcomes.

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Ayisha Farooq Khan; concept, case management, manuscript writing
Lubna jafri; case management, manuscript writing
Saad Shafqat; case management, manuscript revision

All the authors have approved the final version of the article, and agree to be accountable for all aspects of the work.