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Case Report

A case report: primary CNS angiitis

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ABSTRACT

The primary angiitis of the central nervous system (PACNS) is an entity with a very low incidence and prevalence. It affects small and medium sized arteries of the brain parenchyma, spinal cord and leptomeniges resulting in CNS dysfunction. It is defined by inflammation of the cerebral vasculature without angiitis of other organ. Its clinical manifestations are very heterogeneous and make clinical diagnosis difficult. In most cases, a brain biopsy is required. Only the clinical suspicion and the ability to recognize the possible clinical and imagenological patterns of presentation make an accurate diagnosis possible.
We hereby report a case of Primary angiitis of CNS in 35 year old right handed male who presented with ischemic stroke with Left Hemiplegia. The diagnosis of PACNS was made after ruling out most of the causes of secondary CNS angiitis.

Keywords: Primary angiitis of CNS (PACNS), stroke, Vasculitis, Methylprednisolone.

INTRODUCTION

The primary angiitis of the central nervous system (PACNS) is an uncommon disorder of unknown cause that is restricted to the brain and spinal cord, leading to inflammation and destruction of vessels at this level, without evidence of vasculitis outside the central nervous system. An annual incidence of 2.4 cases per million patient/years is reported which is extremely low.[1] PACNS initially termed isolated central nervous system vasculitis was first proposed as separate clinical entity in 1959 by Cravioto and Feigin. The diagnosis remains a challenge, since there are no universally accepted diagnostic criteria and imaging findings may not be specific. Different types of clinical presentation have been described, which makes it even more difficult to identify. Unlike systemic vasculitis, this entity lacks positive autoantibodies. Brain biopsy is required usually to confirm the diagnosis.[2]

Clinicians caring for patients with suspected PACNS should be familiar with its mimics to avoid misdiagnosis. We here report a case of PACNS diagnosed on clinical & imagenological patterns of presentation.

CASE REPORT

A 35 year old right handed male without any relevant previous history presented with three months of progressive headache and declinement in cognition. Two days prior to hospitalization he had sudden onset left hemiparesis and altered sensorium. There was no history of seizures, vomiting, fever or any other complaints. He had no significant past history of hypertension, DM, Tuberculosis, Rheumatic heart disease, HIV or any arthritis.

On physical examination he was drowsy, irritable & had no signs of meningeal irritation. His vitals were stable with pulse 70/min regular, BP 120/80 mmHg & normal respiration. Rest of the general examination was normal. On neurological exam his modified rankins score was 5. Except for altered consciousness with left hemiplegia, no other neurological deficit was present. Other systemic

evaluation did not show any abnormality. His initial CT brain showed acute infarct in right MCA territory involving right temperoparietal and high convexity frontoparietal lobe (Figure 1). MRI brain showed Well defined altered signal intensity lesion in right gangliocapsular region (caudate and basal ganglia) subcortical altered signal intensity in bilateral parieto-occipital region and midbrain right cerebral peduncle (Figure 2 & 3). MRI angiography revealed Right MCA along M1 segment and bilateral PCA irregular (beaded) appearance with significant luminal narrowing with hypoplastic right vertebral artery suggestive of CNS vasculitis**.** (Fig. 4)

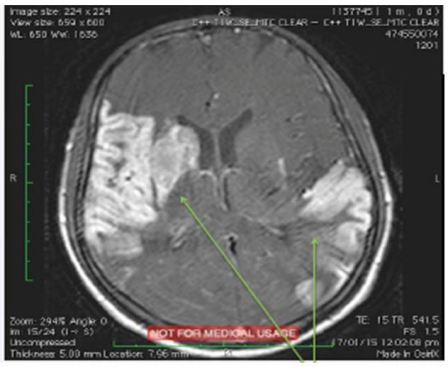

Figure 1: Contrast enhancement showing multifocal Involvement Acute infarct in right MCA territory involving Right temperoparietal and high convexity frontoparietal lobe.

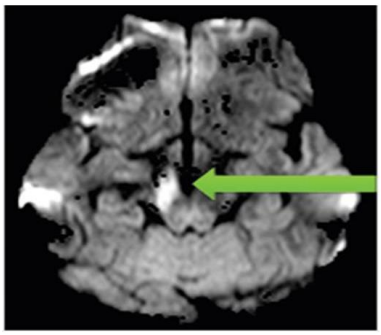

Figure 2: Diffusion weighted restriction showing altered signal intensity in midbrain right cerebral peduncle.

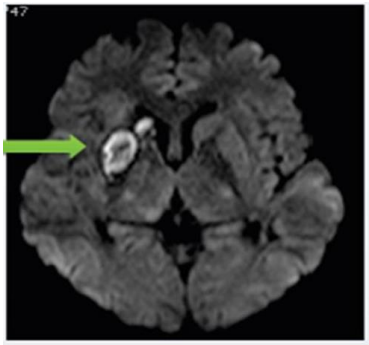

Figure 3: Diffusion weighted restriction altered signal intensity in right caudate and putamen.

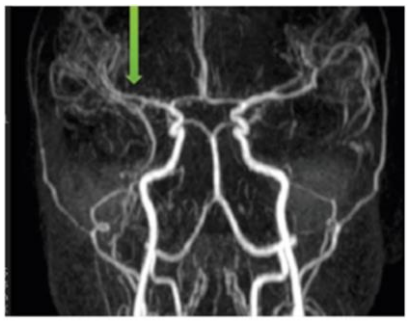

Figure 4: Right MCA along M1 segment along with B/L PCA irregular with significant narrowing (beaded) s/o vasculitis.

So he was investigated for causes of acute stroke in young specially for causes of CNS angiitis. Laboratory examination demonstrated normal Complete blood count, plasma sugar, Serum lipid profile, renal function, liver function & serum electrolytes. His HbsAg, HIV, VDRL status did not show any abnormality. ANA, Anti SSA/SSB, Anti-Phospholipid Antibody, ANCA, RA factor & ASO/CRP were negative. ESR was 08 mm at 1st hr. Sickling was Negative. Tests for Thrombophilia Profile, Complement levels & Serum Cryoglobulins were also normal. Chest X ray, Abdominal sonography, 2D echo, Carotid Doppler & upper & lower limps Doppler did not reveal any abnormality. CSF study revealed colourless, clear fluid with no cobweb. Proteins- 90 mg/dl, Glucose-43 mg/dl, Chloride-116 mEq/l, Cells 3 cells/cumm all lymphocytes suggestive of aseptic meningitis. Gram/ZN/India Ink stains were negative for any micro organism. CSFADA was normal. Brain biopsy could not be done due to non-availability of expertise hand.

So considering clinical presentation, MRI angiographic findings & ruling out common causes of vasculitis without systemic inflammation (ESR and CRP were normal), possibility of primary CNS angiitis was entertained. The patient was treated with bolus of Inj. Methyl prednisolone 1g od x 3 days followed by Tab omnacort 1 mg/Kg body weight OD. His modified Rankin score improved from 5 to 3 and showed increase in strength of motor power in Left upper & lower limb over a period of 6 wks. Patient was discharged on tapering doses of steroids & he is under regular follow up.

DISCUSSION

PACNS is an entity poorly understood and significant challenges remain for diagnosis and treatment.[1] An annual incidence of 2.4 per million people has been recently estimated. PACNS may represent 1.2% of vasculitis involving the CNS However, there has been an increased awareness about this condition which has lead to reporting of more number of cases.[2]

The pathogenesis of PACNS is unknown. The granulomatous nature of the vascular inflammatory lesions in most cases suggests a Th1-mediated response.

PACNS typically involves small-medium sized arteries and veins, especially those located in leptomeninges and subcortical areas. The characteristic histopathologic findings consist of inflammatory infiltration of vessel walls by T lymphocytes and activated macrophages which undergo granulomatous differentiation with giant-cell formation.[1]

The clinical, imaging, and angiography spectra can be very broad. The median age of onset is 50 years, but may affect patients of all ages. The neurological manifestations are diverse, ranging from hyperacute to chronic and insidious. The majority of patients present with subacute manifestations of diffuse CNS dysfunction. Acute presentation is highly unusual. The most common initial symptoms are headache (63%) and cognitive impairment (50%). Focal symptoms usually appear later in the course of the disease and include hemiparesis (44%), stroke (40%), aphasia (28%), transient ischemic attack (28%), ataxia (19%), seizures (16%), dysarthria (15%) and blurred vision or decreased visual acuity (11%). Infrequent manifestations, occurring in less than 10% of patients, include intracranial hemorrhage, amnesic syndrome, spinal cord manifestations such as parapares, quadriparesis, parkinsonism, vertigo, dizziness or cranial nerve palsy. Most patients have multiple manifestations.[3-4]

Heterogeneous patterns and outcomes of the disease have been described, like fulminant disease onset, spinal involvement, prominent leptomeningeal enhancement, and negative cerebral angiography, suggesting that medium-sized vessels are affected. CSF examination reveals evidence for aseptic meningitis in over 90% of patients. First series of PACNS reported in Colombia showed heterogeneous clinical presentation, studied completely & treated properly.[5]

The most important differential diagnosis is the systemic vasculitis, which is characterized by the presence of constitutional symptoms and serological markers indicating systemic inflammation. While in PACNS inflammatory process is limited to the CNS only (See Table 1). Tuberculosis is another important mimic of PACNS. No single laboratory test has sufficient sensitivity or specificity to establish the diagnosis, and high clinical suspicion is necessary. Brain biopsy is required to confirm the diagnosis and exclude other causes. Histologic confirmation of vasculitis is considered the standard for the diagnosis of CNS vasculitis, but this procedure is also limited by several factors. First, the procedure is highly invasive and requires the skills of an experienced neurosurgeon, who might not always be available. Second, the technical aspects of the procedures should be tailored to the individual patient. In patients with suspected GACNS (Granulomatous angiitis of CNS) the procedure of choice is open-wedge biopsy of the tip of the nondominant temporal lobe with sampling of the overlying leptomeninges and underlying cortex. Alternatively, directing the biopsy to an area of leptomeningeal enhancement, when present, might increase the sensitivity. CNS vasculitis is a notoriously patchy disease, which limits the sensitivity of the procedure, and as many as 25% of the biopsies are falsely negative. Finally, the presence of vasculitis in the biopsy specimen should not preclude performing special stains and cultures for occult infections that can produce secondary vascular inflammation.[6] In the present case brain biopsy could not be performed due to lack of expertise.

Table 1: Mimics of Primary Angiitis of the Central Nervous System.

Systemic vasculitis & Connective Tissue disorder	**Neoplasms**
Polyarteritis nodosa	Hodgkin's &Non Hodgkin's Lymphoma
Allergic granulomatosis	Leukemia
Vasculitis with connective tissue disease	Atrial Myxoma
Henoch Schaonlein purpura	Malignant angiotheliomatosis
Wegeners granulomatosis	**Miscellaneous**
Temporal &Takayasu's arteritis	Fibromuscular dysplasia
Behcet's Disease	Moyamoya disease
Systemic lupus erythomatosis	TTP
Sacoidosis	Cerebrovascular atherosclerosis
Lymphomatoid granulomatosis	Embolic disease
Infections	Antiphospholipid syndrome
Vial	Drug exposure (Sympathomimetic drugs)
Bacterial	
Fungal	
Rickettsial	

Based on published studies, the estimated sensitivity of cerebral angiography for detection of vasculitis is between 27% and 90% and for brain biopsy between 36% and 83%. MRI is the main neuroradiographical modality for the workup of patients with suspected PACNS, and generally, the combination of normal findings on MRI and normal CSF analysis has a high negative predictive value for the diagnosis of PACNS.[5] Calabrese & Mallek[7] proposed a series of diagnostic criteria combining, clinical, imaging and histopathologic findings. These include: 1) neurologic deficit that remains unexplained after a vigorous diagnostic workup, including lumbar puncture and neuroimaging studies, 2) angiographic abnormalities highly suggestive of vasculitis or histopathologic evidence of vasculitis within the CNS and 3) no evidence of systemic vasculitis or any other condition to which the angiographic or pathologic findings can be attributed. Our patient was fulfilling all three criteria for PACNS.

A common danger in the workup diagnosis is to start immunosuppressive treatment without establishment of diagnosis or exclusion of other diseases. Unfortunately no

randomised studies of PACNS have been done, and thus all information on treatment is based on retrospective observational data and clinical experience. The efficacy of most immunosuppressive agents such as azathioprine, methotrexate, and rituximab that are used in systemic vasculitis is still unknown or remains elusive in PACNS.[6] The vast majority of case series suggest a high degree of good outcomes when patients are treated with glucocorticoids or glucocorticoids and cyclophosphamide. However, there are some reports using a therapy combining mycophenolate mofetil and steroids allowing control of the disease with disappearance of the neurological abnormalities, restoration of normal daily activities and dramatic improvementin brain MRI abnormalities.[8] Reported mortality of this condition is high. As per literature 14% of 29 patients with biopsy-proven PACNS died or had severe morbidity (Modified Rankin Scale of 5) at follow-up of 1.14 years.[2]

Complete work up except brain biopsy was done in our case. The high clinical suspicion and appropriate diagnostic approach to this rare clinical condition PACNS, can avoid misdiagnosis by physician & more number of cases can be reported.

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