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Case Report

Internal Medicine Section

Neurorickettsioses: A Rare Presentation with Stroke in a Young Adult

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ABSTRACT

Acute stroke-like presentations due to rickettsial infections have been sparsely reported in literature. We report a young patient who presented with high grade fever and acute encephalopathy with right hemiplegia. CT head showed left cerebral, bilateral thalamic and midbrain infarcts. The stroke in young work-up for conventional and non-conventional risk factors including few infections known to cause cerebral vasculitis was negative. He did not respond to empirical antimalarials and antibiotics. With a high index of suspicion of his 'febrile cerebrovasculitis' like presentation, serological test for rickettsia was done and found to be positive. He responded to doxycycline. This case expands the spectrum of presentation of neurorickettsioses and highlights the importance of considering rickettsial vasculitis as one of the potentially treatable causes of infections causing stroke.

Keywords: Endothelial dysfunction, Febrile cerebrovasculitis, Neurorickettsioses, Rickettsia, Stroke-in-young

CASE REPORT

A previously healthy 25-year-old man from rural Karnataka, India a state in southern India presented with high grade fever and severe frontal headache of 8 d duration followed by altered sensorium. On examination, he was febrile with a heart rate of 116/minute, blood pressure was 104/70 mm Hg. There was no lymphadenopathy or rash/eschar. Eyes showed pallor, conjunctival congestion and mild icterus. Neurologically, he was drowsy, arousable; pupils were equal and reactive to light; he had left upper motor neuron type facial paresis with paucity of movements of left upper and lower limbs. His deep tendon reflexes were exaggerated and bilateral plantars were extensor. There were no signs of meningeal irritation. Other systemic examination revealed no abnormality.

Investigations revealed haemoglobin - 6.9g/dl, packed cell volume - 25.5%, red blood cell count - 3.23 million/cubic mm, total count - 2400/ cubic mm, platelets- 17000/cubic mm. Peripheral smear revealed normocytic, hypochromic anaemia with leukopenia and thrombocytopenia (pancytopenia). Blood glucose, renal function tests and serum electrolytes were normal. Serum bilirubin was elevated (total- 3.97; direct-3.62) with normal transaminases. Peripheral smear and QBC (quantitative buffy coat) were negative for malarial parasite. Serological tests for malaria (antigen assays), leptospira, salmonella and dengue were negative. Arterial blood gas analysis was normal. Chest X-ray showed bilateral moderate pleural effusion. Blood culture, sputum and urine culture did not show any growth. Plain CT head showed right posterior cerebral, bilateral thalamopeduncular infarcts [Table/Fig-1]; CT angiogram revealed filling defect at the origin of right posterior cerebral artery (PCA) (P1 segment) [Table/Fig-2]. MRI brain with angiography could not be done due to financial constraints. Serum antinuclear antibody was negative. Cardiac evaluation including echocardiogram and TEE (transesophageal echocardiography) to rule out any embolic source were normal. Transcranial doppler revealed patchy increased cerebral blood flow velocity in right proximal PCA and basilar artery. Relatives did not give consent for conventional angiography.

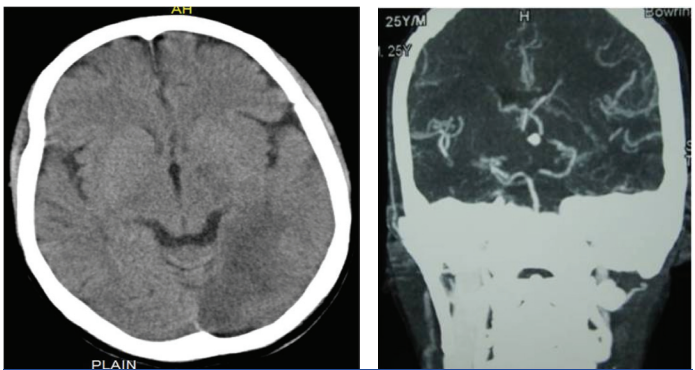
Patient was empirically started on antimalarials at presentation. Platelet concentrates and packed cells were transfused and once platelet counts were normalized, CSF examination done was normal (cell count - 8 lymphocytes per cubic millimeter; protein - 46 mg/dl; glucose - 70 mg/dl; OCB-weakly positive). Bone marrow examination was done for workup of pancytopenia and revealed hypercellular marrow with normoblastic pattern of maturation; no dyserythropoiesis was noted.

With a high index of suspicion of his 'febrile cerebrovasculitis' like presentation, serological test for rickettsia was done and found to be positive. Weil-Felix test was positive (by tube agglutination, to proteus antigen OX19 (1:320); OXK (1:160); OX2 (negative)). A diagnosis of acute ischemic stroke resulting from rickettsiosis with probable cerebral vasculitis was made. Indirect Flourescent antibody assay (IFA), the gold standard investigation could not be done due to non-availability.

Antimalarials were withheld and doxycycline was started. The patient responded with rapid defervescence within 36 h. He was gradually weaned from ventilator over 4 d. Doxycycline was given for 7 d. At discharge, his hemiplegia improved (grade 3/5), he had normal sensorium with normal hemogram, chest X-ray and liver function tests. He showed improvement in muscle power (grade 4/5) during follow up 3 wk later.

DISCUSSION

The complex interplay among infectious diseases, inflammation and stroke is an area of growing interest and ongoing research. It is well established that several infections including *Helicobacter Pylori*, *Chlamydiae*, *Cytomegalovirus*, periodontal anaerobes can directly or indirectly lead to ischemic or hemorrhagic stroke during their course by producing meningeal or parenchymal brain inflammation



[Table/Fig-1]: Plain CT head showed hypodensities in right temporoparietal region and in bilateral thalamopeduncular regions suggestive of infarcts
[Table/Fig-2]: CT angiogram revealed filling defect at the origin of right PCA (P1 segment)

and vasculitis [1]. Acute stroke-like presentations due to rickettsial infections have been sparsely reported in literature [2,3].

Acute febrile cerebrovasculitis, first described by Wenzel et al., is a disorder of unknown cause, probably rickettsial; patients manifest with fever, headache, altered mental status, multifocal neurological signs and CSF pleocytosis [2]. Early signs and symptoms of these infections are non-specific and mimic benign viral illnesses, usually presenting with fever at the outset. Diagnosis primarily requires a high index of suspicion. Linnemann et al., have recommended that evaluation of patients with acute febrile cerebrovasculitis should include rickettsial blood cultures [3].

Rickettsial diseases are reported from various parts of India, though the exact burden is underestimated due to lack of community based studies and availability of specific tests. Our patient was not from any of the known endemic areas for rickettsioses.

The diagnosis of rickettsial fever is made using serology. Though sensitivity and specificity of Weil-Felix test is low, it is still widely used for diagnosis of rickettsial infections due to non-availability of other serologic investigations like IFA, microimmunoflourescence [4].

The treatment of rickettsial vasculitis and hence reducing the morbidity and mortality depend on the bacterial control by antibiotics. With clinical suspicion and supportive laboratory features, we started our patient on doxycycline, the drug of choice for rickettsial infection. The patient showed rapid defervescence and clinically improved significantly.

The pathogenesis of CNS involvement is attributed to vasculitis which is responsible for microvascular leakage, oedema, microhemorrhages and mononuclear cell infilteration around the vessels leading to tissue hypoperfusion and end-organ ischemic injury. Pathologic studies of CNS have shown cerebral vasculitis, perivasculitis with predominant involvement of venules and capillaries. Formation of thrombosis can lead to tissue infarction and hemorrhagic necrosis [5].

CONCLUSION

Rickettsial diseases should be included in the differential diagnosis of patients with fever and acute stroke like presentation. This case highlights that high index of suspicion and prompt early institution of treatment is critical in management of rickettsioses and the consequent vasculitis and hence, reducing the morbidity and mortality.

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