Case Report

Extensive Vasculitis in Tuberculous Meningitis

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Abstract

Tuberculous meningitis causes substantial morbidity and mortality in tropical countries. The various complications reported are hydrocephalus, vasculitic infarcts, tuberculomas, abscesses, and optochiasmatic arachnoiditis. Vasculitis in tuberculosis is basically at the level of lenticulostriate arteries supplying the basal ganglia and terminal cortical branches. In this case report, we present a rare case of tuberculous meningitis with extensive vasculopathy. During hospitalization, she developed acute onset right-sided classical hemiplegia with the inability to speak due to left internal carotid artery occlusion on imaging. The cerebrospinal fluid depicted very high protein levels. The exact pathogenesis of such extensive involvement in tuberculous meningitis substantiates the need for further studies.

Keywords: Hemiplegia, infarcts, tuberculous meningitis, vasculitis

Introduction

Tuberculous meningitis (TBM) is a common cause of morbidity and mortality in South Asian countries. TBM is a dreadful manifestation of tuberculosis. It leads to about 40% of the deaths related to tuberculosis, mainly in developing countries.[1] TBM can manifest with hydrocephalus, vasculitic infarcts, tuberculomas, abscesses, and optochiasmatic arachnoiditis. Vasculitis in TBM is basically at the level of lenticulostriate arteries supplying the basal ganglia and terminal cortical branches.[2] In this case report, we present an unusual case of TBM with extensive vasculopathy.

Case Report

A 26-year-old postpuerperal female (day 13) presented with fever, persistent headache, and vomiting for 1½ months, blurring of vision for 1 month, and altered sensorium for 15 days. There was no history of convulsion, diplopia, dimness of vision, eye pain or discharge, difficulty in swallowing, weakness, and bowel or bladder symptoms. There was no history of significant loss of weight, cough, rash, and joint pain. There is no history of similar illnesses in the past, high-risk behavior, abortion, diabetes, and hypertension.

Her general examination was negative for pallor, icterus, edema, significant lymphadenopathy, rash, joint tenderness, or swelling. The pulse rate was 97 beats/min, regular in rhythm, and normal volume, and all the peripheral pulses were normally palpable, blood pressure of 110/70 mm Hg, temperature of 100.4 F, and respiratory rate of 19/min.

Nervous system examination revealed initial Glasgow Coma Scale (GCS) of E3V4M5 with cranial nerve examination showing bilateral grade 3 papilledema with choroid tubercle [Figure 1], normal pupils, normal ocular movements, with normal limb power, and reflexes with bilateral flexor plantar responses. Neck rigidity and Kernig sign were positive. Her respiratory, cardiovascular, and abdominal examinations were normal except for palpable uterus in hypogastrium.

Her blood investigations which include hematological, renal, and liver functions revealed normal results. The thyroid function test was normal. The markers for HBsAg and HIV-1 and 2 were negative. Cerebrospinal fluid examination revealed 180 cells (90% lymphocyte), protein 1906 mg/dL, glucose 22 mg/dL (corresponding blood glucose 154.1 mg/dL), and cartridge-based nucleic

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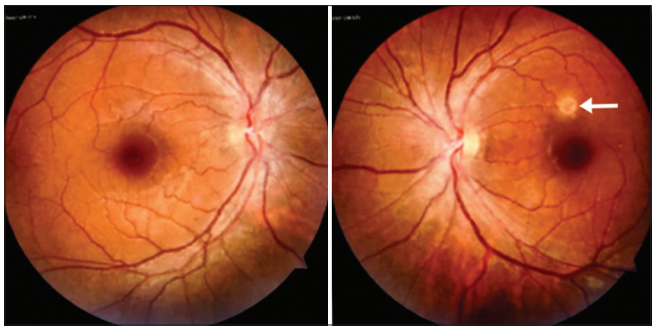

Figure 1: Fundus photography showing evidence of Grade 3 papilledema with the presence of choroid tubercle (white arrow)

acid amplification test (CBNAAT) was not detected. Cryptococcal antigen and fungal stain were negative. Her magnetic resonance imaging (MRI) brain imaging revealed leptomeningeal enhancement with multiple brain tuberculomas and hydrocephalus and she was treated with antitubercular drugs (oral isoniazid 300 mg/day, rifampicin 450 mg/day, pyrazinamide 1250 mg/day, pyridoxine 20 mg/day, and injectable streptomycin 750 mg/day) with steroids (intravenous injection dexamethasone 8 mg thrice daily dosing). The patient was improving and within 5 days, her GCS returned to the normal score of E4V5M6, with reduction in signs of meningeal irritation. However, on day 6, she developed four episodes of generalized tonic-clonic seizures and was treated with levetiracetam (1 g intravenous loading dose, followed by 500 mg twice daily dosing) which eventually controlled her seizures. The next day morning, she noticed acute onset weakness of the right side of the body with the inability to speak and deviation of the angle of the mouth to the left side. Her GCS dropped to E4VAM6 with hemiplegia of the right side (right-sided power 0/5 with extensor plantar on the right side, the other side being normal) with Broca's aphasia.

Her MRI brain and neck revealed left middle cerebral artery (MCA) territory infarct with reducing hydrocephalus, unchanged leptomeningeal enhancement with multiple tuberculoma, and occlusion of the left internal carotid artery (ICA) with hypoplastic left vertebral artery [Figure 2]. CT aortogram was done to look for evidence of vasculopathy elsewhere in the body, which came out to be negative. Her carotid Doppler showed occlusion of proximal left ICA with normal 2D echocardiography of the heart. She was further evaluated for evidence of vasculitis which was found to be negative for antinuclear antibody, antiphospholipid antibody, and rheumatoid factor. She was finally diagnosed with extensive vasculopathy in TBM, presenting with vasculitic infarct. With speech therapy, physiotherapy, and medications for TBM and antiplatelets (aspirin 150 mg/day), she started showing recovery within 2 weeks. At follow-up after 6 months, the patient showed remarkable recovery. The power in her right limbs was 4^{+}/5 and her speech became normal. There was no more episode of convulsion. She could perform her activities of daily living independently.

Discussion

TBM is a serious form of tuberculosis responsible for substantial morbidity and mortality, particularly in tropical countries. The development of infarcts in TBM can lead to a poor outcome.[3] The most common site of involvement is around the basal ganglia through penetrating lenticulostriate arteries and terminal cortical arteries.[4] According to a study by Hsieh and colleagues, 75% of infarcts occurred in the "TB zone" supplied by the medial lenticulostriate and thalamoperforating arteries, whereas only 11% occurred in the "ischaemic zone" supplied by the lateral lenticulostriate, anterior choroidal and thalamogeniculate arteries.[5] The TB zone consisting of the area including head of the caudate, genu and anterior limb of the internal capsule and anteromedial thalamus, while the ischemic zone consisting of the area including the lentiform nucleus, posterolateral thalamus and posterior limb of internal capsule. The development of infarcts can lead to a multitude of clinical presentations, most commonly focal neurological deficits in the form of hemiplegia, cranial nerve palsies, and movement disorders such as chorea, hemiballismus, and tremors.[6] There are multiple mechanisms of such neurological deficits in patients with TBM. First of all, the formation of thick exudates might externally compromise the nearby arterial branches either directly or by reactive vasospasm. Second, there might be an element of tubercular endarteritis.[7] It is well known that tuberculosis, being a chronic infectious entity, can lead to a prothrombotic milieu through excessive production of pro-inflammatory cytokines.[8] The element of significantly increased cerebrospinal protein, in this case, might correlate to the predisposition of vast vasculopathy in tuberculous meningitis.

This 26-year-old female patient of TBM developed an ischemic stroke during hospitalization. Her new brain scans revealed left MCA territory infarct with left ICA occlusion near the bifurcation of the left common carotid artery (CCA). Such a proximal involvement in TBM is rare. However, her further evaluation for other possibilities of vasculitis came out to be negative.

Vasculitic infarcts are an important phenomena in TBM.[9] The involvement of proximal ICA in TBM is a rare observation. The concept of extensive vasculopathy in TBM needs further exploration as the pathological basis of such involvement is not well known at present. However, severely elevated protein in cerebrospinal fluid might predispose to such a phenomena in patients with TBM. There can be future grading system for the predilection of stroke in patients with TBM. In addition, there can be a role of prophylactic antiplatelets, immunomodulatory drugs, and cerebral vasodilators in TBM having a higher predilection for the development of stroke. The role of immunomodulatory drugs other than steroids has not yet been approved in TBM. There have been few case reports of successful use of thalidomide, anti-TNF-alpha agents, interferon gamma, and cyclophosphamide in paradoxical reactions in TBM, where there is evidence of immune dysregulation.[10]

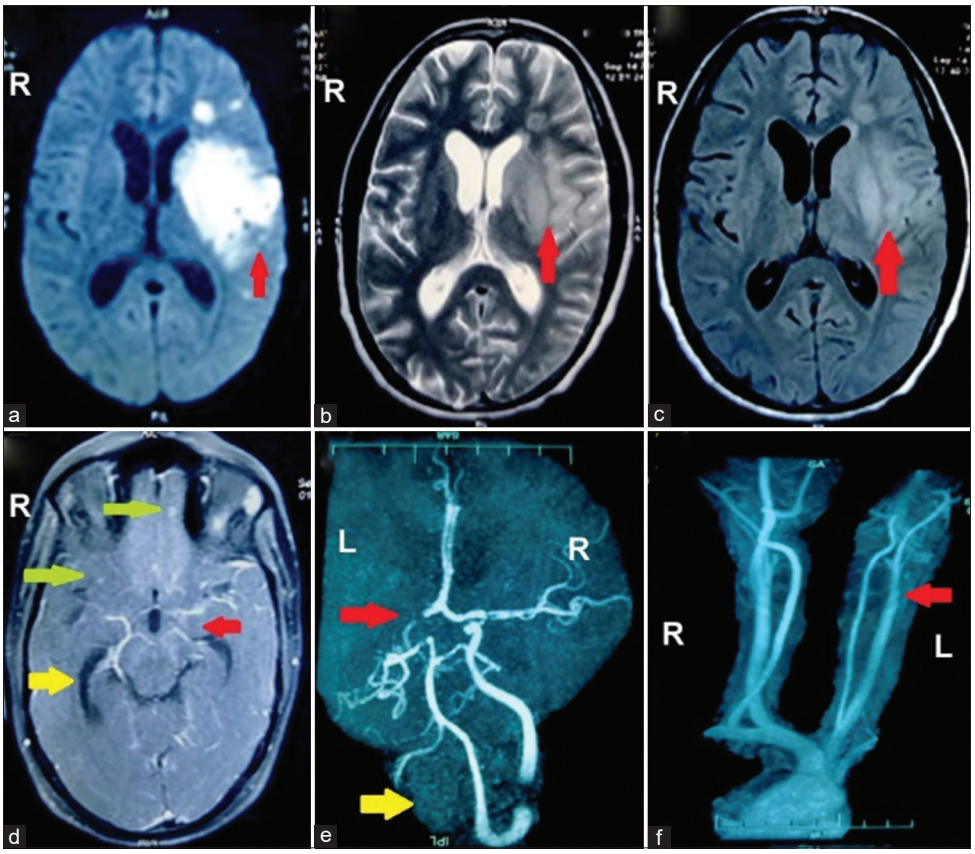

Figure 2: Magnetic resonance imaging of the brain showing (a) DWI restriction in left MCA territory (red arrow), (b) T2-hyperintensity in left MCA territory (red arrow), (c) FLAIR hyperintensity in left MCA territory (red arrow), (d) Gadolinium enhancement of leptomeninges (red arrow), tuberculomas (green arrow), and hydrocephalus (yellow arrow) in T1-contrast, (e) Angiogram of brain-vessels revealing nonvisualization of left ICA (yellow arrow) and left MCA (red arrow), (f) Angiogram of neck vessels showing obscuration of left ICA at origin (red arrow). MCA: Middle cerebral artery, DWI: Diffusion-weighted imaging, FLAIR: Fluid-attenuated inversion recovery, ICA: Internal carotid artery

An extensive study of these associations might help in a better understanding of immunopathogenic mechanisms of vasculitic infarcts in TBM and the role of prophylactic antiplatelets and immunomodulators needs to be explored in such patients with severely elevated cerebrospinal fluid protein.

Research quality and ethics statement

The authors followed applicable EQUATOR Network guidelines (http://www.equator-network.org/), notably the CARE guideline, during the conduct of this report.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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