

Lumbar puncture requirement in acute hemiparesis: Diagnosis of tuberculous meningitis after hemiparesis in a child

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Abstract

Background Infections are an important acquired cause of cerebral arteriopathy. Tuberculous (TB) meningitis leading to infectious cerebral vasculopathy is a rare cause of acute hemiparesis.

Case report A 14-year-old male patient was examined after acute hemiparesis developing within 1 day. Neurological examination revealed total hemiplegia on the left side. Brain MRI findings showed bilateral focal T2-weighted signal hyperintensity in the subcortical and deep white matter regions. There were also areas of restricted diffusion in the right basal ganglia. Although the father had a history of pulmonary TB, the patient had not been given TB prophylaxis because of PPD negativity. At lumbar puncture, opening cerebrospinal fluid (CSF) pressure was 50 cm/H2O, CSF protein 66.9 mg/dL, and glucose 54 mg/dL (concurrent blood glucose 93 mg/dL); 170 polymorphonuclear leukocytes per cubic millimeter were present in CSF. Following tests for TB, treatment was started immediately with four anti-TB drugs. TB PCR of CSF and acid-fast bacteria (AFB) staining in gastric aspirate were positive. At clinical follow-up, the patient was able to walk with support at the end of the first month.

Conclusion Various infectious agents have been reported as causes of cerebral vasculopathy. TB, which affects a significant number of patients worldwide, should be kept in mind in

terms of cerebral vascular complications. Lumbar puncture is essential in order to diagnose TB meningitis.

Keywords Tuberculosis · Stroke · Tuberculous meningitis · Hemiparesis · Child

Introduction

Arterial ischemic stroke is a leading cause of significant disability in childhood. Among the causes of cardiovascular disease, cerebral arteriopathies and serious systemic infections (meningitis and sepsis) are the most common etiologies for arterial ischemic stroke [1]. For these reasons, vasculopathies have recently attracted considerable attention. Infectious agents are the acquired causes of vasculopathy. Varicella, coxsackie A virus, rubella, measles, enterovirus, mycoplasma pneumoniae, and human immunodeficiency virus have previously been reported as factors [2]. We report a case of a child with hemiparesis due to stroke-induced vasculopathy associated with tuberculous meningitis (TBM).

Case report

A 14-year-old male presented with weakness in the left arm and leg developing within 1 day after 1-week headache, followed by fever. His history revealed that his father had started treatment with a diagnosis of pulmonary tuberculous (TB) 1 year previously, and all family members had been administered the purified protein derivative skin test (PPD). Our patient had not been given prophylaxis because of PPD negativity. At physical examination, he was conscious, but muscle strength in the left upper and lower extremities was just one fifth. He had neck stiffness, but no fever. Fundoscopic examination revealed temporal pallor of the optic discs. Other

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vital signs were within normal limits. At laboratory examination, white blood cell count was normal, but CRP at 3.3 mg/dL and erythrocyte sedimentation rate (ESR) at 67 mm/h were elevated. Chest X-ray (Fig. 1) and thoracic ultrasonography demonstrated pleural effusion 13 mm in size in the left cardiophrenic sinus. Brain MRI showed bilateral asymmetrical, focal T2-weighted signal hyperintensity in the subcortical and deep white matter region of the bilateral frontoparietal, left occipital, and temporal lobes (Fig. 2); there were also focal areas of restricted diffusion in the posterior limb of the capsula interna and the posterior and lateral thalamus on the right side (Fig. 3). MR angiography and MR venography were normal. Lumbar puncture was performed in order to rule out infectious agents. CSF opening pressure was 50 cm/H₂O, protein level 66.9 mg/dL, glucose 54 mg/dL, and concurrent blood glucose 93 mg/dL. CSF examination revealed 170 polymorphonuclear leukocytes per microliter and negative gram stain. Combination therapy of ceftriaxone, vancomycin, and dexamethasone was started empirically on suspicion of purulent meningitis. Following tests of CSF and gastric aspirate to investigate TB, treatment was started immediately with four anti-TB drugs (300 mg/day isoniazid, 600 mg/day rifampicin, 1,500 mg/day pyrazinamide, and 1,200 mg/day of ethambutol at the adult dose because the patient weighed 52 kg) without waiting for the test results. Antimicrobial therapy and acyclovir were discontinued because DNA detection by real-time PCR for herpes simplex virus (HSV) and CSF culture was negative. AFB stain of homogenized gastric aspirate was positive for three consecutive days. Although culture of CSF for *Mycobacterium tuberculosis* was negative, PCR was positive.

At laboratory follow-up, hyponatremia evolved on the 7th day of anti-TB treatment. Serum sodium (Na) level was 131 mEq/L, compatible with inappropriate ADH syndrome-related TBM. Following fluid restriction of 1,200 ml/m² per day, Na rose to 134 meq/L on day 5 and 137 meq/L on day 10.



Fig. 1 Chest X-ray showing pleural effusion in the left cardiophrenic sinus

Repeat puncture of CSF on the 10th day of anti-TB therapy revealed a cell count of 50 lymphocytes per microliter, protein 129 mg/dL, and glucose 42 mg/dL (simultaneous with blood glucose of 83 mg/dL). Opening pressure of CSF was measured at 36 cm H₂O. At the end of the first month of anti-TB therapy, MRI of the brain showed slight regression in old lesions in the subcortical and deep white matter of bilateral frontoparietal, left occipital, and temporal lobes (Fig. 2). Faint patchy contrast enhancement was observed in the lesions in the right basal ganglia and thalamus (Fig. 4) and dense nodular contrast enhancement in the lesions in the bilateral parietal lobes. Thicker nodular contrast enhancement on the leptomeningeal surface near the right temporal lobe was thought to be compatible with TBM. There was no ventricular dilatation.

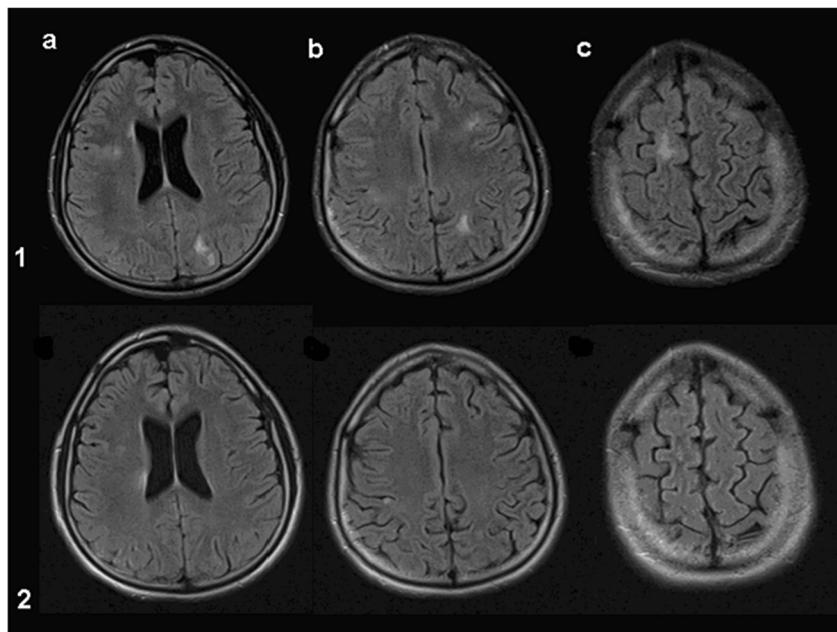
At clinical follow-up, hemiparesis exhibited regression. Muscle strength at follow-ups 10, 20, 28 days later was 2/5, 3/5, and 4/5, respectively. After 4 weeks of treatment, the patient was able to walk with support.

Discussion

Infections in the central nervous system (CNS) can trigger vasculopathy in the CNS. Mycobacteria, spirochetes, varicella zoster, fungal, and parasitic infections and HSV have recently been identified as causative agents. There are several theories regarding the etiology of vasculopathy caused by infectious agents. Although the pathophysiology leading to infectious vasculopathy has not been completely elucidated, one possible mechanism may be infiltration and invasion of the inflammatory subarachnoid exudate or inflammation caused by direct invasion of vessel walls by microorganisms [3]. Immunological involvement via the induction of antigen expression on endothelial cells and the formation of immune complexes may also be important [4]. Locally produced cytokines or other immune mediators may be significant by mediating vasculopathic effects [5]. Chickenpox in particular is a well known cause of stroke. Ueno et al. described a case of a 4-year-old child with monoparesis 3 months after varicella infection and an episode of hemiparesis on the contralateral side 6 months after the infection was reported. That case had basal moyamoya vessels with MCA occlusion and exhibited good prognosis. The authors suggested that chronic progressive stenotic changes in the cerebral arteries might be caused by direct invasion by varicella zoster virus (VZV), and that collateral circulation like moyamoya vessels might develop as a result. They also suggested that this was an inflammatory process of cerebral angitis-related VZV resulting in destruction of the arterial wall [6]. Here, we describe a case of childhood cerebral vasculopathy-related TB infection.

TB is an infection that affects many people worldwide. In 2007, there were an estimated 9.27 million new cases of TB

Fig. 2 FLAIR sequence images before anti-TB treatment (1) and after 4 weeks (2). 1a, 1b, and 1c show the presence of bilateral asymmetrical, focal increased signal intensity in the subcortical, and deep white matter region of the bilateral frontoparietal and left occipital lobe 2a, 2b, and 2c show regression in the lesions



globally and 1.78 million deaths [7]. Incidence of TB in Turkey in 2011 was 29/100,000 according to the 'Ministry of Health 2011 Report on Tuberculosis' [8]. Approximately 10–15 % of all TB infections include CNS involvement [9]. TBM is the most serious form of CNS TB [10]. Vessels near

the circle of Willis are reported to be particularly affected in association with TBM [10]. Basal ganglionic infarctions are the most common due to involvement of perforating vessels [7, 11]. Inflammation, spasms, constriction, and eventually thrombosis cause obliteration of intracranial vessels. The basal exudates strangulate the vessels traversing the CSF, giving rise to obliterative vasculitis [10]. Electron microscopic studies in

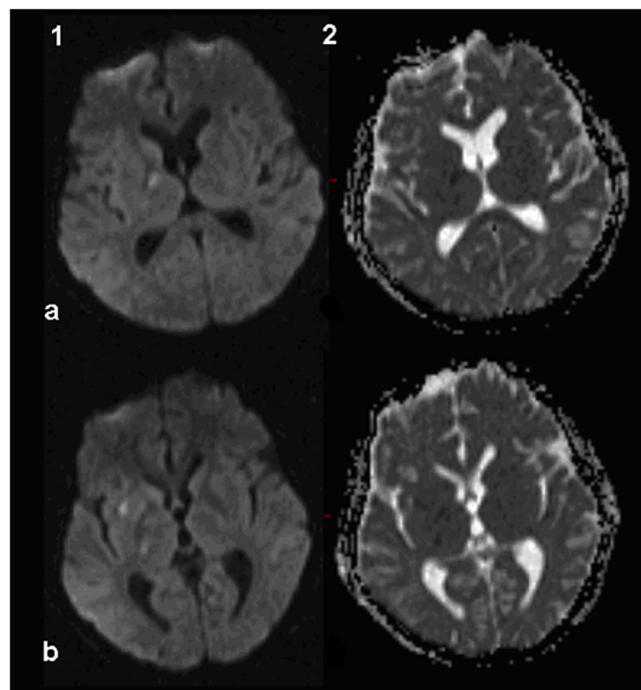


Fig. 3 Diffusion weighted imaging (DWI) (1) and apparent diffusion coefficient (ADC) mapping (2) of the lesions in the right basal ganglia *a*1 hyperintense signal in the posterior limb of the capsula interna in DWI, *a*2 signal hypointensity in the same region in ADC mapping, *b*1 hyperintense signal in the posterolateral of the thalamus and basal ganglia in DWI, *b*2 signal hypointensity in the same region in ADC mapping (These findings denote the diffusion restriction)

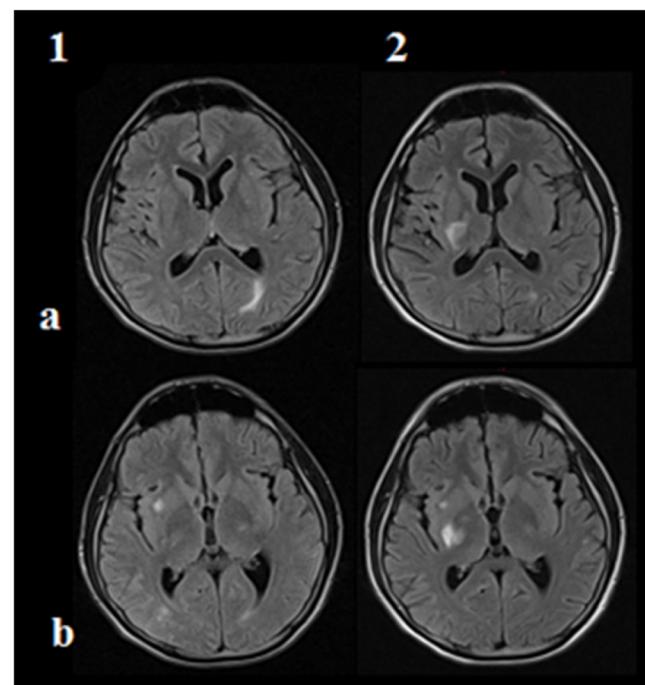


Fig. 4 FLAIR sequence images before anti-TB treatment (1) and after 4 weeks (2). 2a and 2b show signal hyperintensity in the right basal ganglia and thalamus (Note that signal hyperintensity in the left occipital region (1a) regressed 4 weeks later (1b))

the reactive zone around the tuberculoma have confirmed vascular proliferation and vasculitis [7].

In our case, although MR angiography was normal, hemiplegia and infarction in the right basal ganglia were thought to be associated with vasculopathy. Although infarction was observed in the early period in our case, it appears to be more common in cases of longer duration [5]. Arterial narrowing and occlusion are seen in a majority of patients with TBM [10]. Abnormalities suggestive of cerebral vasculitis at MRI are infarctions and white matter hypersignals [4]. Neuroimaging analysis using brain CT with contrast or MRI with gadolinium in TBM may show meningeal enhancement consistent with meningeal inflammation, areas of infarction and hemorrhage, hydrocephalus associated with late complications, and intracerebral tuberculoma [12].

In addition to early clinical suspicion, CSF findings are also important in the diagnosis of TBM. We suggest that a significant increase in CSF protein compared to the number of cells should attract the physician's attention to TBM. In TBM, the CSF typically exhibits a high CSF white cell count, predominantly lymphocytic, with a high protein and low glucose ratio. Initial predominance of neutrophils in the CSF should be kept in mind [13]. TBM may have a poor prognosis. Early clinical suspicion and early treatment are therefore important. CSF findings should be taken into account during assessment.

The tuberculin skin test was negative in our case. Negativity in this test needs not exclude a diagnosis of TBM. The tuberculin skin test may be negative in some patients with comorbid immunosuppressive illness [12]. Although CSF culture was negative for *M. tuberculosis* in our case, diagnosis of TBM was made on the basis of CSF PCR positivity and the presence of AFB stain positivity in the gastric aspirate. Careful bacteriology is as good as or better than the nucleic-acid-amplification assays before treatment commences, but molecular methods may be more useful once antituberculosis drugs have started being used [13].

There are no recommendations for additional treatments supplementary to anti-TB drugs in TBM-induced stroke. Conventional anti-TB drugs and steroids are used. The use of isoniazid, rifampicin, and pyrazinamide is essential at the beginning of TBM treatment, and some institutions use all three drugs for the duration of therapy. There are no established data from controlled trials in terms of a fourth drug. Either streptomycin or ethambutol is mostly recommended. Streptomycin treatment should not be administered to pregnant women or patients with renal impairment. Resistance to this drug is also relatively common worldwide. Incidence of optic neuropathy resulting from ethambutol treatment is less than 3 % at the standard dose of 15–20 mg/kg, but this side-effect should be considered in comatose patients [14]. Although steroids in TBM have been shown to be useful in reducing cerebral inflammation and edema, the role of steroids in preventing cerebral infarction is controversial

[11]. Aspirin and similar studies have not reported any benefit [15].

Vasculopathy of infectious origin must be considered among the causes of stroke. TBM is another of these potential causes. Our case also reveals the importance of prophylaxis against TB in the event of household contact. We suggest that lumbar puncture should be considered in patients with stroke because of the prognostic significance of early treatment in TBM.

Conflict of interest The authors declare that they have no conflict of interest.

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