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Delayed onset cerebral vasculitis from chronic *Schistosoma mansoni* infection in Myanmar: A case report

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Abstract

Neuroschistosomiasis is an infection of the central nervous system caused by *Schistosoma* species and constitute a severe manifestation of the disease. *Schistosoma japonicum* is well-known cause of cerebral schistosomiasis and *Schistosoma mansoni* for spinal schistosomiasis. Although neuroschistosomiasis is not rare, reports on cerebral vasculitis associated with *Schistosoma mansoni* infection is scarce. With regards to schistosomiasis in Asia, most of the published literature has been on *Schistosoma japonicum* and the prevalence of *Schistosoma mansoni* in Asia is not well established. We report here a 54-year-old Rakhine woman with history of diabetes mellitus for more than ten years presenting with three recurrent stroke occurring over 2 months, twelve months after returning to Yangon from Rakhine, an endemic area for *Schistosoma mansoni* infection. Cerebral MRA revealed beaded appearance along left ACA and segmental narrowing beyond terminal ICA both sides, and contrast enhancement was noted at left frontal lobe with restricted diffusion on MRI brain. Serum serology testing for *Schistosoma mansoni* infection was positive. With oral praziquantel and high dose corticosteroid, aphasia and swallowing improved. This is the first report of delayed onset cerebral vasculitis associated with chronic *Schistosoma mansoni* infection in Asia.

Keywords: Asia, Stroke, Cerebral vasculitis, *Schistosoma mansoni*, Corticosteroid, Praziquantel

INTRODUCTION

Schistosomiasis is a parasitic infection by blood flukes (trematodes) of the genus *Schistosoma*. It is the third leading endemic parasitic disease in the world with an estimated prevalence of 250 million worldwide.[1] In Asia, three species of *Schistosoma* are known to cause human disease. *Schistosoma japonicum* is the most prevalent, followed by *Schistosoma mekongi* and *Schistosoma malayensis*.[2] *Schistosoma mansoni* is endemic across sub-Saharan as well as southern Africa, the Middle East, South America and the Caribbean. *Schistosoma mansoni* infection has been given little attention in Asia including Myanmar.[3] Neuroschistosomiasis is an infection of the central nervous system caused by *Schistosoma* species and constitute a severe manifestation of the disease. Neuroschistosomiasis caused by *S. mansoni* can present with acute schistosomal encephalopathy, pseudotumoral encephalic schistosomiasis and spinal cord schistosomiasis.[4] Although neuroschistosomiasis is not rare, *S. mansoni* infection is still an under-recognized cause of cerebral vasculitis especially in Asia. We report here a diabetic woman presenting with recurrent stroke due to delayed cerebral vasculitis caused by chronic *S. mansoni* infection.

CASE REPORT

A 52-year-old Rakhine lady with known history of diabetes mellitus for 10 years, presented to our hospital in April 2019 with two days duration of sudden onset cognitive impairment with recent memory deficit, difficulty in calculation, disorientation and behavioural changes. She denied headache, vomiting and fever. She had no meningeal signs, cranial nerve palsies, motor and sensory deficit. Her MMSE was 24/30. Other

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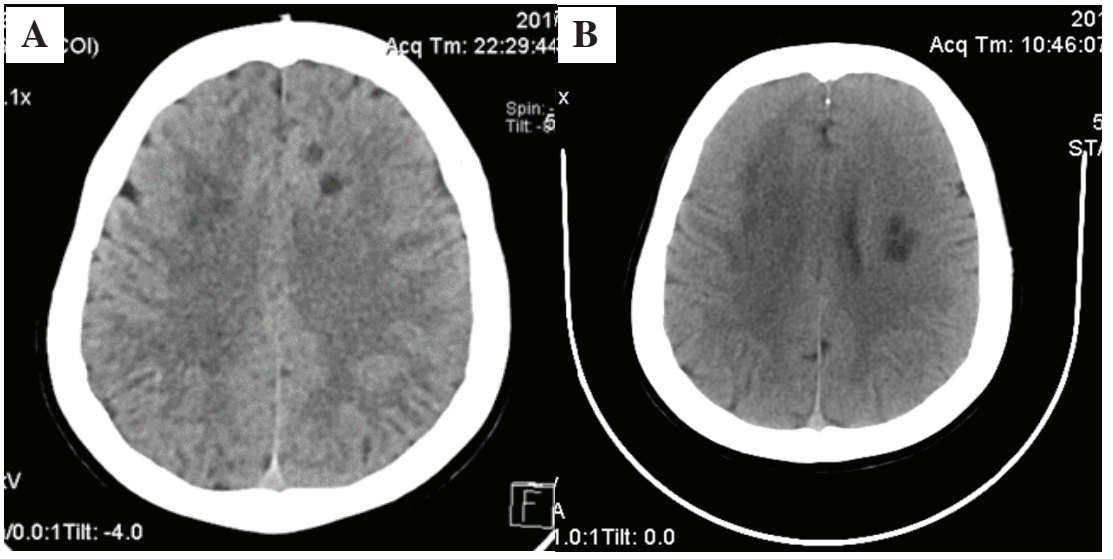

Figure 1. CT (brain) of the patient. A. Axial image showing bilateral multiple hypodense lesions. B. Appearance of new lesions over left central semiovale on repeat scan 3 weeks after first admission with development of right hemiparesis.

examination was unremarkable. Non-contrast CT scan of the brain showed bilateral multiple hypodense lesions. Because of the presence of cerebrovascular risk factors, she was diagnosed with multifocal cerebral infarcts. Three weeks later, she developed dysarthria, right-sided hemiplegia and right-sided upper motor neuron facial palsy. New hypodense lesions were found on repeated non-contrast CT of the brain. (Figure 1, 2)

MRI brain with contrast, MRA and MRV were also performed, showing contrast enhancement of the left parasagittal superior frontal hyperintensities in T2WI. Lumbar puncture was performed showing normal protein (0.35 g/dl), normal sugar (50 mg/dl) and four lymphocytes. CSF was also tested for common virus and bacteria and the results were all negative. CSF for Xpert MTB/Rif as well as for oligoclonal bands were also negative, as well as serum serology for Japanese B encephalitis virus.

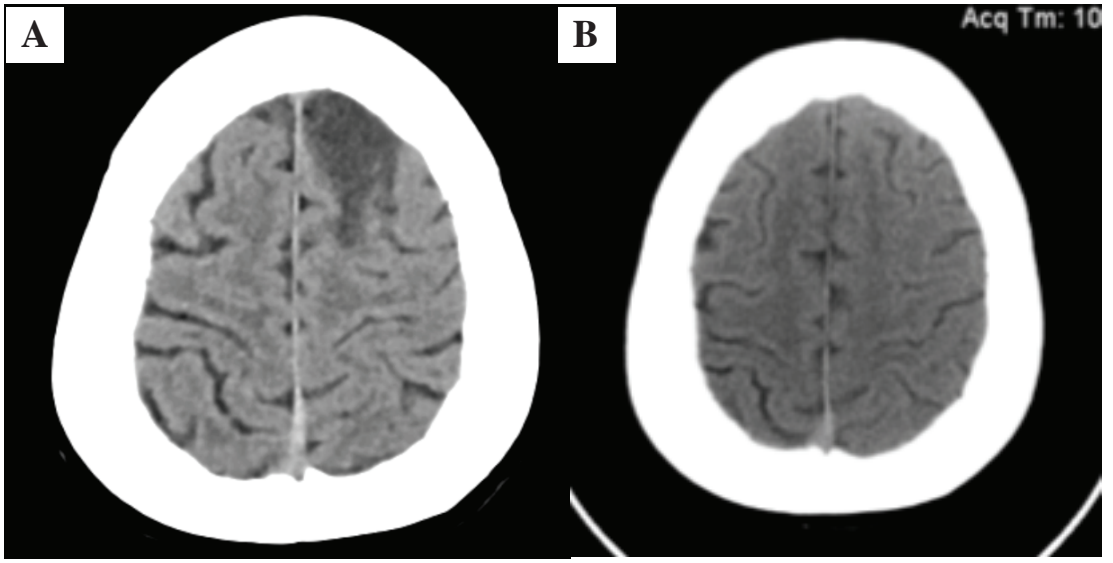

Figure 2. CT (brain) of the patient. A. Axial image showing moderate-sized hypodense lesion over left superior frontal lobe on first admission. B. Disappearance of the lesion on repeat scan 3 weeks after first admission with development of right hemiparesis.

As there was restricted diffusion on DWI/ADC of the left frontal lesion, and segmental narrowing on both sides beyond terminal ICA, and beaded appearance along left ACA, the patient was thought to have disseminated cerebral vasculitis. (Figure 3) Systemic autoimmune disease screening and serum for typhus serology testing was done and the results were negative. IV methylprednisolone 1G daily for 3 days was initiated for possible primary CNS angiitis. The night after the first day of methylprednisolone, her motor deficits worsened followed by global dysphasia, urinary incontinence and aspiration.

Transthoracic as well as transoesophageal echocardiogram were done, and they showed no thrombus or no vegetation. Blood was sent for thrombophilia screening and the results were negative. As there was schistosomiasis outbreak in Rakhine state, Myanmar in 2018, and she visited her hometown one year ago on the same period, when she ate snails, swam in seawater and was also exposed to pond, serum ELISA for *Schistosoma mansoni* was performed and was positive. In repeated haematological testing, there was persistent eosinophilia at two times upper limit of normal. Stool and urine were negative for ova. She was treated as neuroschistosomiasis as she had neurological symptoms with previous exposure to Schistosoma infection.[5] She was given 40mg/kg of praziquantel in two divided doses 4 hours apart together with high dose corticosteroid therapy (oral dexamethasone 16 mg daily) for 9 weeks with tapered dose over another 6 weeks. Follow up MRI brain and MRA was taken 6 weeks after first dose of praziquantel where a new lesion was found at left frontal operculum with restricted diffusion suggestive of new cerebral infarct with no significant changes on narrow cerebral arteries and clinically without any relapse. Therefore, second dose of praziquantel was given. There was no further relapse and no more eosinophilia on complete blood count in the last follow up at 6 months after second dose of praziquantel, when she could walk with aid.

DISCUSSION

Humans is the definitive host and freshwater snails are the intermediate hosts of *Schistosom*a. Infection is usually acquired through activities such as swimming, bathing, fishing, farming, and washing clothes in fresh water.[6] *S. japonicum* causes more clinical cerebral involvement than *S. mansoni*. Severe cases of acute encephalitis and multiple distal border zone ischaemic infarctions due to cerebral vasculitis have been proposed to occur during primary infection with *S. mansoni*.[4] However, cerebral vasculitis associated as a delayed manifestation of chronic *S. mansoni* infection is rare. To our knowledge, there was only one previous case reported of a delayed cerebral vasculitis causing infarct in a French woman who developed dysphasia and right hemiparesis 6 months after return from Bukina-Faso. MRI brain showed left junctional infarct and multiple hyperintense lesion in the

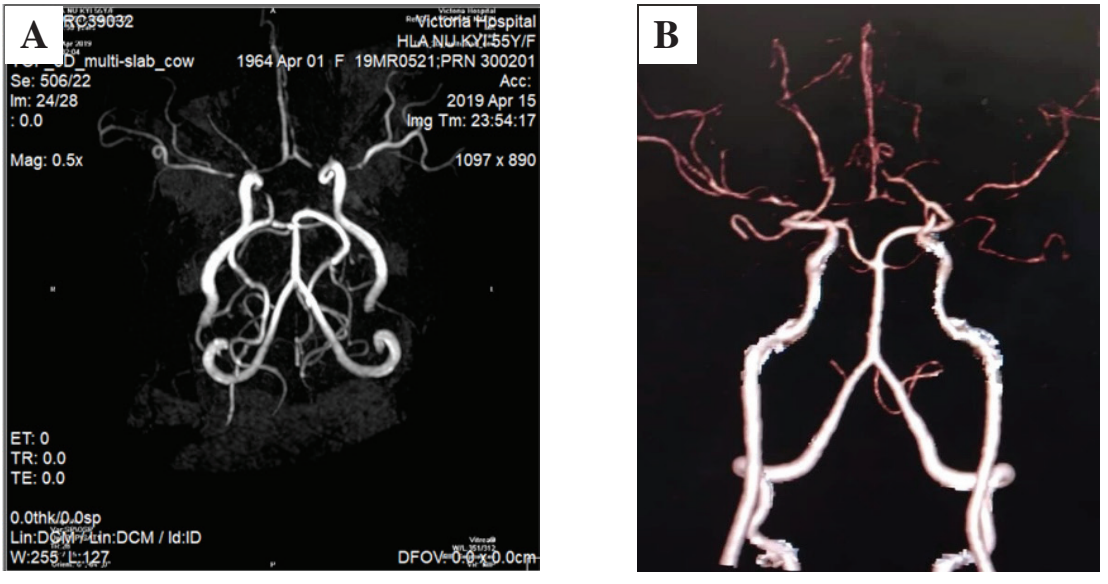

Figure 3. A. MRA (brain) of the patient. B. CTA (brain) of the patient showing segmental narrowing on both sides beyond terminal internal carotid artery (ICA)

left hemisphere. MRA showed bilateral internal carotid artery stenosis.[7] In our patient, the vasculitis involving left ACA and both ICAs occurred with a latency period of one year after exposure. In the study done by Pittella, two forms of cerebral vascular changes were observed in cerebral schistosomiasis caused by *S. mansoni* infection. Five out of fifteen cases had vascular wall changes. Among them, four showed arteritis with fibrinoid necrosis either involving arterial wall completely or in segments with ova in one case and granuloma in another case. In the other one case, arterial wall thinning, interruption of the internal elastic membrane, aneurysmal dilatation of the lumen, intimal thickening and vascular wall destruction with perivascular lympho-histiocytic infiltrate were identified.[8] This suggests that in the cerebral arterial lesions in *S. mansoni*, the pathology process include necrotizing vasculitis and interaction of ova with endothelial cells to provoke an inflammatory reaction in the vascular wall.

Diagnosis of neuroschistosomiasis is challenging and diagnostic standards have not been established. Diagnostic approaches include the identification of ova excretion in faeces or urine or in biopsy material from the urinary bladder or rectum in combination with immunological testing. However, a positive serology with previous exposure in endemic area, together with neuroimaging and neurological symptoms should form reasonable basis of diagnosis of neuroschistosomiasis as in our patient.[5] Praziquantel is the treatment of choice for all *Schistosoma* species. Effective praziquantel dosage regimen is 40 mg/kg orally in two divided doses over one day (2 x 20 mg/kg doses 4-hours apart) for *S. mansoni*. Corticosteroids and anticonvulsants maybe needed as adjuvants to praziquantel in neuroschistosomiasis.[5] In our patient, with two doses of 40mg/kg/dose and high dose steroids, her deficits improved especially speech and swallowing on discharge and can walk with aid on 6 months follow-up.

In conclusion, we describe the atypical presentation of neuroschistosomiasis with latency of one year after exposure to *S. mansoni* infection with cerebral vascular narrowing. The neurovascular involvement indicate the need to include neuroschistosomiasis in the differential diagnosis of cerebral vasculitis.

DISCLOSURE

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Conflict of interest: None

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