**CASE REPORT**

Infectious causes of acute ischemic stroke: pathomechanisms and distribution of brain infarct

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**ABSTRACT**

Infectious diseases and stroke are common and a great health problem worldwide. However, relatively few studies have focused on direct infectious causes of acute stroke, and the exact mechanisms of acute stroke associated with infections are poorly understood. Herein, we present several infectious organisms that are probable causes of stroke. Different pathomechanisms of stroke and neuroimaging features of infection by these organisms are discussed. Specifically, the distribution of cerebral infarction suggests that infections could be a direct cause of acute stroke. These include cerebral convexity probably due to vasculitis in bacterial meningitis, deep infarcts due to endarteritis and inflammation in neurocysticercosis, and exudates in tuberculous meningitis, as well as hemodynamic borderzone infarct due to large vessel vasculitis by direct invasion of fungal infection. We suggest that prompt and appropriate control of these organisms could prevent ischemic stroke.

**Keywords:** Cerebral infarction; Meningitis; Neuroimaging; Stroke; Vasculitis

**INTRODUCTION**

Infectious diseases remain a great health problem in developing countries and the proportion of infection-related strokes is possibly greater in these nations [1]. Furthermore, over the last decades, the number of immunocompromised patients has increased in part due to the use of immunosuppressive treatments (e.g., post-organ transplantation) and human immunodeficiency virus (HIV) infection.

Some infectious pathogens may act as risk factors and can trigger stroke through different mechanisms in their acute phase. Most studies to date have focused on the role of chronic infections/inflammation as a risk or trigger factor for stroke and atherosclerosis, or on the control of post-stroke infection [2-6]. Relatively, fewer studies have focused on direct infectious causes of acute stroke [7,8]. Consequently, the exact mechanisms underlying acute stroke associated with infection are poorly understood.

Here, we introduce several cases with various intracranial infections that caused acute ischemic stroke. Different pathomechanisms of stroke and different neuroimaging features associ-
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Bacterial meningitis
A 62-year-old man developed general weakness and a fever/chilling sensation. He was taking prednisolone and azathioprine due to immunoglobulin G4-related sclerosing cholangitis and pancreatitis. Twelve days after the onset of fever, he developed mental changes and speech disturbance. Cerebrospinal fluid (CSF) examination showed elevated intracranial pressure (> 30 cmH₂O) and white blood cell (WBC) count 38,400/µL (polymorphonuclear neutrophils [PMNs] 82%, lymphocytes 3%). Brain magnetic resonance imaging (MRI) showed meningeal enhancement and fluid collection. Based on the CSF study and MRI findings, he was diagnosed as having bacterial meningitis, and underwent external ventricular drainage. Antibiotic and steroid therapy were started. CSF culture revealed *Klebsiella pneumonia*. The fever subsided, but the patient remained severely disabled (Fig. 1).

Fungal infection
A 70-year-old woman developed swelling in her left ocular region followed by ocular pain, left ptosis, and diplopia 2 days later. She had diabetes and hypertension. Two weeks later, right hemiparesis and aphasia developed. A physical examination revealed no fever, and black necrotic mucosal eschar and mucosal ulceration were observed in the nasal cavity. A neurological examination showed decreased left visual acuity (light perception), complete ophthalmoplegia, and mild (grade 4+) right hemiparesis and global aphasia. CSF pressure was normal, but WBC was 25/µL (PMNs 43% and lymphocytes 36%) and protein level was 57.1 mg/dL. MRI showed acute infarct on the left borderzone area and occlusion of the previously intact left distal internal carotid artery with wall enhancement. Cranial MRI showed infiltrative enhancing lesions involving the left cavernous sinus, orbital apex, and optic nerve, suggestive of invasive fungal sinusitis. A nasal cavity biopsy from the right middle turbinate was performed, which revealed invasive aspergillosis. The patient received antiplatelet agents, voriconazole, an antifungal agent, and hydration. Infarct growth was observed within the borderzone area, and the patient continued to present with global aphasia and severe right hemiparesis (Fig. 2).

Tuberculous meningitis
A 48-year-old female presented with fever and headache. On the 2nd day after admission, she developed mental changes...
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Prevalent causes of acute ischemic stroke include vasculitis, arteritis, or cardiac sources. Syphilis, tuberculosis, endocarditis, and neurocysticercosis are atypical causes of ischemic stroke. Neurocysticercosis has been described in up to 20% of patients presenting with stroke and has been associated with multiple presentations, including acute ischemic stroke.

A 48-year-old woman with tuberculous meningitis. Diffusion-weighted image (DWI) at initial examination and follow-up showing acute infarcts on left medulla and right thalamus, respectively. Magnetic resonance angiography (MRA) showing normal large cervicocephalic vessels.

Parasite infection
A 59-year-old man experienced transient dysarthria that lasted 30 minutes. He had no history of illness, except hypertension. The neurological examination was unremarkable. MRI showed acute infarcts on the right basal ganglia and corona radiata, and multiple enhancing cystic lesions on the basal cistern. Hydrocephalus and calcified cystic nodules in the cisternal space were also observed. High-resolution MRI showed occlusion of the bilateral proximal middle cerebral arteries (MCAs), as well as circular enhancement and thickening of the MCAs, anterior cerebral arteries, and the distal internal carotid arteries; suggesting vasculitis. CSF showed WBC 8/µL (PMNs 47%, lymphocytes 35%, eosinophils 1%) and protein 77.2 mg/dL. An enzyme-linked immunosorbent assay (ELISA) test for parasite antibodies was positive for cysticercosis. Plain X-ray showed multiple elongated oval shaped, rice grain appearance calcifications within the bilateral leg muscles. Other tests, including malignancy and ring finger protein 213 (RNF213) gene variant for Moyamoya disease, were negative. Albendazole, praziquantel, and prednisolone were started after diagnosis of cysticercosis-related vasculitis. The patient remained functionally independent and free from recurrence (Fig. 4).

Written consent by the patients was waived due to a retrospective nature of our study.

DISCUSSION
Although anecdotal evidence exists to support a link between most infectious pathogens and stroke, certain pathogens display more robust associations, such that causation is probable [7].

Bacterial meningitis is a serious and life-threatening disease. The occurrence of stroke is associated with worse outcomes in patients with bacterial meningitis. Streptococcus pneumoniae and Neisseria meningitidis are the most common pathogens, although Klebsiella pneumoniae was identified in our case. Infarction can develop weeks after initial diagnosis of meningitis. The arterial involvement in patients with bacterial meningitis is explained by vasospasm of large arteries and vasculitis of small arteries. In our case, proximal large cerebral vessels were spared, and infarcts typically involved the bilateral superficial cortical areas, suggesting that vasculitis involved small MCA branches on the cerebral convexity, rather than large cerebral vessels such as the MCA trunk. Other possible mechanisms include endocarditis/septic emboli and intra-arterial clotting. Because bacterial menin
In conclusion, the causal relationship between infections and stroke remains unclear. In this study, we presented several infectious organisms for which causality is deemed relatively high. Cases presented in this study showed that the pathomechanisms of stroke differ between pathogens. Specifically, the distribution of cerebral infarction suggests that infections could be a direct cause of acute stroke. Examples discussed here include cerebral convexity probably due to vasculitis in bacterial meningitis, deep infarcts due to endarteritis and inflammation in neurocysticercosis, and exudates in tuberculous meningitis, as well as hemodynamic border zone infarct due to large vessel vasculitis by direct invasion of fungal infection. We propose that proper control of these organisms could prevent ischemic stroke.

**CONFLICTS OF INTEREST**

No potential conflict of interest relevant to this article was reported.
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Acquisition, analysis, or interpretation of data: WL, JK, JZ, OYB.
Drafting the work or revising: WL, OYB.
Final approval of the manuscript: OYB.

REFERENCES