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Stroke presenting as a rare complication of neurosarcoidosis in a young adult male: A case report

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Abstract
A 29-year-old Filipino-Chinese man with pathologically diagnosed neurosarcoidosis experienced right-sided weakness and slurring of speech. Neuroimaging showed a subacute infarction at the left paramedian pons. Pharmacotherapy included steroids, immunosuppressants, and anticoagulants. Three-month follow-up showed no progression of focal neurologic deficits. Stroke is rare in neurosarcoidosis and typically relates to granulomatous inflammation with a predilection for the perforator arteries. Neurosarcoidosis generally responds well to corticosteroids; however, combination therapy with additional immunosuppression is recommended to reduce the risk of relapse on steroid weaning. This report aims to highlight the occurrence of stroke as a rare complication of an equally rare disease entity in neurosarcoidosis.

Keywords: stroke, infarct, cerebrovascular disease, neurosarcoidosis, case report

Introduction

Apart from its usual causes, ischemic stroke may be caused by vasculopathic processes associated with underlying rheumatologic or inflammatory diseases, infections, drug reactions, malignancies, or granulomatoses [1]. Neurosarcoidosis is an example of granulomatous inflammation of primarily small and medium-sized blood vessels [2]. Neurosarcoidosis, a multisystemic disease that may involve the brain, spinal cord, meninges, cranial, or peripheral nerves, occurs in approximately 5% of sarcoidosis patients, with approximately 50% presenting with neurologic disease at the time of diagnosis [1, 2]. Rarely, stroke can occur in neurosarcoidosis and we are unaware of similar reported cases in the Philippines. One reported stroke case from elsewhere presented with acute cerebral infarction resulting from cardiac thromboembolism secondary to sarcoid cardiomyopathy [3]. The remaining 2 patients had stroke arising as a complication of diagnosed neurosarcoidosis [4, 5]. This case report aims to highlight the occurrence of ischemic stroke in a rare case of neurosarcoidosis.

Case Report

A 29-year-old Filipino-Chinese male, with a medical history of neurosarcoidosis controlled with steroids, consulted four days after the onset of speech difficulty and right-sided weakness. He was a nonsmoker with a healthy lifestyle, and apart from the pathologically diagnosed neurosarcoidosis from an eyelid nodule three years prior, he did not have any significant medical or surgical history. The details of the clinical and pathological profile of this patient has been reported elsewhere [6] (Figure. 1).

At the time of evaluation, the patient denied recent weight loss, fever, chills, rashes, cough, or headaches. General examination was unremarkable aside from nodular lesions on both upper and lower eyelids. Neurological evaluation showed normal comprehension, with intact naming and repetition. It also revealed sluggish pupillary light reflex in the left eye, right eye ophthalmoparesis, facial diplegia, and mild pronator drift in the right limbs. The remainder of the examination, including reflexes, sensation, coordination, and gait, were intact.

Imaging showed areas of restricted diffusion in the left paramedian pons without evidence of stenosis or atherosclerosis in bilateral carotid arteries or large intracranial vessels via magnetic resonance angiogram (MRA) with contrast (Figure 2). Laboratory tests showed elevated total cholesterol at 307 mg/dL. Echocardiography showed only minimal pericardial effusion with no thrombus that could relate to a possible source of embolism. Immunologic profile (rheumatoid factor and anti-nuclear antibodies) were negative. Further work-up showed positive serum angiotensin converting enzyme (SACE), elevated protein C and decreased protein S activities.

Pharmacotherapy ranged from steroids coupled initially with azathioprine which was then recently shifted to mycophenolate mofetil. Anticoagulant medication in the form of rivaroxaban was started at 10 mg/tab once daily and slowly titrated to 20 mg/tab once daily.

Follow-up after 3 months showed no progression of focal neurologic deficits, with a National Institute of Health Stroke Scale (NIHSS) score of 5 and a Modified Rankin Scale (MRS) score of 1

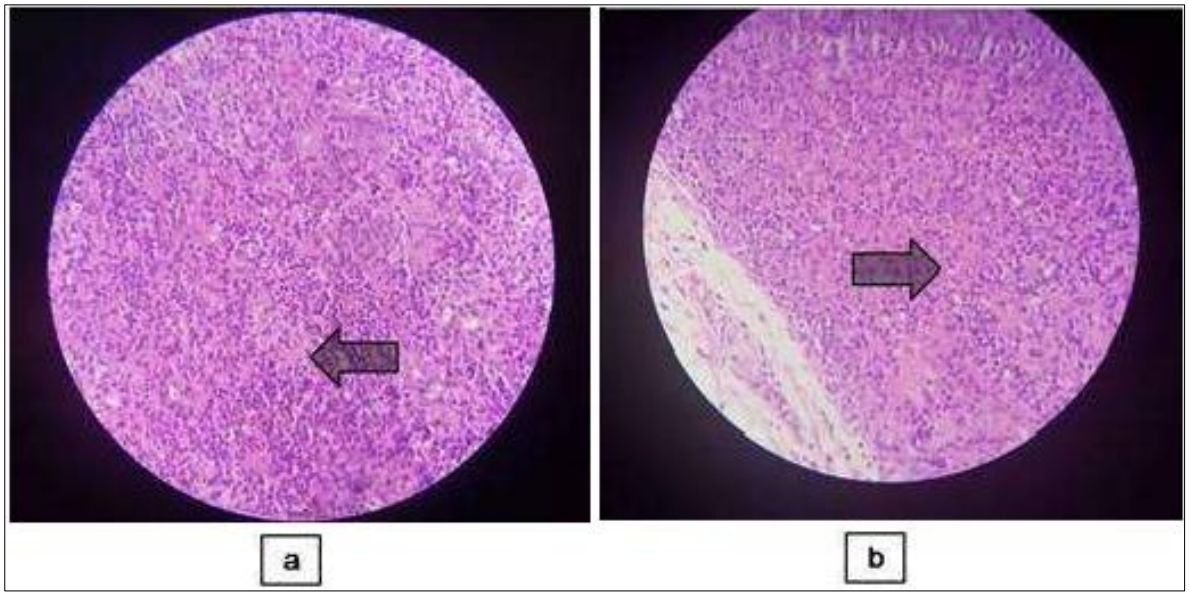

Fig 1: Images of the patient's biopsy of the eyelid nodules. a and b. Granuloma formation with aggregates of epithelioid histiocytes (arrow) surrounded by chronic inflammatory cells

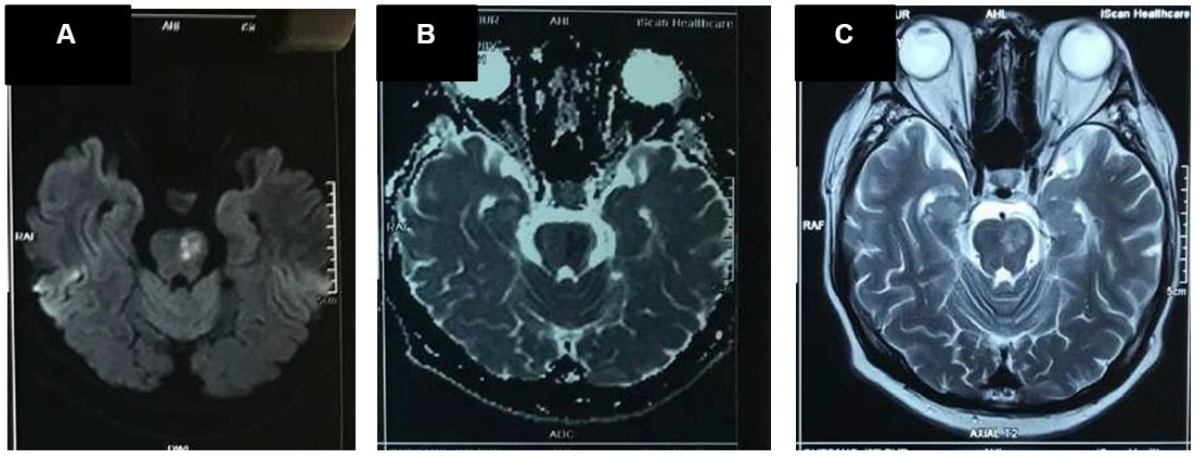

Fig 2: Cranial MRI at the time of evaluation showing subacute infarction in the left paramedian pons. A. diffusion weighted imaging (DWI), B. apparent diffusion coefficient (ADC), C. T2 weighted fluid attenuated inversion recovery (T2-FLAIR)

Discussion

Majority of strokes due to neurosarcoidosis in literature have occurred in young people. The most typical presentation is strokes due to occlusion of small or medium-sized arteries, although large cerebral arteries can also be involved [1]. Although transient ischemic attacks (TIAs) and strokes rarely develop in patients with neurosarcoidosis, pathologic studies show evidence of vascular involvement. Parenchymal granulomas invade blood vessel walls, with vasculitic disruption of the media and internal elastic lamina. Panarteritis often leads to thrombosis, granulomatous vessel stenosis or occlusion, clearly associated with small brain infarcts [2]. Despite these pathological findings, the low incidence of neurovascular complications in neurosarcoidosis is intriguing [4]. Vasculitis preferentially involves vessels the caliber of perforating arteries, which explains why— as seen in our patient—cerebral angiography is usually normal in neurosarcoidosis [7]. Three types of arterial pathology have been described: granulomatous angiopathy, granulomatous arteritis and fibrinoid necrosis of the wall [8]. Reported abnormalities in fibrinolysis and coagulation include decreased protein C and increased tissue thromboplastin and factor VII activities. Increased thrombin-activatable fibrinolysis inhibitor and decreased plasminogen activator activities were also noted. These observations provide additional explanations for the development of cerebral infarction in neurosarcoidosis. The discrepancy between the frequent neuropathological findings of vasculopathy and the rarity of clinical stroke in neurosarcoidosis may reflect the chronic nature of the inflammation [2].

Treatment aims to suppress inflammatory activity, allowing for neurological recovery while also preventing further relapse. No randomized controlled trials guide optimal treatment of neurosarcoidosis, so treatment options are based on previous case series and extrapolation of results from trials in systemic sarcoidosis [5]. Although corticosteroids are usually highly effective and are considered the mainstay of treatment for symptomatic neurosarcoidosis, long-term use is limited by many potential adverse effects. Treatment with other forms of immune-modulating drugs can shorten exacerbations and alleviate

symptoms. Combination therapy with corticosteroid-sparing agents is therefore recommended early in patients with significant central nervous system (CNS) involvement to reduce risk of relapse on steroid weaning [5]. Examples of adjunct or alternative drugs include methotrexate, cyclophosphamide, azathioprine, cyclosporine, mycophenolate mofetil, and chlorambucil. Since TNF-a plays a central role in both sarcoidosis- associated inflammation and inflammation-associated thrombogenicity, agents that specifically decrease TNF-a activity may also be considered for cases that progress despite first- line therapy. One such medication is pentoxifylline which inhibits TNF-a production from macrophages. Other agents include thalidomide and infliximab [2]. However, adverse effects such as infection and allergic reactions can limit the use of TNF-a antagonists [5].

It is prudent to address all applicable stroke risk factors to treat patients. Clinicians should attend to features that may point to its diagnosis, including young age, leptomeningeal involvement, and evidence of extra-neurological involvement. As more progress is being made in understanding the pathogenesis of neurosarcoidosis and stroke, it is recommended that further investigation be done for acute treatment strategies and additional preventative regimens. In sarcoidosis, stroke is associated with a high risk of permanent neurological impairment (up to 50% of patients) and a high mortality rate (23%). Relapses are common and require effective and likely prolonged courses of treatment [9].

Conclusion

In summary, we have presented a rare occurrence of ischemic stroke in an equally rare disease, neurosarcoidosis. A positive response to novel oral anticoagulants on top of immunosuppressants improved the patient's clinical outcome. While not seen seen in this present case, cerebrovascular events may be the first manifestation of neurosarcoidosis.

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