

Moyamoya Angiopathy Presenting with Cerebrovascular Stroke post-COVID-19 Vaccination

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Abstract Despite being uncommon, thrombotic complications from COVID-19 vaccinations that cause cerebrovascular events have been extensively studied. Moyamoya angiopathy (MMA) is a progressive intracranial vasculopathy that is responsible for causing recurrent strokes. This report analyzes a case of cerebrovascular stroke post-COVID-19 vaccination (inactivated-Sinovac) in a middle-aged Asian female. The patient was administered two doses of Sinovac, followed by one dose of the Pfizer vaccine, which led to the diagnosis of Moyamoya disease. The report aims to study MMA in a patient exhibiting exacerbated symptoms post-vaccination, thereby forming a basis for research regarding the safety of COVID-19 vaccinations in patients with pre-existing intracranial vasculopathy. Although such a correlation may not necessarily imply causality, caution must be exercised till future robust observations are obtained, especially considering the possibility of a shared inflammatory pathophysiological foundation between MMA and COVID-19 vaccinations.

Keywords: *moya moya, vaccination, stroke, COVID-19, angiopathy*

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1. Introduction

An increased incidence of thrombotic events, including stroke, has been reported in patients with coronavirus disease (COVID-19), although the characteristics and outcomes of the patients who experienced strokes are not adequately known. There has been evidence of a higher incidence of thrombotic events, including stroke, in COVID-19 patients; however, there is insufficient information available regarding the patient characteristics and outcomes of patients who experienced strokes.

Since the beginning of the epidemic, there have been numerous reports about the potential for stroke and cerebrovascular disease to exacerbate SARS-CoV-2 infection. Scientists, regulators, and governments worldwide have worked together to speed up the development of multiple SARS-CoV-2 vaccines. [1].

One of the most important developments and breakthroughs in the fight against the pandemic was the creation of vaccines against SARS-CoV-2. However, as our knowledge of the side effects of vaccines continues to expand, many cerebrovascular events in close temporal association with vaccinations are being reported.

Moyamoya angiopathy (MMA) is an uncommon, chronic condition that is characterized by the progressive narrowing of the intracranial portion of the internal carotid artery (ICA), or proximal anterior cerebral artery (ACA),

and/or middle cerebral artery (MCA). At the base of the brain, it is accompanied by the formation of aberrant collateral vessels, which usually resemble a "puff of smoke." [2]. It has been suggested that an inflammatory state initiates and enhances the changes that MMA exerts on the cytokine pathways [3].

MMA is a type of vasculitis brought on by immune-mediated vascular injury and inflammatory response through anti- and pro-inflammatory mediators. Anti-inflammatory mediators - such as IL-4, IL-10, IL-13, IFN- α , and TGF- β - lead to acute aggravation of MMA by affecting vascular reactivity and auto-regulation. Meanwhile, pro-inflammatory mediators - such as IFN- β , IFN- γ , TNF- α , IL-1, and IL-6 - influence the initiation, often causing severe and sudden progression of MMA. Pro-inflammatory mediators activate the RNF-dependent signal transducing pathway. Therefore, in genetically predisposed patients, any acute systemic inflammatory response will likely result in intimal vascular smooth muscle cell hyperplasia, which narrows the lumen and causes neovascularization by rapidly increasing endothelial cells. In a study by Das et al., 64.3% of MMA patients with COVID-19 infection had worsening neurological symptoms. [4].

We herein report the case of a middle-aged female patient who suffered from acute ischemic stroke; she was later diagnosed with MMA. We observed neurological symptoms occurring in close temporal association with the Pfizer vaccine preceded by the Sinovac vaccination.

2. Case Presentation

The patient was a 43-year-old Pakistani female with a past medical history of HTN. She presented to our neurology clinic in June 2022 for further workup and evaluation, having visited a hospital two days prior for the sudden onset of left facial deviation with speech difficulty and a tingling sensation in the left arm. The symptoms continued for a few minutes and then subsided completely (transient ischemic attack).

Additionally, the patient history suggested a sudden onset of speech difficulty three months prior to visiting our hospital that continued for a few days. In March 2022, before developing these symptoms, the patient received a third dose of the COVID-19 vaccination (Pfizer). Additionally, she received the first two doses of the Sinovac vaccine on May 30, 2021, and July 1, 2021, respectively. An MRI of her brain was conducted, and the patient was diagnosed with acute ischemic stroke, for which she was evaluated and treated.

3. Physical Examination

The neurological examination was normal, and no focal neurological deficits were found.

4. Investigations

We evaluated the case extensively for secondary causes. The complete blood count – including platelet count, erythrocyte sedimentation rate (ESR), serum electrolytes, blood sugar, and lipid profile – was normal, as was the C-reactive protein level. Anti-nuclear antibody (ANA) and vasculitis screen were negative, including anti-phospholipid antibodies, p-ANCA, c-ANCA, and lupus anticoagulant. Thyroid function tests and coagulation profile were normal, and screening for hyper-coagulable state was negative. Chest X-ray, electrocardiogram, and echocardiography were also normal. Carotid Doppler ultrasound showed no significant stenosis. The work-up revealed no potential source for thrombo-embolism.

Follow-up revealed that the patient was stable on medications with no neurological problems at that time.

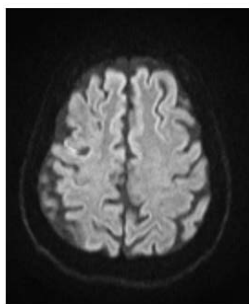


Figure 1A

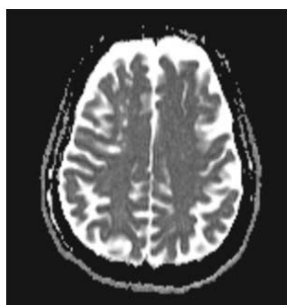


Figure 1B

Figure 1A and 1B. Magnetic resonance imaging (MRI) of the brain revealed diffusion-weighted image (DWI) hypointense signal in the high right frontal region with corresponding changes in apparent diffusion coefficient (ADC) as chronic infarction.

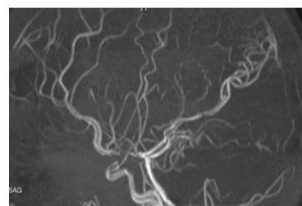


Figure 2A



Figure 2B

Figure 2A and 2B. Magnetic resonance angiography (MRA) revealed irregularities in the small bilateral cavernous part of the internal carotid artery in both calibers. It also showed a narrowing proximal left middle cerebral artery with collateral vessel formation suggestive of Moyamoya angiopathy.



Figure 3A



Figure 3B

Figure 3A and 3B. Magnetic resonance angiography (MRA) revealed irregularities in the small bilateral cavernous part of the internal carotid artery in both calibers. It also showed a narrowing proximal left middle cerebral artery with collateral vessel formation suggestive of Moyamoya angiopathy.

5. Discussion

An estimated 1.4% of COVID-19 cases suffered from strokes. Thus, COVID-19 infection has been observed to be a risk factor for stroke. The major mechanisms implicated are hypercoagulability, vasculitis, and cardiomyopathy. Compared to COVID-19 infection, the adverse cerebrovascular effects seen with COVID-19 vaccinations are much less. Among the several reported cases of vaccine-associated cerebrovascular events, cerebral venous sinus thrombosis appears to occur more frequently than arterial stroke [4].

Though arterial stroke following COVID-19 vaccination has been documented, it is rare. However, it may not be so uncommon in cases that are genetically predisposed to or have pre-existing vasculopathy. MMA has been intensively studied in terms of inflammatory pathophysiology in genetically predisposed patients, thereby leading to progressive vaso-occlusive disease. According to a few documented reports, COVID-19 infection enhances MAA symptoms. Thus, based on the inflammatory etiopathogenesis of MAA, it can be extrapolated that COVID-19 vaccinations can similarly have an effect on the symptoms associated with MMA. These case reports form the basis for further research on the complex interplay of COVID-19 vaccinations and neurological destabilization in patients having vasculopathy of inflammatory pathophysiology [5].

As proposed earlier, the aberrant inflammatory pathway activation due to vaccines can probably influence these down-signaling pathways, thus leading to similar aggravation of Moyamoya symptoms.

Previous studies have noted the occurrence of strokes following varicella and influenza vaccination, and it was anticipated that, like their natural infections, these vaccines, too, can lead to intracranial angiopathy resulting in narrowing and occlusion of vessels and resultant ischemic stroke [5].

A similar mechanism could be involved in other vaccines, causing a hypercoagulable state leading to thromboembolism. Therefore, more data is needed to establish the precise correlation between COVID-19 vaccinations and cerebrovascular events.

6. Conclusion

Currently, there is no proven association between cerebrovascular accidents and COVID-19 vaccinations. Furthermore, the available data has limitations like under-reporting, differential reporting, and non-reported or undiagnosed concomitant COVID-19 infection. These

factors preclude establishing a cause-effect relationship. Therefore, additional research in the form of controlled studies is required to establish an accurate relationship between COVID-19 vaccinations and cerebrovascular accidents.

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