

Adult Moyamoya Syndrome as A Manifestation of Varicella-Associated Cerebral Vasculopathy: A Case Report

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ABSTRACT

Moyamoya disease (MMD) is a rare cerebrovascular disorder characterized by progressive large intracranial artery narrowing and development of small vessel collaterals. Moyamoya syndrome (MMS) refers to the angiographic findings of MMD with predisposing medical conditions. Varicella-associated cerebral vasculopathy (VACV) is a severe complication of varicella zoster virus (VZV) infection and its association with MMS is rare in adult. We report on a case of a 55-year-old lady who presented with progressively worsening dysphasia and left lower limb weakness following a week of right herpes zoster ophthalmicus infection. The initial Magnetic Resonance Imaging (MRI) of brain demonstrated features of encephalitis with micro abscesses. Her serial repeated MRI brain imagings subsequently demonstrated worsening of cerebral infarctions with right internal carotid artery stenosis and basal ganglia collaterals suggestive of Moyamoya vasculopathy. This case highlights the rare association of VACV with MMS and should be considered as a potential serious complication in patients with VZV infection.

Keywords

Hemiparesis, Moyamoya syndrome, Varicella zoster

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INTRODUCTION

Moyamoya disease (MMD) is a unique, rare cerebrovascular condition characterized by progressive steno-occlusive disease at the terminal portions of the bilateral internal carotid arteries and their proximal branches with prominent collateral artery formation.¹ The latter has a smoky characteristic appearance on angiography and hence named 'moyamoya', a Japanese word which means puffy. It was first described in 1957 and was later termed in 1969 by Suzuki and Takaku.¹

The aetiology is unknown² and it is found to be commoner among the Asians though cases have been reported around the world.¹ Moyamoya syndrome (MMS) on the other hand is referring to the moyamoya-like vasculopathy with associated underlying diseases. These include various conditions which can be causative or syndromic such as atherosclerosis, meningitis, brain tumours, neurofibromatosis type 1, systemic lupus

erythematosus and thyroid diseases.² Both MMS and MMD may manifest in two types of clinical presentations; ischemic and haemorrhagic.² Among the Asian population, MMS is commoner in the adult whereas the latter is commoner in children.² Varicella zoster virus infection has been reported in the past as one of the precipitating factors in MMS. Nonetheless, varicella-associated cerebral vasculopathy (VACV) with moyamoya vasculature is very rare and there are currently three cases reported in adults.³ Herein, we intend to report on a case of adult MMS as a severe complication of VACV.

CASE REPORT

Our patient was a 55-year-old lady who had the comorbidities of long-standing diabetes mellitus, hypertension, dyslipidaemia and non-toxic multinodular goitre. Her diabetes mellitus was poorly controlled with a

recent Haemoglobin A1c (HbA1c) of 11.2%. She was otherwise an independent housewife. She initially presented to us with a two-week history of progressive left-sided limb weakness. There was no history of constitutional symptoms or fever. Her initial contrast-enhanced Computed Tomography (CT) brain imaging at presentation showed multiple non-enhancing brain lesions with involvement of corpus callosum. She was then started on antiplatelet therapy with a higher dose of statin. She was brought to the Emergency Department by their family members after a month due to worsening limb weakness and a change of behaviour. She was noted to be less talkative and active. There was also a one-week history of rash with blistering lesions over the right forehead and eyelid. Clinically, she was mute with dense hemiparesis over the left limbs.

On examination, there was right periorbital oedema with dermatomal distribution of erythematous, scaly lesion over the trigeminalophthalmic nerve distribution (Figure 1). A diagnosis of right herpes zoster ophthalmicus was made and she was started on topical as well as intravenous acyclovir therapy. She underwent Magnetic Resonance Imaging (MRI) of the brain which showed a serpiginous peripherally enhancing lesion extending from the right side of the vertex until the right side of the corpus callosum, with minimal crossover towards the contralateral side. A separate but similar looking lesion at the right frontal white matter region with abnormal fluid-attenuated inversion recovery (FLAIR) hyperintense signal within the ependymal lining.

The initial findings of MRI were suggestive of encephalitis with presence of micro abscess. MR Angiography (MRA) showed no signal observed from the C4 segment of right internal carotid artery (ICA) with M1 segments of both middle cerebral arteries appeared small in calibre. Her cerebrospinal fluid (CSF) analysis demonstrated lymphocytosis which was further suggestive of viral encephalitis; protein 0.94 g/L (0.15-0.45 g/L), glucose 4.3 mmol/L (2.2-3.9 mmol/L) with CSF glucose to serum ratio of 0.49, neutrophil count 0/uL and lymphocyte count 50/uL.

An initial diagnosis of brain abscess due to varicella zoster virus infection was made. She was observed to have dynamic clinical progress during her hospital admission. Her limb weakness remained at power of 0 out of 5 over the left side. However, her Glasgow Coma Scale (GCS) fluctuated between 9 to 15. These were due to the verbal components; she was mute at most times, stuttering some times and had perseveration of speech at times. The latter two could be the manifestations of frontal lobe lesions. She underwent serial MRI brain imagings to assess her clinical progress which was however showing worsening cerebral infarctions. Nonetheless, the infection resolved. The right ICA, middle cerebral artery (MCA) and posterior cerebral artery (PCA) appeared small in caliber with presence of multiple collateral vessels. These findings were summarized in Figure 2, 3 and 4.

A diagnosis of moyamoya syndrome precipitated by varicella zoster virus infection was made. In view of her comorbidities, the pharmacological therapy was opted rather than a surgical approach. She completed six weeks duration of acyclovir therapy and was started on tablet clopidogrel 75mg and atorvastatin 40mg daily. She was followed up in the outpatient clinic whereby she received multidisciplinary team engagement. She demonstrated clinical improvement in her cognition with residual mild to moderate dysphasia and left hemiplegia.



Figure 1: Herpes zoster rash at presentation with (a) ophthalmic branch of trigeminal nerve and (b) nasociliary branch involvement which innervated cornea, lateral dorsum and tip of the nose (Hutchinson's sign)

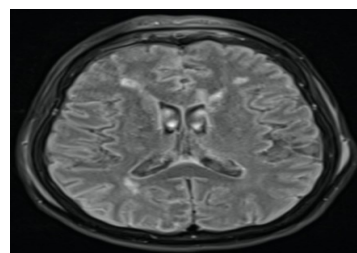


Figure 2: MRI brain in axial FLAIR sequence at presentation showed generalized hyperintensities along the gyri suggestive of Ivy sign.

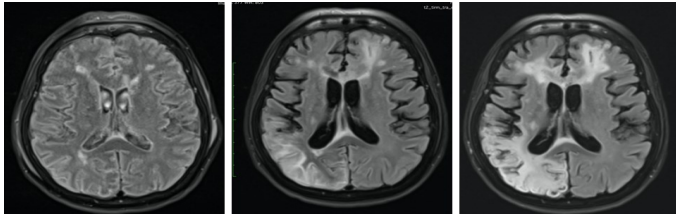


Figure 3: MRI brain in FLAIR sequences at (a) initial presentation, (b) one month and (c) two months follow-up showed progressive and extensive abnormal hyperintense signals predominantly on the right side of the brain parenchyma.

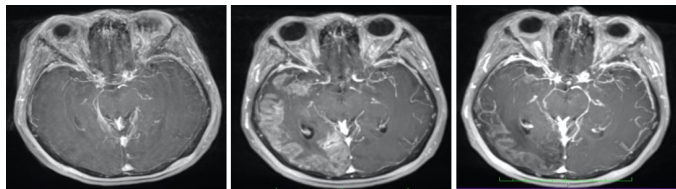


Figure 4: MRI brain in multiplanar reformation (MPR) axial section post contrast T1-weighted images (a) at presentation, (b) at one month and (c) at two months follow-up. The yellow arrows showed small caliber of both MCA with multiple collateral vessels.

DISCUSSION

We report the rare case of adult MMS secondary to varicella zoster virus infection. VZV has varieties of manifestations ranging from encephalitis to aneurysms and the cases are underreported.⁴ Historically, the earliest cases of VZV dated back in 1959 and in 1974, where Gordon et al. reported severe stenosis of carotid siphon on the angiographic study following ipsilateral herpes zoster ophthalmicus in a case of hemiplegia.^{5,6}

MMS is a unilateral disease as opposed to MMD which tends to have bilateral involvement. However, the contralateral side is usually eventually involved in 40% of the cases.⁷ The underlying pathophysiology remains unknown and the vessel occlusion described in MMS is likely due to luminal thrombosis combined with smooth muscle cells hyperplasia.⁴ Hougin et al. proposed double hit theory for MMS.

In predisposed individuals, a trigger-like infection or immune disorder will result in inflammation with subsequent cerebral vessels' narrowing.⁸ ICA stenosis may persist and vessel remodeling may continue following the trigger.⁴ While luminal narrowing mostly resolves with treatment of VZV, the ICA stenosis may remain with moyamoya vasculature remodeling in susceptible patients.⁸

Moyamoya is essentially diagnosed by a combination of clinical and radiographic findings with angiography has been the criterion standard investigation.⁹ This disease carries a high impact to the patients albeit the rarity with progressive neurological deficits (sensorimotor, speech and cognitive) and physical disabilities. As for other rare diseases, the diagnosis can be missed by incomplete work-ups and absence of suspicion such as during acute stroke presentation in the emergency setting or in asymptomatic cases.¹⁰ The lack of information on the disease natural history and pathophysiology contributes to the heterogeneity and uncertainties in patient management.¹⁰ The available treatment strategies are shared between MMD and MMS and they consist of surgical as well as pharmacological surgical stroke prevention therapy with combination of symptomatic drugs.

Treatment strategies are based on the physicians' or surgeons' experiences as well as center tools.¹⁰ To date, there is no available curative therapy to regress the occlusive arterial lesions. In selected patients, revascularization surgical therapy is recommended. Antiplatelet therapy has been shown by recent Japanese studies to effectively improve cerebral perfusion in symptomatic adult patients with ischaemic moyamoya angiopathy.¹⁰ Cilostazol was associated with a more significant reduction of mortality as compared to other antiplatelet agents. The use of antithrombotic strategies in acute setting has limited recommendation due to the increased risk of haemorrhage and mortality. MMS is associated with considerable morbidity though disputable and aggressive treatment is imperative.

CONCLUSION

VZV with Moyamoya vasculature is a serious yet rare complication of VZV infection. Insufficient awareness among healthcare providers about the disease entity results in notably delayed or incorrect diagnosis and inappropriate management. Due to its progressive nature of MMS, early suspicion and prompt diagnosis as well as management are crucial to improve the patients' clinical outcome.

REFERENCES

1. Li J, Jin M, Sun X, et al. Imaging of Moyamoya Disease and Moyamoya Syndrome: Current Status. *J Comput Assist Tomogr.* 2019;43(2):257-263. doi:10.1097/RCT.0000000000000834
2. Dou Z, Chen H, Cheng H, Liu G. Moyamoya syndrome after bacterial meningitis. *Pediatr Investig.* 2018;2(2):134-136. doi:10.1002/ped4.12048
3. Husari K, Sguigna P, Shang T. Adult Moyamoya Syndrome Caused by Varicella Zoster Virus Infection: A Case Series (P6.251). *Neurology.* 2017;88 (16 Supplement):P6.251. http://n.neurology.org/content/88/16_Supplement/P6.251.abstract
4. Kumar S, Pillai S V. Moyamoya syndrome as a manifestation of varicella-associated cerebral vasculopathy-case report and review of literature. *Child's Nerv Syst.* 2019;35(4):601-606. doi:10.1007/s00381-019-04091-6
5. Amlie-Lefond C, Gilden D. Varicella Zoster Virus: A Common Cause of Stroke in Children and Adults. *J Stroke Cerebrovasc Dis.* 2016;25(7):1561-1569. doi:10.1016/j.jstrokecerebrovasdis.2016.03.052
6. Nagel MA, Jones D, Wyborny A. Varicella zoster virus vasculopathy: The expanding clinical spectrum and pathogenesis. *J Neuroimmunol.* 2017;308:112-117. doi:10.1016/j.jneuroim.2017.03.014
7. Yeo LLL, Söderman M, Cornelissen SA, Bhogal P, Steinberg A, Andersson T. Angioplasty and stenting of adult onset Moya-moya disease. *Interdiscip Neurosurg Adv Tech Case Manag.* 2019;15:60-65. doi:10.1016/j.inat.2018.10.013
8. Houkin K, Ito M, Sugiyama T, et al. Review of Past Research and Current Concepts on the Etiology of Moyamoya Disease. *Neurol Med Chir (Tokyo).* 2012;52(5):267-277. doi:10.2176/nmc.52.267
9. Sharma A, Soneji N, Farah G. Clinical and angiographic findings in moya moya. *Am J Case Rep.* 2014;15:147-151. doi:10.12659/AJCR.890222
10. Canavero I, Vetrano IG, Zedde M, et al. Clinical management of moyamoya patients. *J Clin Med.* 2021;10(16):1-20. doi:10.3390/jcm10163628