Dear Editor,

Symptomatic carotid disease with more than 50% stenosis usually causes neurological symptoms in the form of minor stroke or transient ischaemic attacks in the ipsilateral anterior circulation territory and the most common location of plaque is in the carotid bifurcation and proximal internal carotid artery (ICA).\(^1\) The mechanism of stroke is an artery to artery embolism, thrombosis or hemodynamic fluctuations. Azygos anterior cerebral artery (AACA) is a variant of Willisian circle anatomy characterised by absence of the anterior communicating artery (ACom) and the bilateral anterior cerebral arteries (ACAs) join to form a single trunk which travels superiorly in the interhemispheric fissure and has implications in the arterial haemodynamics. We report a case of left ACA territory infarction caused by right ICA stenosis in a patient with azygous ACA.

**Case Report**

A 55-year-old gentleman with past history of hypertension and dyslipidaemia for the last 5 years, poorly compliant to treatment, with acute onset right-sided weakness of predominantly lower limb along with speech disturbance, presented outside the window period. On examination, the patient had apathy, global aphasia, right upper motor neuron facial weakness and right-sided weakness predominantly in the lower limb. CT brain at admission showed evolved infarct in the left ACA territory involving the left parasagittal frontal lobe [Figure 1]. CT angiogram showed right ICA hypodense plaque causing about 80% stenosis at origin and azygous ACA with occlusion of the left division of azygos ACA [Figure 1]. Cardiac evaluation including 2D-echo and 24 hours Holter monitoring were normal. MR plaque imaging of the right ICA plaque showed lipid-rich core without any ulceration or intraplaque haemorrhage. The patient was managed with dual antiplatelets, statins and antihypertensives. In view of the symptomatic right carotid stenosis, carotid revascularisation was considered. Over the next 1 month, the patient improved to NIHSS of 9 and modified Rankin scale of 3. He is planned for right carotid endarterectomy.

**Discussion**

Anterior circulation comprises of ACA and middle cerebral

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artery (MCA) formed from ICA. The ACAs are connected by the ACom which is a primary collateral along with the posterior communicating artery in cases of occlusions or stenosis in the vascular network. Arteria termatica or AACA was first described by Wilder with a reported incidence of less than 2%. AACA is characterised by A1 segments of bilateral ACAs joining to form a single stem (A2 segment) which ascends in the interhemispheric fissure as a result of the persistence of the embryonic median artery of the corpus callosum. The anatomical variations in the ACA were described by Baptista. Type I anomaly is the true azygos ACA, from which ACA branches supply both hemispheres. Type II anomaly is the bihemispheric ACA, where both right and left ACA are present, but most of the major branches to the bilateral hemispheres arise from one ACA and the other one is rudimentary. In type III, an accessory ACA arises from Acom. Our patient had a Type I anomaly.

The left ACA territory infarct could be explained by right ICA stenosis due to the coexistent true azygos ACA with probable embolisation from the right ICA plaque as the mechanism causing the infarct and thus the aetiology of stroke is large artery atherosclerosis. In a patient with high-grade carotid stenosis, with infarct in the opposite hemisphere, carefully analysing the vascular anatomy may give a clue to the aetiology which can help in the management of the patient.

**Conclusion**

AACA is a rare variant, which can produce unilateral or bifrontal infarctions. The anatomical variations in the ACA should be carefully looked into in cases of ACA territory strokes that affect the arterial haemodynamics and a proper etiological evaluation aids in the optimal management of the patient.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Acknowledgements**

We thank Mr. Krishnakumar N for his assistance in obtaining high quality images.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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Submitted: 26-Apr-2021   Accepted: 06-Aug-2021   Published: 13-Jan-2022

MTHFR Deficiency: A Potentially Treatable Cause of Adult-Onset Hereditary Spastic Paraparesis

Dear Editor,

A 27-year-old man born out of nonconsanguineous parentage [Figure 1: Pedigree chart] with normal developmental history presented with history of insidious onset, slowly progressive spastic paraparesis for the past 3 years. At the onset, he noticed difficulty in getting up from squatting position, which was associated with stiffness of lower limbs. One year into the illness, he noticed difficulty in walking especially on uneven surfaces with history of slippage of footwear with awareness. There was no associated sensory, upper limb, bowel, bladder, or cranial nerve involvement or cognitive decline. There was no history of similar symptoms in the family. Physical examination revealed grade 1+ spasticity and exaggerated deep tendon reflexes involving both lower limbs.

Magnetic resonance imaging (MRI) brain revealed symmetric T2/FLAIR hyperintensity involving periventricular and deep white matter of bilateral posterior parietal region [Figure 2]. MRI cervicodorsal spine was normal. Possibilities of infective, noninfective inflammatory metabolic myelopathies, genetic and degenerative leukoencephalopathies were considered. Nerve conduction studies and visual evoked potentials were normal. Routine hematological and biochemical blood tests were normal, as were levels of serum cortisol, vitamin B12, and folate. VDRL and HIV were nonreactive. ANA and ENA profile were negative. Fasting plasma homocysteine levels were significantly elevated (136.25 µmol/L; normal 3.3–11.3) with normal methionine levels (5.917 µmol/L; normal 5 to 75). Urine for gas chromatography and blood liquid chromatography and mass spectrometry were normal. Next generation sequencing was ordered with suspicion of Hereditary Spastic Paraparesis (HSP)/Leukodystrophy which showed mutations of MTHFR gene on exome 11 (c.1671_1672dupTG) and exome 3 (c.459C>G), clinching the diagnosis of Homocystinemia due to MTHFR deficiency. Genetic testing in the parents revealed the former mutation in the mother and the latter in the father. The patient was started on oral vitamin B12 1500 mcg/day, folate and pyridoxine supplementation, with some symptomatic improvement.

5,10-Methylenetetrhydrofolate reductase (MTHFR) deficiency is a rare, autosomal recessive, potentially treatable metabolic disorder that usually manifests in the childhood, but can present in adulthood very rarely. Hypomethioninemia may decrease global methylation reactions in the central nervous system, hence possibly affecting myelin, as attested by white matter abnormalities often found in cerebral MRIs of these patients. In a case series of 24 patients with adolescent/adult-onset MTHFR deficient patients, the mean age of onset was 22.4 ± 12.1 years. At presentation, gait disturbances (46%) were the most common symptom followed by epilepsy (29%), cognitive decline (21%), psychosis (12%), encephalopathy, and stroke (4% each). The mean homocysteine was 177.3 ± 49.5 micromol/L. Although severe hyperhomocystenemia, often associated with hypomethyoninemia, helps in suspicion of this disease, confirmation of the disease requires genetic analysis. However, there is usually a significant delay from onset to diagnosis (mean 5.75 years). Although radiology might help in early diagnosis, they aren't specific for any particular disease. The most common radiology finding was white matter abnormalities seen in 70% of patients in

Figure 1: Pedigree Chart

 DOI: 10.4103/aian.aian_307_21