CASE REPORT

An unusual aetiology for internuclear ophthalmoplegia

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Dr Ihtsham ul Haq,
ihq@wakehealth.edu**SUMMARY**

Typical causes of internuclear ophthalmoplegia (INO) include arterial infarcts, demyelinating conditions, inflammation and trauma. We here report the unique case of a 33-year-old man with INO of the right eye caused by infarction of the right midbrain, confirmed by diffusion-weighted MRI. At presentation he displayed impaired adduction of the right eye with normal movement of the left. CT angiogram revealed an underlying developmental venous anomaly (DVA), raising the concern of venous infarction. His symptoms improved with aggressive management of blood pressure and risk factors. The patient had vascular risk factors—smoking, hypertension and dyslipidaemia—and we theorise that the hyalinised and inelastic walls of our patient's DVA were more vulnerable to the thrombogenic effects of his risk factors, predisposing him to this event. Venous infarcts owing to DVA are rare. To our knowledge INO secondary to venous infarct has not been reported, and should be considered in the differential of such cases.

BACKGROUND

Arterial infarcts and central nervous system demyelinating conditions like multiple sclerosis are relatively common events, and are the most frequently identified underlying aetiologies in internuclear ophthalmoplegia (INO).^{1–2} By contrast, a developmental venous anomaly (DVA) is a generally benign vascular malformation that rarely occurs in the brainstem and rarely leads to infarction.³ Our patient developed a unilateral right INO owing to ipsilateral infarction in the right midbrain in the region of a DVA, a previously unreported event in the literature.

Diagnosing DVA and venous infarctions poses a diagnostic challenge. They can have heterogeneous imaging characteristics, leading to misdiagnosis as tumours or demyelinating diseases and to unnecessary biopsies with the attendant negative effects on patient care and outcome.^{4–6} This case suggests that venous infarction secondary to DVA may be an additional aetiology for brainstem ischaemia, and considered in the differential diagnosis, even in the absence of known hypercoagulable or inflammatory states.

CASE PRESENTATION

A 33-year-old Caucasian man with a medical history of well-controlled chronic migraines (2–3/year) and hypertension presented with acute onset of diplopia. He took an oral dose of sumatriptan after he had developed diplopia, assuming it could be due to his migraine. He denied any headache,

focal weakness, dysarthria, facial droop, numbness, paresthesias or loss of consciousness. He was taking verapamil 240 mg once daily for his migraine prophylaxis and sumatriptan 50 mg as needed for abortive treatment of his migraine headaches. At presentation he had diplopia with left gaze so that he preferred to look to his right. In primary gaze his right eye was down and out. Convergence was preserved. Examination of his extraocular movements revealed only impaired adduction of the right eye and slow saccades in the right eye upon adduction compared with the abducting left eye. There was no nystagmus of the left eye upon abduction. The remainder of his eye movements was normal. There was no right-sided ptosis and his pupils were symmetric and reactive to light. Funduscopy was normal as was the remainder of the rest of the cranial nerve exam. He displayed normal strength, normal sensation, normal deep tendon reflexes with bilateral flexor plantar responses and normal coordination. His initial CT scan of the head was normal and he was admitted to the hospital for further workup.

On the day after admission the patient's eye was no longer out and down. His diplopia had mildly improved but he continued to compensate by tilting his head to the right. He had impaired adduction of the right eye and slow compensatory saccades in the right eye upon adduction consistent with INO.

His medical history was significant for chronic migraine and hypertension. He had dyslipidaemia in the past, with hypertriglyceridaemia in the range of 215–237 mg/dl and hypercholesterolaemia ranging from 156 to 165 mg/dl. High-density lipoprotein (HDL) and low-density lipoprotein were within normal limits. He was not receiving treatment for his hypertriglyceridaemia at presentation.

His family history was significant for: multiple family members with hypertension and type 2 diabetes mellitus, migraine and hypertension in his mother, a paternal grandmother with multiple myeloma and a paternal grandfather with three myocardial infarctions. The patient smoked one-half pack of cigarettes per day and drank beer or wine three times a week.

INVESTIGATIONS

On admission he had an MRI of the brain performed, which showed restricted diffusion in the midbrain (figure 1A) at the level of CNIII with corresponding hypointensity on the apparent diffusion coefficient sequence (figure 1B), consistent with an acute infarction. A vascular structure was identified

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Figure 1 (A) Axial diffusion weight imaging sequence, showing bright signal in the right midbrain. (B) Corresponding apparent diffusion coefficient sequence showing hypointense lesion in the right midbrain. (C) Axial T2 sequence, showing venous anomaly in the right midbrain. (D) Axial T1 postcontrast sequence, demonstrating the venous anomaly in the right midbrain.

adjacent to this region on axial T2 (figure 1C) and postcontrast T1 MRI (figure 1D). CT angiogram of the head further characterised this finding, demonstrating the presence of tiny right midbrain intraparenchymal venous structures (caput medusa) in the region of the right oculomotor nucleus, draining into a prominent collector vein coursing along the right cerebral peduncle, which in turn drained into the superficial venous drainage (figure 2), consistent with a DVA. Further workup included a normal transthoracic echo, transcranial Doppler and carotid ultrasound. Serum blood work revealed an HbA1C of 5.7, C reactive protein of 1.6, triglyceride level of 215 and HDL of 40.

Figure 2 CT angiogram of the head demonstrating the presence of subtle tiny right midbrain intraparenchymal venous structures (caput medusa) in the region of the right oculomotor nucleus, draining into a prominent collector vein coursing along the right cerebral peduncle, which in turn drained into the superficial venous drainage.

Lipoprotein(a) levels were normal. His thyroid-stimulating hormone level was normal. Testing for Factor V Leiden and Factor II 20210 mutations returned negative. A urine drug screen did not show evidence of drug use.

DIFFERENTIAL DIAGNOSIS

Multiple sclerosis and arterial infarcts are the most common causes of INO, but the MRI did not support these diagnoses. Trauma, infection and tumour are other potential causes of INO but were inconsistent with the history and imaging. A CT angiogram was performed to look for vasculitis, but showed only the venous infarct secondary to DVA seen on the MRI. Cavernous angioma could be another consideration in the differential diagnosis; however, there were no characteristic imaging findings on the MRI and CT angiogram as described in the discussion below. The rest of the brain imaging did not reveal features suggestive of small vessel arterial disease.

TREATMENT

On admission the patient's blood pressure ranged between 140 and 160 mmHg systolic. His sustained release verapamil was increased from 240 to 360 mg. After this dose increase his systolic blood pressure ranged between 130 and 140 mmHg. Low-dose aspirin 81 mg once daily was initiated. He declined statin therapy, instead choosing to try lifestyle and dietary modification first for his dyslipidaemia.

OUTCOME AND FOLLOW-UP

During admission the patient's symptoms improved with the management of his blood pressure. On discharge he was instructed to pursue stroke risk reduction: smoking cessation, blood pressure control, life style/dietary modification, and to avoid the use of triptans for his migraines.

DISCUSSION

We believe that the ocular deficits in our patient can be explained by a right-sided unilateral INO. He did not have any other features of isolated third nerve palsy: ptosis, pupillary dilatation or limitation of movements of other eye movements (inferior oblique, superior rectus and inferior rectus). Ischaemic lesions tend to affect the medial longitudinal fascicle (MLF) in a unilateral manner because they reflect the segmental distribution involvement of the paramedial branches of the basilar artery (BA).⁷ The midbrain is supplied by branches arising from the posterior cerebral artery, upper BA and the superior cerebellar artery.⁷ The MLF is often affected in patients with embolic stroke occurring in the posterior circulation, usually with the concomitant involvement of other structures such as the pons, thalamus and the cerebellum.^{7 8}

Infarcts limited to the midbrain are rare. In one 24-subject prospective study exploring the MRI and angiogram features in patients presenting predominantly with INO, the pathology was predominantly pontine in 92%. Only two had predominantly midbrain lesions.⁸ In a prospective study of pure midbrain infarction ataxia was the most frequent clinical manifestation and INO was present in only 13% of patients.⁷ In all reviewed case series the presumed cause of INO was an arterial brainstem infarct.⁸ None had an identified underlying venous anomaly infarct, as we observed in our patient.

Our case demonstrates that midbrain infarcts may be associated with a developmental venous anomaly. DVAs are generally benign vascular malformations that rarely become symptomatic.³ DVAs are vascular variations of the venous drainage system in which a collection of veins lacking elastic tissue drain into a large collecting vein.⁷ Most are incidentally discovered. DVAs can be seen in association with a coexisting cavernous malformation or cavernoma³ which have a characteristic appearance as a circumscribed high-attenuation sometimes calcified lesion on CT, with a reticulated 'popcorn ball' appearance on MRI and peripheral rim of hemosiderin⁹ not seen in this case. Though haemorrhagic transformation is known to be a common complication of venous infarcts,^{5 10} ischaemic infarctions have also been reported.⁵ The most likely aetiology for these events appears to be thrombosis of the collecting vein. This was demonstrated by angiography of an endoluminal clot in a DVA collecting vein in a patient with an acute cerebellar infarction.¹¹ Hypercoagulable states such as pregnancy, oral contraceptives, protein C or S deficiency, antithrombin deficiency and factor V Leiden mutation may be risk factors for developing venous infarcts in DVA.⁵ Though our patient had no evidence of hypercoagulability, he did have risk factors for arterial infarction: cigarette smoking-half PPD, HTN and dyslipidaemia. We theorise that the already hyalinised and inelastic walls of our patient's DVA were more vulnerable to the effects of his

cigarette use and dyslipidaemia and predisposed him to his ischaemic event.

It should be noted that venous infarcts can have heterogeneous imaging characteristics, leading to misdiagnosis as tumours or demyelinating diseases, and unnecessary biopsies, with the attendant negative effects on patient care and outcome.⁴⁻⁶ Our case presents a subtle manifestation of a potentially life-threatening but treatable problem.

Learning points

- ▶ Acute ischemia in the midbrain may be associated with complications of DVA.
- ▶ Venous infarcts in the brain stem resulting in internuclear ophthalmoplegia are rare, but can occur.
- ▶ It is important to recognise DVAs early; large DVAs may be prone to bleeding and require surgical intervention. Smaller DVAs may be followed closely.

Competing interests None.

Patient consent Obtained.

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