CASE REPORT

Mystery of a cryptogenic stroke solved by an abdominal angiogram

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SUMMARY

Despite advances in the field of imaging and diagnostics, the incidence of cryptogenic stroke is still around 30–40% in modern stroke databases. Our patient presented with recurrent midbrain infarcts over 3 years and was initially labelled as a patient with cryptogenic stroke. His blood investigations were normal, work up for autoimmune disorders was negative, CT brain angiogram was normal and a two-dimensional echo showed a small patent foramen ovale with a left to right shunt. He later presented with a right perinephric haematoma and an abdominal angiogram revealed multiple microaneurysms of the renal arteries, coeliac trunk and the mesenteric arterial system. The feeding renal artery was embolised. A diagnosis of polyarteritis nodosa was made. The patient was subjected to digital subtraction angiography of neck and intracranial vessels, which revealed multiple microaneurysms in internal and external carotid artery territory. He was discharged with steroids and azathioprine.

BACKGROUND

With the advent of MRI and other modalities of imaging, the pathophysiology of stroke and the functional significance of structural lesions in the brain are now well understood. Despite these advances, the incidence of cryptogenic stroke is still around 30–40% of all ischaemic strokes in most modern stroke databases and registries.^{1–6} By definition, cryptogenic stroke refers to an infarct in the brain that is not attributable to a source of definite cardio embolism, large artery atherosclerosis or small artery disease, despite extensive vascular, cardiac and serological evaluation.⁷ It is very pertinent that the aetiological factors contributing to these cryptogenic strokes be identified and addressed, lest the patient returns with recurring cerebrovascular accidents. We report one such patient who came to us with recurring brainstem strokes whose aetiology was elusive until a surgical emergency revealed the diagnosis.

CASE PRESENTATION

A 21-year-old man presented to us with sudden onset diplopia. He had no comorbid illness. There was no significant history apart from an operation for right-sided chronic suppurative otitis media 8 months prior to this admission. On examination, his blood pressure was normal. He had evidence of internuclear ophthalmoplegia on the left side with upbeat nystagmus. The rest of the clinical examination was unremarkable. He had no demonstrable

skin lesions. MRI of the brain revealed a lesion in the midbrain, with T2 hyperintensity and diffusion restriction (figure 1)—suggestive of an acute infarct—and the MR angiogram was normal. His renal functions were within normal limits. A complete blood count, erythrocyte sedimentation rate, lipid profile, blood sugars and ECG were within normal limits. A two-dimensional echo was also normal. This being a young stroke, we proceeded with a transoesophageal echocardiogram, which showed evidence of a small patent foramen ovale, with left to right shunt. The cardiothoracic surgeons advised routine follow-up. The patient was discharged with antiplatelets. His diplopia and internuclear ophthalmoplegia (INO) cleared over the next 2 months on follow-up.

Four months later he was readmitted in the hospital with gaze evoked nystagmus to left and left cerebellar signs. Brain MRI this time revealed a diffusion-restricted lesion in the midbrain posterior to the red nucleus. There was also evidence of contrast enhancing lesions in the right subcallosal cortex. MR angiogram was normal. With these MRI pictures, a differential diagnosis of cryptogenic stroke/demyelination/granulomatous lesion/early neurocysticercosis was suspected. Cerebrospinal fluid

Figure 1 Diffusion-weighted MRI showing infarct in the midbrain.

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(CSF) analysis was normal and oligoclonal bands were negative. HIV, hepatitis B surface antigen and hepatitis C virus were negative. The patient's CSF antibody for neurocysticercosis by ELISA was negative and he was discharged on antiplatelets and glucocorticoids.

One month later, the patient was readmitted with clinical features of right INO. His cerebellar signs had disappeared. A repeat MRI of the brain showed a midbrain infarct. There was also a nodular lesion in the interpeduncular cistern and suprasellar cistern, which was thought to be granulomatous as it minimally enhanced on contrast administration. There was also a focal mild old subarachnoid haemorrhage in the right temporal sulcal spaces (which was attributed to his right mastoid surgery). This time, the possibility of vasculitis was suspected, however, there were no external markers for this. Antinuclear antibodies, double-stranded DNA, c-antineutrophil cytoplasmic antibody (ANCA) and p-ANCA were negative. A CT angiogram of neck and intracranial vessels did not reveal any demonstrable lesions. The patient was continued on antiplatelets and steroids.

Two months later, he presented with steroid-induced acneiform lesions. His INO had cleared. The steroids were stopped and he was continued on antiplatelets. Four months later he presented with a history of melena and drop in haemoglobin. The antiplatelets were stopped and upper gastrointestinal endoscopy was normal. The patient was asymptomatic for 1 year.

One year later, the patient was admitted to the emergency room with acute right flank pain. Examination revealed right renal angle tenderness. CT of the abdomen revealed a right perinephric haematoma (figure 2). Abdominal angiogram showed multiple microaneurysms in B/L kidneys, spleen, and superior mesenteric and coeliac arteries. The renal vessel that was responsible for the perinephric haematoma was identified and embolised (figure 3).

The following year, the patient was readmitted to neurology department with diplopia. On examination, he had right INO, and MRI revealed midbrain infarct. With a history of recurrent brainstem infarcts and evidence of microaneurysms in the abdominal arterial system, the possibility of polyarteritis nodosa (PAN) was suspected. The patient was then subjected to four vessel digital subtraction angiography of the neck and intracranial vessels, which revealed multiple microaneurysms in the internal and external carotid artery branches (figure 4). A renal biopsy was deferred in view of a high risk of postprocedural

Figure 3 Right renal angiogram showing evidence of microaneurysms.

bleed. The rest of the autoimmune markers were negative. The patient was discharged with a diagnosis of probable PAN. He was started on steroids and azathioprine. Antiplatelets were withheld in view of the risk of potential rupture of the microaneurysms.

TREATMENT

The patient was started on azathioprine and steroids. Antiplatelets were withheld in view of the risk of potential rupture of the aneurysm.

OUTCOME AND FOLLOW-UP

The patient has been on azathioprine for the past 4 months, during which he has not had a stroke. Nerve conduction studies conducted during follow-up showed evidence of symmetrical sensorimotor neuropathy in bilateral lower limbs.

DISCUSSION

PAN was first described by Kussmaul and Maier⁸ in 1866, when they discovered palpable nodules along the course of arteries in their patients. Central nervous system manifestations of PAN are uncommon, with the incidence of stroke being extremely rare.⁹ In our patient, it was initially difficult to arrive at a diagnosis—the MR angiogram was normal, the vasculitis work up was

Figure 2 CT of the abdomen showing a perinephric haematoma in the right kidney.

Figure 4 Multiple microaneurysms in the branches of the carotid artery.

Box 1 American College of Rheumatology criteria for polyarteritis nodosa (PAN)¹⁰

Weight loss >4 kg
 Livedo reticularis
 Testicular pain/tenderness
 Myalgias
 Mononeuropathy or polyneuropathy
 Development of hypertension with the diastolic blood pressure higher than 90 mm Hg
 Elevated blood urea nitrogen or creatinine
 Presence of hepatitis B surface antigen or antibody in serum
 Arteriogram showing aneurysms or occlusions of the visceral arteries
 Biopsy of small-sized or medium-sized artery showing the presence of granulocytes or granulocytes and mononuclear leucocytes in the artery wall
 Classified as PAN if at least 3 of the 10 criteria are present.

negative and the American College of Rheumatology (ACR) criteria for PAN (box 1)¹⁰ were not fulfilled. Our suspicion of PAN was heightened when the patient presented with a right perinephric haematoma. This is a well-documented presentation of PAN.^{11–13} When he was subjected to an abdominal angiogram, the patient showed multiple microaneurysms in bilateral kidneys, splenic, coeliac and superior mesenteric artery territor-

Learning points

- The unusual clinical points in our patient were the four episodes of reversible brainstem dysfunction with MRI findings, the nature of which could be diagnosed only on evolution of the pathognomonic perinephric haematoma; an abdominal angiogram distant from the site of stroke helped us arrive at the diagnosis.
- Our case also establishes the fact that sometimes a clinical presentation, though distant from our practising specialty, might be the only clue to help us arrive at the diagnosis.
- A stroke is termed cryptogenic only if 'extensive' investigations fail to reveal an aetiology. This case demonstrates that extensive work up is not only limited to the initial presentation of stroke but is also required during follow-up so as to establish the aetiology of the stroke.

ies. The next time he was admitted for a stroke, the cerebral angiogram revealed microaneurysms in external and internal carotid artery branches. Ideally, a renal biopsy would have helped us with the diagnosis, but since there was a risk of a postprocedural bleed, it was deferred. Angiographic demonstration of microaneurysms is an accepted feature for diagnosing PAN.¹⁴ The treatment options of PAN include steroids and other immunomodulators such as cyclophosphamide and azathioprine.

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