Granulomatosis with polyangiitis presenting as ischaemic stroke

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Granulomatosis with Polyangiitis (GPA) is a necrotising granulomatous vasculitis. We describe a case of GPA with cerebral involvement and review the literature.

DECLARATIONS

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Case report

A 59-year-old man presented with symptoms of intermittent nasal obstruction and reduced hearing. He had a history of type II diabetes mellitus, managed with oral hypoglycaemic agents with no evidence of diabetic complications. He also reported well-controlled hypertension. There was no personal or family history of cardiovascular disease.

Biopsies of the nasal mucosa showed evidence of vasculitis with fibrinoid changes within the vessels and endarteritis obliterans, in keeping with a diagnosis of GPA. Arthralgia and non-visible haematuria were noted and he was commenced on prednisolone 40 mg daily.

Six days later, he presented to his local hospital with acute onset of left-sided weakness without higher level dysfunction in keeping with a right-sided lacunar infarct. Computed tomography of his head and carotid dopplers were both normal. He was treated with high-dose aspirin (300 mg daily) and dipyridamole. However, he was noted to have an elevated creatinine at 191 μmol/L which did not settle with discontinuation of his antihypertensive agents. Six months prior to presentation his renal function was normal. He was therefore transferred to our nephrology centre for further management.

On admission he had persistent mild left-sided limb and facial weakness. His arthralgia had settled on low dose steroids and he denied pulmonary symptoms. His chest X-ray was clear and there was no vasculitic rash. Urine microscopy showed RBC casts and antineutrophil cytoplasmic antibody (ANCA) was strongly positive (1:320 titre). A diagnosis was made of GPA with renal and nervous system involvement and he was commenced on cyclophosphamide 2 mg/kg daily and prednisolone 60 mg daily. In view of his persistent neurological signs, he was commenced on plasma exchange for presumed cerebral vasculitis.

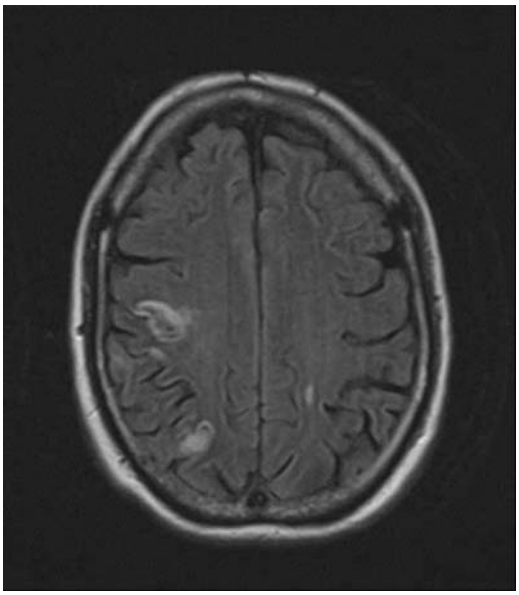
Magnetic resonance imaging (MRI) of his head (with gadolinium contrast) showed small areas of acute cortical infarction with bilateral enhancement but particularly in right parietal/occipital area (Figure 1). The intracranial vasculature appeared normal. The nature and distribution of the infarcts favoured a vasculitic cause for the patient's symptoms and signs.

The patient's symptoms of weakness improved rapidly with this treatment, as did his creatinine which on discharge was 129 μmol/L. He completed 7 sessions of plasma exchange. By one month post discharge his creatinine had settled to his pre-morbid level of function with falling ANCA titres and continued clinical improvement in his limb and facial weakness.

Discussion

GPA is a systemic necrotising granulomatous vasculitis, typically affecting small vessels associated with the presence of ANCA. Localized GPA (defined as affecting the respiratory tract only) is seen in <5% patients and ANCA positivity is seen in only 50% of these patients.[1] A more specific diagnostic marker is the presence of ANCA directed against proteinase 3 (ANCA-PR3) which is seen in 95% patients with generalized GPA.[1]

Figure 1
MRI scan, with suppression of cerebral spinal fluid (CSF) signal, demonstrates high signal lesions in the right fronto-parietal cortex and the left deep white matter. Appearances are consistent with vasculitis



Characteristically GPA involves the kidneys and respiratory tract but may also affect the nervous system. Around 50% of patients experience some form of neurological involvement.[2,3] This is most commonly (~50%) a peripheral neuropathy which can be a motor, sensory or mixed picture.[3] Cranial neuropathies are also frequently seen (~40%), typically involving the optic, facial, trigeminal and acoustic nerves.[2,3] Involvement of the central nervous system (CNS) is rare, but intracerebral haemorrhage, seizures, meningeal irritation and mass lesions as a result of granuloma formation are well documented sequelae of GPA. Damage to the arterial wall in GPA can lead to intracranial aneurysm formation and haemorrhage or vascular occlusion due to inflammatory injury to the endothelium.[4] Cerebral vessel occlusion by granulomata has also been reported.[2,5] Thrombolysis is contraindicated in such cases as there is a high risk of haemorrhagic transformation.[4] Cerebral vasculitis may therefore mimic the more common atherosclerotic or hypertensive cerebral events, consequently requiring a high degree of clinical suspicion to make the correct diagnosis.

MRI is key to diagnosing cerebral vasculitis. Multiple infarcts of varying ages in more than one vascular territory are highly suggestive of an underlying inflammatory process.[6] The MRI appearances do not identify the cause of the vasculitis and localized primary CNS vasculitis/angiitis of the CNS is well recognized.[3,7,8] Cerebral vessel wall thickening and enhancement and intramural contrast uptake on standard MRI has also been frequently observed[6,7] but as yet, there are no studies demonstrating the specificity of these findings to permit negation of biopsy in the absence of other features of vasculitis.

There have been case reports of ischaemic stroke associated with GPA, but generally these are associated with extensive areas of infarction,[5,9] symptoms suggestive of a diagnosis of GPA such as haemoptysis, or other atypical features such as seizure predating the hemiparesis.[3]

Patients with small vessel vasculitis (including GPA) are known to be at higher risk of venous thromboembolic events, but a recent study[10] also suggested increased risk of cardiovascular events, independent of traditional cardiovascular risk factors.

A full review of the evidence for treatment options is beyond the scope of this article. However, cerebral vasculitis is a marker of severe disease activity, indicating the need for plasma exchange in addition to the standard induction immunosuppressive regime of cyclophosphamide (or rituximab) plus glucocorticoids. Treatment response is best indicated by an improvement in symptoms (e.g. headache) rather than resolution of neuroimaging findings, which may remain unchanged. A lack of new lesions developing is highly supportive of treatment response and a follow up MRI should be organized four to six weeks after commencing treatment.

In conclusion, patients with GPA may present with neurological symptoms, including those suggesting cerebral ischaemia. Vasculitis may be a risk factor for cardiovascular events but symptoms may be due to active cerebral vasculitis. This can only be reliably diagnosed with an MRI scan. We therefore suggest that this should be part of the standard investigations for a patient presenting with signs of cerebral ischaemia in whom vasculitis is known or suspected.

References

1 Lamprect P, Gross WL. Wegener's granulomatosis. *Herz* 2004:**29**;47–56

2 Yuan J, Guan H-Z, Wu Q-J. Neurological manifestations of 33 patients with Wegener's granulomatosis. *Chinese Journal of Neurology* 2004:**37**;428–30

3 Roncallo F, Turtulici I, Bisio N, Inglese M, Bartolini A. Wegener's granulomatosis with cerebral vasculitis. *Rivista di Neurobiologia* 1997:**43**;775–81

4 Wisniewska M, Czlonkowska A. The role of vasculitis in stroke. *Udar Mozgu – Problemy Interdyscyplinarne* 2008:**10**; 8–14

5 Satoh J, Miyasaka N, Yamada T, *et al.* Extensive cerebral infarction due to involvement of both anterior cerebral arteries by Wegener's granulomatosis. *Annals of the Rheumatic Diseases* 1988:**47**;606–11

6 Kuker W, Gaertner S, Nägele T, *et al.* Vessel wall contrast enhancement – a diagnostic sign of cerebral vasculitis. *Cerebrovascular Diseases* 2008:**26**;23–9

7 Birnbaum J, Hellmann DB. Primary angiitis of the central nervous system. *Archives of Neurology* 2009:**66**; 704–9

8 Ferro JM. Vasculitis of the central nervous system. *Journal of Neurology* 1998:**245**;766–76

9 Savitz JM, Young MA, Ratan RR. Basilar artery occlusion in a young patient with Wegener's Granulomatosis. *Stroke* 1994:**25**;214–6

10 Morgan MD, Turnbull J, Selamet U, *et al.* Increased incidence of cardiovascular events in patients with antineutrophil cytoplasmic antibody-associated vasculitides – a matched pair cohort study. *Arthritis and Rheumatism* 2009:**60**;3493–500