LETTERS

Antiphospholipid antibody syndrome associated with primary angiitis of the central nervous system: report of two biopsy proven cases

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PPrimary angiitis of the central nervous system (PACNS) remains one of the most challenging forms of vasculitis.

Its diagnosis requires the presence of an acquired neurological deficit, classic angiographic evidence consistent with vasculitis or histopathological demonstration of angiitis within the central nervous system (CNS), and no evidence of systemic vasculitis or another autoimmune, infectious or malignant process.¹ Antiphospholipid syndrome (APS) involves recurrent arterial or venous thrombosis, pregnancy loss, and repeated detection of anticardiolipin antibodies or lupus anticoagulant at least 6 weeks apart.² APS may result in neurological complications such as stroke, migraine, chorea, seizures or transverse myelitis. There has been no reported association between APS and PACNS. We present the first two cases of PACNS and simultaneous APS.

Patient 1 is a 76 year old man presenting with headaches, mental status changes progressing to somnolence, and neurological deficits, including dysarthria and right sided hemiparesis. Patient 2 is a 62 year old man who presented with mental status changes progressing to stupor and right sided hemiparesis. Magnetic resonance imaging of the brain in patient 1 showed four areas of recent infarction affecting both hemispheres, whereas in patient 2 it showed extensive white matter changes. Ischaemic and embolic causes were excluded. Investigation of possible infections was unrevealing. Autoimmune serologies were negative, except for the dilute Russell viper venom test (dRVVT), which was prolonged in both patients (table 1). Patient 1 also had a prolonged partial thromboplastin time (PTT), and patient 2 had a positive hexagonal phase platelet neutralisation assay (HPPNA).

Hospital course for patient 1 was complicated by extensive left arm deep vein thrombosis and pulmonary embolisation. Patient 1 had a negative cerebral angiogram. Brain biopsy established the diagnosis of PACNS in both patients (fig 1). Treatment consisted of intravenous corticosteroids 1 g daily for 3 days followed by a tapering oral regimen, oral cyclophosphamide, and warfarin. The mental state normalised in

both patients. The focal neurological deficits partially improved in patient 1, but completely resolved in patient 2, including the areas of previous abnormal intensity on magnetic resonance imaging. After 1 year cyclophosphamide was replaced with mycophenolate mofetil in patient 2 and he remains asymptomatic. More than 6 months after presentation, the dRVVT continued to be prolonged in both cases, PTT was raised in patient 1 only.

PACNS affects the small and medium sized arteries and, less commonly, the veins and venules of the brain and leptomeninges. Two cases of CNS vasculitis and APS have been described in patients with systemic lupus erythematosus (SLE).^{2,3} Neither of our patients had any clinical or serological evidence to suggest a diagnosis of SLE. Studies have shown an increased prevalence of anticardiolipin antibodies and lupus anticoagulant in patients with giant cell arteritis.⁴ Espinosa *et al* suggested that these antibodies could be induced by the exposure of phospholipids at the outer membrane of endothelial cells during inflammation.⁵ On the other hand, Ruffatti *et al* reported on three patients with giant cell arteritis and APS, with thrombotic phenomena and persistent serological abnormalities; all three were positive for anticardiolipin antibodies and two for β_2 microglobulin.⁶ Our patients did not have symptoms consistent with temporal arteritis.

In summary, PACNS has not been previously associated with APS. Therefore, these two patients constitute the first report of PACNS associated with APS. In both patients, the lupus anticoagulant persisted for more than 6 months after the initial presentation, confirming the diagnosis of APS. Both patients markedly improved when immunosuppressant drugs and anticoagulation were started and remain stable 2 years after their initial presentation.

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Table 1 Laboratory results of APS testing

	PTT	HPPNA	dRVVT	KCT
Normal range	25–34.0*	<8.0	31.8–46.4	79–131.0*
Patient 1				
Baseline	40.7	6.8	60.0	89.0
After 6 months	36.2	6.8	60.0	89.0
Patient 2				
Baseline	32.3	9.0	71.2	
After 6 months	28.7	0.0	55.2	103.0

PTT, partial thromboplastin time; HPPNA, hexagonal phase neutralisation assay; dRVVT, Russell's viper venom test; KCT, kaolin clotting time.

*Clotting times in seconds.

Figure 1 Patient 1: Brain biopsy of patient 1 shows granulomatous perivascular inflammation with lymphocytes, macrophages, and multinucleated giant cells (A). Immunocytochemistry shows that the macrophages and the multinucleated cells are positive for CD68 (B). Panels A and B are at the same magnification. Patient 2: Brain biopsy sample from patient 2 shows that the meningeal and cortical vessels walls are positively stained by Congo red (A) and become apple-green in polarised light (B). Immunocytochemistry shows that these vessel walls are positive for β -amyloid (C). Some of these vessels show chronic perivascular inflammation, often including multinucleated giant cell (arrow in D).

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