SHORT REPORT

Eosinophilic vasculitis in an isolated central nervous system distribution

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J Neurol Neurosurg Psychiatry 2007;**78**:85–88. doi: 10.1136/jnnp.2005.085191

Background: Eosinophilic vasculitis has been described as part of the Churg–Strauss syndrome, but affects the central nervous system (CNS) in <10% of cases; presentation in an isolated CNS distribution is rare. We present a case of eosinophilic vasculitis isolated to the CNS.

Case report: A 39-year-old woman with a history of migraine without aura presented to an institution (located in the borough of Queens, New York, USA; no academic affiliation) in an acute confusional state with concurrent headache and left-sided weakness and numbness. Laboratory evaluation showed increased cerebrospinal fluid (CSF) protein level, but an otherwise unremarkable serological investigation. Magnetic resonance imaging showed bifrontal polar gyral-enhancing brain lesions. Her symptoms resolved over 2 weeks without residual deficit. After 18 months, later the patient presented with similar symptoms and neuroradiological findings involving territories different from those in her first episode. Again, the CSF protein level was high. She had a raised C reactive protein level and erythrocyte sedimentation rate. Brain biopsy showed transmural, predominantly eosinophilic, inflammatory infiltrates of medium-sized leptomeningeal arteries without granulomas. She improved, without recurrence, when treated with a prolonged course of corticosteroids.

Conclusions: To our knowledge, this is the first case of non-granulomatous eosinophilic vasculitis isolated to the CNS. No aetiology for this patient's primary CNS eosinophilic vasculitis has yet been identified. Spontaneous resolution and recurrence of her syndrome is an unusual feature of the typical CNS vasculitis and may suggest an environmental epitope with immune reaction as the cause.

Eosinophilic vasculitis has been described as part of the Churg–Strauss syndrome, but affects the central nervous system (CNS) in only 6–7% of cases.[1 2] Presentation in an isolated CNS distribution is rare. We present a case of eosinophilic vasculitis isolated to the CNS.

CASE REPORT

A 39-year-old woman with a history of migraine without aura presented to an institution (located in the borough of Queens, New York, USA; no academic affiliation) in an acute confusional state with concurrent headache and left-sided weakness and numbness. A lumbar puncture showed acellular cerebrospinal fluid (CSF) with a slightly increased protein concentration. She was treated presumptively for herpes encephalitis on the basis of an increased herpes simplex virus (HSV)-2 IgG titre in the serum and CSF (IgM not analysed and CSF polymerase chain reaction negative), as well as bifrontal polar gyral-enhancing brain lesions on magnetic resonance imaging (MRI). Her symptoms resolved over 2 weeks without residual deficit. After 18 months, the patient presented again with a similar constellation of symptoms, including acute-onset headache, confusion, left visual field flashes, and left-sided numbness and weakness. An MRI showed new occipital–parietal leptomeningeal-enhancing lesions; lumbar puncture again showed acellular CSF with raised protein concentration (128 mg/dl). She was transferred to The Neurological Institute of New York for further management.

The patient worked at a perfume counter and identified odours of certain perfumes as a trigger for her migraine attacks. She had no respiratory complaints including asthma, rash, constitutional symptoms or allergies. Other than a multivitamin, she took no drugs regularly, including non-prescription supplements. Further history and physical examination showed no features suggestive of systemic vasculitis, including lymphadenopathy or rash. Neurological examination was notable for mildly impaired attention, a left homonymous lower quadrantanopsia, left hemiparesis and left patchy hemihypesthesia.

Brain MRI showed right occipital, anterior frontal and bilateral parietal cortical lesions with leptomeningeal enhancement on the T1-weighted post-contrast images (fig1A, black arrowheads). Gradient echo showed patchy low signal in sulci, consistent with persistent intracellular deoxyhaemoglobin or methaemoglobin. FLAIR images showed high signal of the cortical mantle as well as the subarachnoid space in the adjacent gyri (fig1B, white arrowheads) that showed prolonged diffusion rates on diffusion-weighted images and apparent diffusion coefficient maps, consistent with inflammatory oedema or subacute ischaemia. The bifrontal lesions observed on MRI during the patient's previous hospitalisation were faintly visible on the FLAIR sequence (fig1B, white arrow) and showed low signal in the sulci on the gradient echo images, consistent with haemosiderin deposition from a prior haemorrhage.

Serum inflammatory markers were increased, with erythrocyte sedimentation rate 35 mm/h (normal range 0–22 mm/h) and C reactive protein level 92.6 mg/l (normal <3 mg/l; table 1). The patient had a normal blood count including only 1% eosinophils. Serum electrolytes, creatinine, liver enzymes and urine analysis were also normal. Antithyroglobulin and antimicrosomal antibodies were not detected. Stool was negative for ova and parasites. CSF examination showed 2 leucocytes/mm^3 (100% lymphocytes), 300 erythrocytes/mm^3, a protein level of 119 mg/dl and normal glucose. CSF cultures were negative, as were polymerase chain reaction studies for HSV-1 and HSV-2 and varicella zoster virus. Serum rapid plasma reagin was non-reactive and the patient was HIV negative. Rheumatological studies, including antinuclear antibodies, anti-DNA, anti-extractable nuclear antigens, antineutrophil cytoplasmic (cANCA, pANCA), rheumatoid factor and lupus anticoagulant, were negative. A DNA analysis was carried out

Abbreviations: CSF, cerebrospinal fluid; CNS, central nervous system; HSV, herpes simplex virus; MRI, magnetic resonance imaging

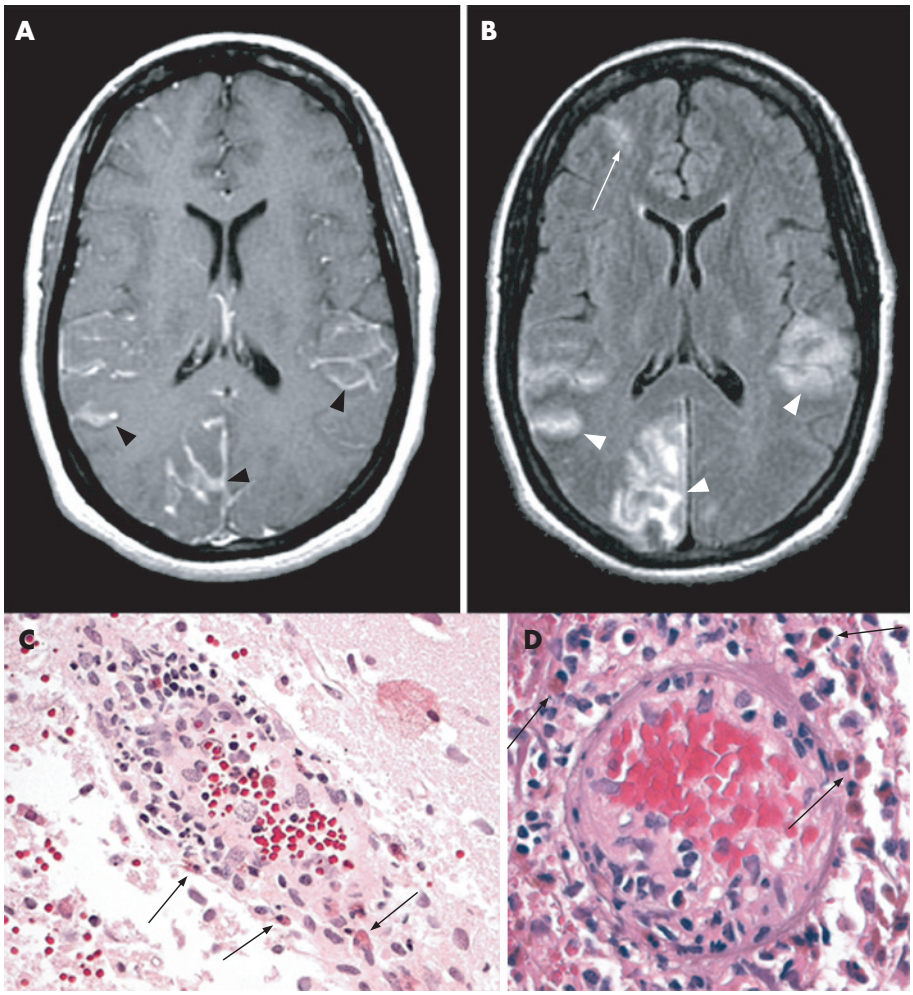

Figure 1 (A) Brain magnetic resonance imaging (MRI) post-gadolinium T1 sequence shows right occipital, anterior frontal, and bilateral parietal cortical lesions with leptomeningeal enhancement on the T1-weighted images (black arrowheads). (B) FLAIR image shows high signal of the cortical mantle as well as the subarachnoid space in the adjacent gyri (white arrowheads). The bifrontal lesions observed on MRI during the patient's previous hospitalisation show evolution (white arrow). (C, D) Histological examination shows transmural, predominantly eosinophilic, inflammatory infiltrates of medium-sized leptomeningeal arteries (black arrows). Small cortical vessels showed focal fibrinoid necrosis and swollen endothelial cells, without granulomas.

to look for mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS), but there was no A3243G mutation. Cerebral angiography showed no evidence of focal arterial narrowing. Computed axial tomography of the chest was normal.

Brain biopsy showed transmural, predominantly eosinophilic, inflammatory infiltrates of medium-sized leptomeningeal arteries (fig1C, D, black arrows). Small cortical vessels showed focal fibrinoid necrosis and swollen endothelial cells, without granulomas. Immunoperoxidase staining for amyloid-β peptide in cortical and subpial vessels showed no evidence of amyloid angiopathy. Gram stain, bacterial culture, staining for acid-fast bacilli and mycobacterial culture of the brain biopsy were all negative. No viral inclusions were identified, and immunohistochemical stains for HSV-1, HSV-2 and varicella were negative.

The patient received high-dose intravenous dexamethasone with rapid improvement in symptoms. She had normal erythrocyte sedimentation rate and C reactive protein levels within 2 weeks of steroid therapy, and was discharged on a prednisone taper followed by a low maintenance dose. One year later she has mild residual left-sided sensory loss without recurrence of symptoms; MRI showed gyral volume loss and encephalomalacia.

DISCUSSION

Eosinophilic vasculitis is a feature of certain rheumatological conditions, but is rare in an isolated CNS distribution.[3] Stroke caused by vasculitis is well described in the Churg–Strauss syndrome, which is characterised by multisystem granulomatous eosinophilic vasculitis accompanied by peripheral eosinophilia and a history of asthma.[4] Granulomatous eosinophilic vasculitis accompanied by mild peripheral eosinophilia has been observed in parenchymal and leptomeningeal vessels affected by cerebral amyloid angiopathy.[5] Eosinophilic temporal arteritis and claudicating systemic arteritis, associated with a 24% peripheral eosinophil count, was reported with vasculitic vertebrobasilar stroke, although no aetiology was identified.[6] Here we describe a non-granulomatous eosinophilic vasculitis of the CNS with no accompanying eosinophilia of the peripheral blood or CSF, and no involvement of other organ systems. Given their similarities, her two isolated episodes may probably be due to the same disorder. Lack of peripheral eosinophilia argues against systemic infection or drug reaction. The absence of granulomas further distinguishes this case histopathologically from nearly all other reported cases of isolated CNS vasculitis. Although her MRI findings could indicate focal lobar oedema with haemosiderin deposition, the

Table 1 Laboratory studies on the patient

	Prior illness (outside hospital, 1 year earlier)	Current illness				
		D2 (outside hospital)	D4 (presentation to our institution)	D5	D9	Reference range
Blood						
WBC			5.7			3.54–9.06×10^9/l
Hgb			12.2			12.0–15.8 g/dl
MCV			92.8			79–93.3 fl
Plt			168			165–415
Lymphocytes			11			20–50%
Neutrophils			80			40–70%
Monocytes			8			4–8%
Eosinophils			1			0–6%
Basophils			0			0–2%
Na			139			136–146 mM/l
K			4.1			3.6–5.0 mM/l
Cl			109			102–109 mM/l
CO_2			20			25–33 mM/l
BUN			11			7–20 mg/dl
Cr			1.3			0.5–0.9 mg/dl
Glucose			119			79–105 mg/dl
Ca			8.5			8.4–9.8 mg/dl
P			2.9			2.5–4.3 mg/dl
Mg			1.9			1.5–2.3 mg/dl
CK			168			39–238 U/l
Total protein			6.4			6.7–8.6 g/dl
Albumin			3.7			4.0–5.0 g/dl
Total bilirubin			0.4			0.30–1.30 mg/dl
Direct bilirubin			0.1			0.04–0.38 mg/dl
AST			19			12–38 U/l
ALT			10			7–41 U/l
Alkaline phosphatase			45			33–96 U/l
TSH			8.06			0.34–4.25 μU/ml
T4			7.13			5.41–11.66 μg/dl
Free T4			1.0			0.8–1.8 ng/dl
T3			58			76.91–134.74 ng/dl
ESR		48	35			0–20 mm/h
CRP			92.6			<3 mg/l
Homocysteine			5.3			4.4–10.8 μmol/l
B12			346			279–996 pg/ml
Arterial lactate			1.1			0.50–1.60 mM/l
RF			<9.5			<15
RPR			NR			
ANA			Negative			
Angiotensin-converting enzyme					26	9–67 U/l
Anti-DNA Ab			12			<25 IU/ml negative
Anti-ENA (includes anti-SS-A/Ro, SS-B/La, SM, U1RNP, SCL-70, and Jo-1			2.0			0.0–19.9 negative
P-ANCA			0			<6
C-ANCA			0			<2
Anti-cardiolipin Ab (IgG and IgM)			Negative			
C3			111			83–177 mg/dl
C4			31			16–47 mg/dl
CH50			194			50–150%
Quantitative IgA					239	70–350 mg/dl
Quantitative IgG					1120	700–1700 mg/dl
Quantitative IgM					180	50–300 mg/dl
Antithyroglobulin antibody					Negative	
Antimicrosomal antibody					Negative	
HIV-1 and HIV-2 ELISA			Negative		Negative	
CMV IgM			0.11			>0.90 positive
EBV IgG			5.42			>1.10 positive
Anti-HAV IgG			Positive			
Anti-HAV IgM			Negative			
HBSAg			Negative			
Anti-HBV surface			Negative			
Anti-HBV core			Negative			
Anti-HCV			Negative			
HSVI Ab			>5.00			0.00–0.89
HSV II Ab			4.35			0.00–0.89
Lyme Ab			0.64			<1.00
Cerebrospinal fluid						
WBC		2		4		per mm^3
Lymphocytes				92		%
Neutrophils				8		%
Monocytes				0		%

	Prior illness (outside hospital, 1 year earlier)	Current illness: D2 (outside hospital)	Current illness: D4 (presentation to our institution)	Current illness: D5	Current illness: D9	Reference range
Eosinophils				0		%
Basophils				0		%
Cytology	No malignant cells			No malignant cells		
Macrophages				4		Per 100 WBC
RBC		58		350		Per mm^3
Glucose		64		51		40–70 mg/dl
Protein		124		119		15–45 mg/dl
Lactate				2.0		0.6–2.20 mM/l
Pyruvate				0.10		0.04–0.13 mM/l
HSV 1 and 2 PCR	Negative			Negative		
VZV PCR				Negative		
West Nile virus PCR				Negative		
St Louis encephalitis PCR				Negative		
Eastern equine encephalitis PCR				Negative		
Cache Valley and California serogroup viruses PCR				Negative		
Enterovirus PCR				Negative		
EBV PCR				Negative		
CMV PCR				Negative		
IgG				16.4		0.5–6.0 mg/dl
IgG/total protein				13.8		6.0–13.0%

Ab, antibody; ALT, alanine aminotransferase; AST, aspertate aminotransferase; ANA, antinuclear antibodies; BUN, blood urea nitrogen; CMV, cytomegalo virus; CRP, C reactive protein; EBV, Epstein–Barr virus; ENA, extractable nuclear antigens; ESR, erythrocyte sedimentation rate; HAV, hepatitis A virus; Hgb, haemoglobin; HSV, herpes simplex virus; Ig, immunoglobulin; MCV, mean corpuscular volume; NR, not reported; PCR, polymerase chain reaction; Plt, platelet count (×1000); RF, rheumatoid factor; RPR, rapid plasma reagin; TSH, thyroid-stimulating hormone; VZV, varicella zoster virus; WBC, white blood cell count.

condition argues against cerebral amyloid angiopathy or amyloid-β-related angiitis, which has been recently described as a reversible cerebral amyloid angiopathy leucoencephalopathy syndrome with associated angiitis.[7 8] No aetiology for this patient's primary CNS eosinophilic vasculitis has yet been identified. Spontaneous resolution and recurrence of her syndrome is an unusual feature of the typical CNS vasculitis and may suggest an environmental epitope with immune reaction as the cause.

ACKNOWLEDGEMENTS

We have no financial or other disclosures to report, but are grateful to Timothy S Lo, MD, of the Neurological Institute, College of Physicians and Surgeons of Columbia University, for his assistance with this report.

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Competing interests: None declared.

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Received 8 December 2005
Revised 27 June 2006
Accepted 29 June 2006
Published Online First 22 August 2006

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