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J Neurol Neurosurg Psychiatry published online September 22, 2010

doi: 10.1136/jnp.2009.198283

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Published online September 22, 2010 in advance of the print journal.

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LETTER

Intracranial aneurysms associated with hyperimmunoglobulinaemia E (Job) syndrome: report of two cases

Hyperimmunoglobulinaemia E (HIES) syndrome is a rare immunodeficiency disease inherited as a single locus autosomal dominant trait with variable expression¹ presenting with multisystem infections.² The diagnosis is based on a scoring system assessing multiple features such as chronic eczema, recurrent pyogenic skin and lung infections, significantly increased serum levels of immunoglobulin E (>2000 IU), peripheral eosinophilia, characteristic faces, joint hyperextensibility, and pathological long bone fractures.¹ Treatment includes medical and surgical management of the infections and, in severe cases, intravenous administration of immunoglobulin or recombinant interferon gamma. Central nervous system (CNS) abnormalities such as lacunar infarctions, Chiari type 1 malformations, cerebritis and parenchymal and subarachnoid haemorrhage (SAH) are common in this syndrome.²

Despite the known CNS involvement,² this syndrome has not been previously described in the neurosurgical literature. We present two cases with known HIES with aneurysmal SAH and discuss possible causes of aneurysm formation.

CASE REPORTS

Both patients with confirmed diagnosis of HIES were followed up at the Warren Grant Magnuson Clinical Center under protocol 93-1-0119 with informed consent.

Case 1

A 29-year-old woman was admitted presenting with persistent headaches over a 2-week period, accompanied by transient right-sided weakness and loss of consciousness. In the interim, she had multiple severe skin infections, cavitary pulmonary aspergillosis and facial cellulitis. Her Hunt and Hess grade on admission was 4 (World Federation of Neurological Surgeons grade 4+; Glasgow coma score 8), accompanied by mild nuchal rigidity, right sensory deficits and right-sided hyperreflexia (3+/4) without Babinski sign. The initial cranial computed tomographic (CCT) scan was unremarkable; the follow-up MRI revealed a previous ischaemic infarction in the anterior segment of the left temporal lobe and in the left insular cortex associated with haemorrhagic changes. One week later, a subsequent MRI demonstrated enlargement of the infarction, which included the left basal

ganglia and the adjacent frontal cortex; magnetic resonance arteriography revealed occlusion of the left middle cerebral artery (MCA). The MCA infarction was considered to have been exacerbated by haemorrhage into the area of the thrombosed MCA. After the patient's further clinical deterioration. A CCT showed acute hydrocephalus and evidence of SAH in the left Sylvian fissure and suprasellar cisterns (Fisher grade 2). A right frontal ventriculostomy yielded haemorrhagic, xanthochrome cerebrospinal fluid. Cerebral arteriography revealed a 5-mm aneurysm on the left anterior temporal artery and occlusion of the left MCA at the level of the trifurcation. Surgery of the aneurysm was postponed because of the patient's high surgical risk and poor clinical prognosis. Unfortunately, the patient's hemiparesis and consciousness quickly deteriorated, and she died. Autopsy revealed an extensive SAH secondary to rupture of a mycotic aneurysm and infarction in the distribution of the left MCA. Microscopic and microbiological studies of the left MCA showed invasive aspergillosis with severe necrotising inflammation of the arterial wall (figure 1A) and fragmentation of the internal elastic lamina (figure 1B). The right internal carotid, middle cerebral and basilar arteries were separately examined and revealed marked degenerative changes consisting of

deposits of atheromatous debris within the intima with no signs of active infection (figure 1C). These changes were accompanied by fragmentation of the internal elastic lamina (figure 1D). Examination of the aorta, renal arteries, hepatic arteries and smaller vessels showed no abnormalities of the internal elastic lamina.

Case 2

A 35-year-old woman was previously found to have HIES at age 11 years. Three days before admission, she experienced typical SAH-related history of extreme and persistent headaches (Hunt and Hess grade 2). The CT scan revealed an SAH in the left Sylvian fissure (Fisher grade 3). Cerebral arteriography confirmed mirror aneurysms at the internal carotid artery bifurcation. On the fourth day after SAH, the ruptured neck of the aneurysm was successfully clipped. Postoperatively, the patient had a transient right-sided hemiparesis and was discharged without neurological deficits on postoperative day 6. One month later, the aneurysm of the contralateral internal carotid artery bifurcation was electively clipped, and a postoperative arteriogram confirmed its complete occlusion. During the uneventful period of neurosurgical management, the patient was monitored for signs of

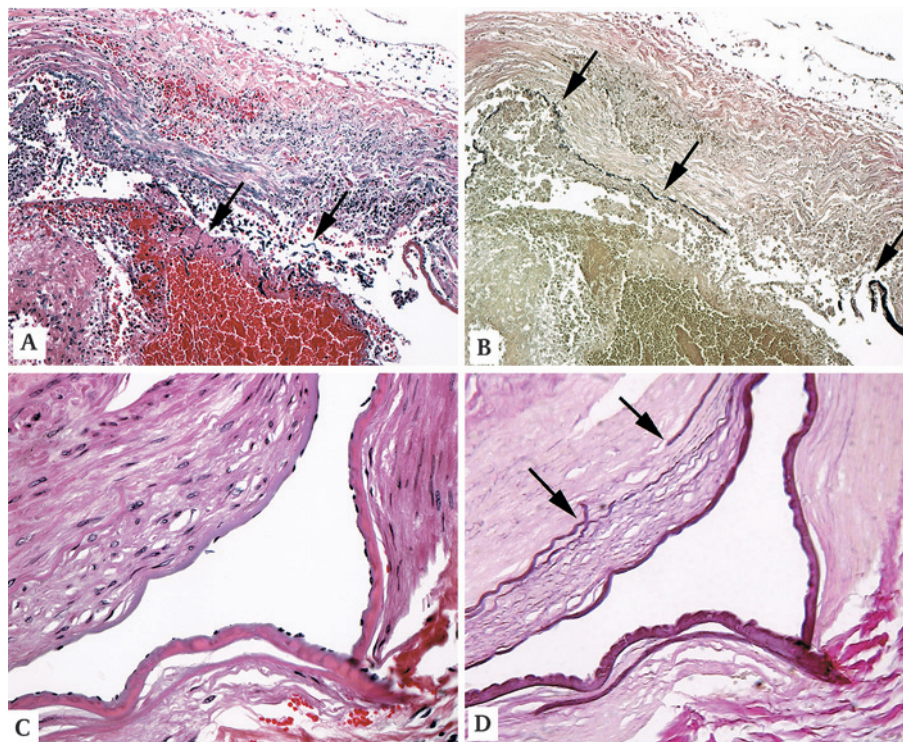


Figure 1 (A, B) Photomicrograph of the left MCA revealing the presence of mycotic infection in the vessel wall (arrows; haematoxylin and eosin, magnification $\times 10$) (C) with severe destructive inflammatory changes and fragmented internal elastic lamina (arrows; van Gieson, magnification $\times 10$) (D). (C, D) Photomicrograph of the right MCA with marked degenerative changes without inflammation in the intima (haematoxylin and eosin, magnification $\times 20$) (E). Photomicrograph (van Gieson, magnification $\times 20$) (F) revealing splitting of the internal elastic lamina (arrows) and deposition of atheromatous debris.

infections, and prophylactic antibiotic was administered before every invasive procedure.

DISCUSSION

In case 1, aneurysm formation had an infectious background directly related to the immunological disorder. Pathological findings suggest that mycotic aneurysm formation due to fungal infection might be facilitated by pre-existing changes in the artery wall characteristic for aneurysm formation. Development of coronary artery, thoracic aorta and bronchial aorta aneurysms in patients with HIES further supports this hypothesis.² Although without strong evidence, other genetic syndromes characterised by congenital connective tissue abnormalities have been associated with the risk of aneurysm formation: Marfan syndrome, polycystic kidney disease and Ehlers–Danlos disease type 4. The lack of a properly developed smooth muscle layer (media) and/or disruption of the internal elastic lamina result in development of intracranial aneurysms in both animal models³ and humans.² Thus, underlying vascular connective tissue changes together with the aggressive angioinvasive nature of aspergillus, directly related to its ability to digest elastic tissue by producing elastase, may facilitate destruction of potential barriers to fungal infection and increase the risk of infectious aneurysm formation.⁴

Because the annual rate of aneurysmal SAH in the USA is approximately 30 000 and the second patient exhibited no signs of CNS infection, the presence of the saccular mirror aneurysms may be coincidental with

possible linkage to the pathophysiological feature of HIES. Nevertheless, the presence of collagen and elastic lamina changes with frequent peripheral aneurysm formation suggests the likelihood of a higher incidence of intracranial aneurysm formation in patients with HIES.² An explanation for the lack of reported cases of intracranial aneurysm in HIES, despite the possible increased risk of incidence, may be the relatively short lifespan of patients (mean 26.5 years),¹ which precludes development and subsequent diagnosis of aneurysms.

Because CNS involvement and headaches are rather common symptoms in HIES,⁵ it is of value to be aware of HIES as a rare cause of brain infections and mycotic aneurysm formation, and special vigilance is advocated to avoid overlooking a possible SAH in these patients. Although a direct link between HIES and the development of cerebral aneurysms may not exist and because this syndrome is rare, some patients might benefit from neurosurgical management.

Acknowledgements This research was supported by the Intramural Research Program of the National Institutes of Health, National Institute of Neurological Disorders and Stroke. ARF was supported by a grant from the Swiss National Science Foundation. The authors gratefully acknowledge Dr Nicolaus J Patronas, John I Gallin and Tung Nguyen for their participation in the early stages of this work.

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Funding This study was funded by the National Institutes of Health and the Swiss National Science Foundation.

Competing interests None.

Ethics approval This study was conducted with the approval of both patients who were followed up at the Warren Grant Magnuson Clinical Center under protocol 93-I-0119.

Provenance and peer review Not commissioned; externally peer reviewed.

Received 26 October 2009

Revised 17 February 2010

Accepted 15 March 2010

J Neurol Neurosurg Psychiatry 2010; **■**:1–2.
doi:10.1136/jnnp.2009.198283

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