LETTERS TO THE EDITOR

Obstructive hydrocephalus due to benign cysts of the thalamus: report of two patients

Benign cysts of the thalamus compressing the posterior third ventricle are an unusual cause of obstructive hydrocephalus. We report two patients with symptomatic hydrocephalus due to such cysts and discuss the pathogenesis and treatment of these rare lesions.

A 35 year old woman (patient 1) presented with a one month history of intermittent and severe frontal headaches, nausea, difficulty reading, and numbness and weakness of the left arm and leg. Physical examination disclosed bilateral papilloedema and constriction of the temporal visual fields. Slight weakness was present in both upper limbs. The left lower limb was hyperreflexic. The remainder of the neurological examination was normal.

Brain CT showed obstructive hydrocephalus due to a $3 \times 3 \times 2$ cm cyst within the right thalamus compressing and shifting the posterior third ventricle to the left (figure). Transependymal diapedesis of CSF was present. Brain MRI showed the cyst fluid to be similar in intensity to CSF on all pulse sequences; the cyst wall failed to enhance with gadolinium. No communication existed between the cyst and the third ventricle or subarachnoid space.

The presence of papilloedema prompted urgent placement of a right ventriculoperitoneal shunt. Two days later, CT guided stereotactic aspiration of the cyst yielded 16 ml of colourless fluid without evidence of tumour, haemorrhage, or infection.

Postoperatively, the headaches resolved and vision returned to normal. The weakness and numbness also abated. The cyst was fully collapsed on CT 48 hours after aspiration and remained unchanged 19 months postoperatively.

Axial T2 weighted MRI shows the cyst in the right thalamus compressing the posterior third ventricle. Transependymal diapedesis of CSF is present. The cyst fluid is similar in intensity to CSF.

For five months, a 72 year old woman (patient 2) experienced progressive gait ataxia, urinary incontinence, and disorientation. She denied headaches, nausea, vomiting, visual, sensory, or motor complaints. Physical examination showed her to be slow to respond and oriented only to person. Gait was unsteady and assistance was needed for ambulation. The remainder of the neurological examination was normal.

Brain CT and MRI of the head showed hydrocephalus due to a $2.5 \times 3 \times 2$ cm cyst in the right thalamus identical in characteristics to the cyst of patient 1.

A CT guided stereotactic aspiration of the cyst was performed and 14 ml of colourless fluid obtained. A biopsy of the cyst wall showed a lining composed of a single layer of ependymal cells. Brain CT 72 hours postoperatively showed that the cyst did not collapse. A right ventriculofugular shunt was placed nine days later for persistent hydrocephalus.

Postoperatively, mentation, gait, and urinary continence improved, and one year later the neurological examination was normal. Brain MRI 24 months postoperatively showed no change in the size of the cyst.

Benign intracerebral or subarachnoid cysts lined by a single layer of ependymal or choroidal cells, with or without cilia, are classified as neuroepithelial cysts. These can occur throughout the CNS but are most common adjacent to the ventricles or the subarachnoid space, especially of the frontal lobes. The persistence of the cysts in both of our patients after shunting shows the characteristic lack of communication of neuroepithelial cysts with the subarachnoid space and ventricles.

Obstruction of the posterior third ventricle by the mass effect of the thalamic cysts led to obstructive hydrocephalus in both patients. Presenting signs were of increased intracranial pressure with papilloedema, loss of visual fields, and headaches in patient 1 and gait disturbance, change in mentation, and incontinence in patient 2 mimicking normal pressure hydrocephalus. Numaguchi *et al* reported two patients with smaller left thalamic cysts which were not associated with signs of increased intracranial pressure.² In addition to increased intracranial pressure from obstructive hydrocephalus, thalamic cysts produce neurological signs due to compression of the posterior thalamus. Patient 1 had contralateral lower extremity hyperreflexia, whereas one of the patients reported by Numaguchi *et al* had contralateral face and hemicranium pain.¹

Neuroepithelial cysts are considered to arise from the pinching off of a diverticulum from the neuroepithelium lining the primitive ventricular system, producing intracerebral or subarachnoid heterotopic rests of ependymal or choroidal cells. Friede and Yasargil suggest that the pinched off diverticulum is composed of a short segment of neuroepithelium of the wall of the neural tube equivalent to the tela choroidea, explaining the variation found in neuroepithelial cyst wall structure.² A cyst derived from the wall of the neural tube away from capillaries and choroid plexus would be lined with a ciliated or non-ciliated epithelium directly abutting glia, as in patient 2, whereas a basement membrane would be present if the segment of displaced neuroepithelium was adjacent to vascular structures.

Neuroepithelial cysts typically become symptomatic around the fourth decade of

life.³ It is perplexing that the onset of symptoms from such a congenital rest should be delayed; however, once symptoms start, they tend to progress rapidly.² The short duration of symptoms in both of our patients suggests cyst enlargement. The electron microscopic finding of pinocytotic vesicles in the cyst epithelium suggests transcellular fluid transport and supports the hypothesis of active fluid secretion into the cyst.⁴ The failure to enlarge early in life may indicate communication of the cyst with the ventricles or subarachnoid space which closes off in later life.

The goal of surgical treatment of thalamic cysts causing hydrocephalus is cyst decompression to alleviate obstruction of the third ventricle. Surgical options include cyst ventriculostomy, cyst-peritoneal and cyst-subarachnoid shunts, fenestration of the cyst to the ventricle, and stereotactic aspiration. Stereotactic cyst aspiration is a reasonable initial procedure for cyst decompression, supported by the continual collapse of the cyst in patient 1. If the cyst is not successfully decompressed by aspiration, the cyst or ventricular system can be shunted. It is not known why simple aspiration of a secreting cyst maintains collapse although recurrence of neuroepithelial cysts in other locations of the brain has been reported two to eight years after aspiration.⁵

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Antineutrophil cytoplasmic antibodies and the optic-spinal form of multiple sclerosis in Japan

A high incidence of the optic-spinal form of multiple sclerosis (OpS-MS) has been said to be one of the characteristic features of multiple sclerosis (MS) in Japan, whereas other aetiologies such as vasculitis should be considered in patients diagnosed with OpS-MS. Because antineutrophilic cytoplasmic antibodies (ANCAs) may be implicated in the pathogenesis of vasculitis,¹ we investigated ANCAs in serum samples from 13 patients with a diagnosis of clinically definite multiple sclerosis, who also had acute transverse myelopathy² and severe optic neuropathy (worse eye with maximal visual acuity less than 20/200) during their clinical course, and were in the active phase. The cerebrum, brainstem, and cerebellum were unaffected in all of the 13 patients. Serum samples from 26 other patients with conventional multiple sclerosis, and from nine patients with monophasic acute transverse myelopathy of unknown aetiology, also in

Demographical and laboratory findings of patients with OpS-MS

Patient	Sex	Age	AAO	Duration	p-ANCA	c-ANCA	ANA	aCL
1	F	79	76	2y 8m	—	—	1:80	—
2	F	57	48	8y 6m	—	—	—	—
3	F	61	58	3y 5m	+	—	1:320	+
4	F	27	20	6y 8m	—	—	—	+
5	F	56	56	5m	—	—	1:80	—
6	F	34	27	7y	—	—	—	—
7	M	36	30	6y	+	—	—	—
8	F	66	46	24y	—	—	—	—
9	F	56	52	4y 8m	+	—	—	—
10	M	21	19	2y 4m	—	—	—	—
11	F	58	46	11y 9m	+	—	1:320	—
12	M	58	55	3y 2m	+	—	1:640	—
13	F	54	52	2y	+	—	1:160	—

OpS-MS = the optic-spinal form of multiple sclerosis; AAO = age at onset; duration = duration of the illness; ANA = antinuclear antibody; aCL = anticardiolipin antibody.

the active phase, served as controls. Any patient taking an immunosuppressive drug or steroids during the month before the time of blood sampling was excluded. Serological testing for autoantibodies (rheumatoid factor (RF), anti-nuclear antibody (ANA), anti-double stranded DNA antibody, anti-Ro antibody (SS-A), anti-La antibody (SS-B), anticentromere antibody, antiribonucleoprotein antibody, and anticardiolipin antibody (aCL)) was performed in all patients. We considered an ANA titre of 1:80 or more by indirect immunofluorescence on Hep-2 cells as positive. Patients who were serologically positive for ANA without any other evidence of collagen diseases were enrolled in this study. Tests for anti-HTLV-1 antibodies were negative in all patients. The 13 patients with a diagnosis of OpS-MS comprised three men and 10 women aged between 21 and 79 (mean 51.0 (SD 16.7)) years. The age at onset of disease ranged from 19 to 76 (mean 45.0 (SD 16.7)) years and the duration of the illness ranged from 0.5 to 24 (mean 6.3 (SD 6.1)) years. The 26 patients with conventional multiple sclerosis comprised eight men and 18 women aged between 23 and 66 (mean 42.2 (SD 13.8)) years. The age at onset of disease ranged from 16 to 59 (mean 31.9 (SD 14.5)), and the duration of the illness ranged from 0.3 to 43 (mean 10.2 (SD 9.1)) years. In nine patients with acute transverse myelopathy, there were four men and five women aged between 21 and 59 (mean 40.2 (SD 13.3)) years. ANCA were detected by standardised indirect immunofluorescence,³ and were examined by the same experienced investigator (SM) without the knowledge of the clinical profiles. Two different staining patterns of ANCA were investigated: a cytoplasmic pattern (c-ANCA), and a perinuclear pattern (p-ANCA).¹

The table summarises the immunological laboratory findings of the 13 patients with a diagnosis of OpS-MS. Six of the 13 (46.2%) were positive for p-ANCA and no patients were positive for c-ANCA. Six patients were ANA positive, four among the p-ANCA positive patients and two among the p-ANCA negative patients ($p = 0.29$). Four patients were both p-ANCA positive and ANA positive and two patients were p-ANCA positive but ANA negative. Age at onset, age at the time of blood sampling, and duration of illness were similar between p-ANCA positive and p-ANCA negative patients. Titres of ANCA were not detectable in serum samples from the 26 patients with conventional multiple sclerosis and the nine patients with acute transverse myelopathy. Samples were positive for ANAs in three (11.5%) of the 26 patients with conventional multiple sclerosis and in none of the nine patients with acute trans-

verse myelopathy. Among the 39 patients in this study, the p-ANCA positive rate was similar between men and women. The mean age at blood sampling for p-ANCA positive patients was 53.8 (SD 9.0) years, and for negative patients, 43.5 (SD 15.6) ($P = 0.13$). The mean duration of illness of p-ANCA positive patients was 5.2 (SD 3.5) years and for negative patients, 9.6 (SD 8.8) years ($P = 0.23$). The p-ANCA positive patients were older at onset of disease (mean 48.8 SD (10.0) years) than p-ANCA negative patients (mean 33.9 (SD 16.2) years) ($P = 0.038$). The ANA positive rate was significantly higher in p-ANCA positive patients (4 of 6; 66.7%) than in p-ANCA negative patients (3 of 33; 9.1%) ($P = 0.018$). The p-ANCA positive rate was significantly higher (46.2%) in the 13 patients with OpS-MS than in the 26 patients with conventional multiple sclerosis ($P = 0.0005$). The ANA positive rate was significantly higher in patients with OpS-MS (46.2%) than in patients with conventional multiple sclerosis (11.5%) ($P = 0.04$). Other tests for autoantibodies were negative in all 48 patients.

We found a significantly higher p-ANCA positive rate (46.2%) among patients with a diagnosis of OpS-MS, compared with that (0%) among the 26 patients with conventional multiple sclerosis ($p = 0.0005$), and p-ANCA was not detectable in serum samples from the nine patients with acute transverse myelopathy of unknown aetiology, suggesting that the positivity for p-ANCA was not an epiphenomenon. As p-ANCA may be involved in the pathogenesis, at least of vasculitis,¹ a possible pathogenetic role of ANCA associated vasculopathy in patients with p-ANCA positivity should be considered. Six of the 13 patients with OpS-MS, were ANA positive, among whom four were p-ANCA positive and two were p-ANCA negative. Other collagen screening studies were negative. Although ANAs can produce a staining pattern in indirect immunofluorescence that is difficult to distinguish from that of p-ANCA⁴ and the frequency of positive ANAs was significantly higher in patients with positive p-ANCA than in patients with negative p-ANCA, two patients were p-ANCA positive without being ANA positive. This indicated that being ANA positive could not explain the p-ANCA positivity. The ANA positive rate among patients with OpS-MS was also significantly higher (46.2%) than that among patients with conventional multiple sclerosis (11.5%) in our series. Therefore, vasculopathy may play an important part in patients who are positive for p-ANCA, ANAs, or both. Further investigations on the antigenic specificities of p-ANCA which were positive in this study are also important.^{4,5}

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Cerebral venous sinus thrombosis associated with factor V gene mutation

Activated protein C resistance, caused by a mutation in the gene coding for protein C cofactor (factor V), has recently been found to be a major cause of familial thrombophilia.¹ One previous case of cerebral venous thrombosis, occurring in a woman taking the oral contraceptive pill who was a heterozygous carrier of the factor V mutation, has been described.² We present a case of cerebral venous thrombosis in a patient homozygous for the factor V mutation who was taking hormone replacement therapy.

A 45 year old woman was admitted with a two day history of headache. On the morning of admission she awoke with vomiting and an unsteady gait. Later that morning she became drowsy. She was premenopausal, had a history of migraine, and was a non-smoker. She had started hormone replacement therapy (oestradiol and oestradiol with norethisterone acetate) three months earlier for premenstrual exacerbations of migraine. There was no history of deep vein thrombosis, but a paternal grandmother had had a deep venous thrombosis, and her mother had had two episodes of thrombophlebitis. A brother (later found to be homozygous for the factor V mutation) had recently had a thrombosis of a superficial short saphenous vein. Neither her father nor her two other brothers had a history of venous thrombosis. On examination she was conscious but verbal responses were limited to "yes". She had roving eye movements with intact reflex ocular movements. There was a left hemiplegia. Both plantar responses were extensor.

Brain CT showed hypodensity within both thalami, the right internal capsule, and the left parietal region consistent with infarction. Lateral and third ventricles were