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Slowly progressive Foix–Chavany–Marie syndrome associated with chronic herpes simplex encephalitis

Foix–Chavany–Marie syndrome (FCMS) is characterised clinically by automatic voluntary dissociation of orofacial motility. It is caused by bilateral anterior opercular lesions and its aetiology is heterogeneous.[1]

Clinically, most cases of FCMS can be divided into three categories—*developmental*, *acute/subacute*, and *transient*.[2] The most common cause of the developmental form is congenital bilateral anterior opercular dysplasia. The acute/subacute form is usually caused by infection in the CNS or cerebrovascular disease. The underlying pathogenesis of transient form is epilepsy. Rare variant cases of FCMS presenting with a slowly progressive clinical course have also been reported.[3] We describe the clinical features of a patient with adult onset, slowly progressive FCMS, thought to be associated with chronic herpes simplex encephalitis.

A 29 year old Japanese woman developed epilepsy of generalised tonic-clonic type at the age of 15 and had been taking anticonvulsants for 14 years. She had had a normal pregnancy and delivery. Developmental assessment during schooling showed normal motor and psychological ability.

At the age of 27, she presented with dysarthria and dysphagia, which deteriorated gradually during the following 18 months. She also had difficulty with fine movements of her right arm at the age of 29. On admission, her voluntary orofacial motility was disturbed bilaterally, while emotional and involuntary facial movements were well preserved. Movement of the pharynx was slightly disturbed and gag and pharyngeal reflexes were reduced. She had difficulty in moving her tongue laterally. The other cranial nerves were normal. There was no sensory deficit or weakness in the limbs. Deep tendon reflexes of her right arm were slightly increased and her plantar responses were flexor. Rapid alternating movements of the right arm showed some clumsiness. A full scale IQ on the Wechsler adult intelligence scale, revised (WAIS-R) was 80, with a verbal IQ of 85 and a performance IQ of 78. There was no similar disorder in her family members.

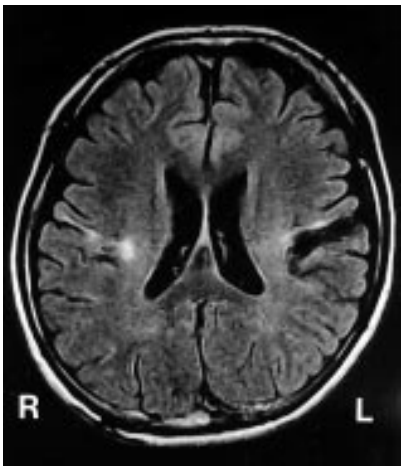

Figure 1 Magnetic resonance imaging on FLAIR sequences, showing linear high intensity lesions in the rolandic area bilaterally and severe atrophy of the operculum bilaterally. Diffuse atrophy of the frontotemporal lobes was also observed.

The concentration of IgG (7.9 mg/dl) and the IgG index (1.89) in the CSF were increased, while the protein level in the CSF (30 mg/l) and the cell count (2/mm^3) were normal. IgG antibody titres for herpes simplex virus (HSV), measured by enzyme linked immunosorbent assay (ELISA) in the serum (64.6) and CSF (6.4), were also raised. The serum to CSF ratio of the HSV IgG titre was decreased at 10.1, and the IgG index for HSV was increased at 3.28. IgM was negative. Polymerase chain reaction (PCR) methods did not reveal genomes for HSV 1 or 2 in the CSF. Antibodies to other virus were not detected and antibody testing for HIV was negative in the serum.

An EEG showed generalised mild slowing without paroxysmal activity. Magnetic resonance imaging (MRI) on FLAIR sequences revealed bilateral linear high intensity lesions in the rolandic area and severe atrophy of the operculum bilaterally, in addition to mild frontotemporal lobe atrophy (fig 1). These lesions on T1 weighted sequences showed no contrast enhancement after gadolinium administration. There was a partial defect in the body of the corpus callosum.

Treatment with acyclovir was begun but was suspended immediately because of a drug eruption. Treatment with intravenous vidarabine for 14 days was tried twice, and transient decreases of both IgG antibody titre and the IgG index for HSV in the CSF were observed on each occasion. There was no further deterioration in her neurological state after these treatments.

Comment

Neurological examination in our patient showed automatic voluntary dissociation of orofacial motility in addition to a disturbance of movement of the pharynx and tongue. An MRI study showed involvement of the opercular and rolandic regions bilaterally. This combination of clinical and neuroradiological features is typical of FCMS. However, our patient is unusual for two reasons. First, the clinical course of the FCMS was of adult onset and was slowly progressive; this type of deterioration has not been reported previously either in congenital dysplasia or in acquired acute/subacute CNS event such as stroke or infection.[1] Although some cases with adult onset and a slowly progressive course have been reported, the aetiology of those cases remained obscure.[3] Second, elevation of the IgG antibody titre and the IgG index for herpes simplex virus in the CSF showed the presence of chronic herpes simplex encephalitis. The temporal lobe is the favoured region for this. FCMS with an acute clinical course caused by herpes simplex encephalitis has been reported.[4]

Transient decreases in both IgG antibody titre and the IgG index for HSV after intravenous vidarabine were observed on both occasions the treatment was given. Although the correlation between increased IgG antibody for herpes simplex virus in the CSF and the chronic cerebral disturbance has not been verified, these observations support the view that chronic herpes simplex encephalitis remained active in our patient and could have been responsible for her neurological impairment. The clinical features—including the slowly progressive clinical course, the negative results of PCR testing for HSV, and the normal protein level and the cell count in the CSF—suggest that herpes simplex encephalitis was not the direct cause of the damage in the affected region. It is possible that persistent HSV infection may induce inappropriate activation of the immune system, resulting in neurocytotoxity because of cross reactivity.

Our patient had both a partial defect of the corpus callosum and epilepsy. This combination is often observed in patients with congenital cerebral dysplasia. However, the onset of developmental FCMS is always in the early infant period and is usually associated with delayed psychomotor milestones or mental retardation.[5] Thus the pathogenesis in our patient is very unlikely to be explained on the basis of simple congenital dysplasia. The association between a partial defect of the corpus callosum and epilepsy in FCMS could be explained by the presence of herpes simplex virus infection dating from the fetal period. Although a necropsy proven case of FCMS that was probably caused by chronic herpes simplex encephalitis has been reported before,[2] the clinical course in that case was not slowly progressive. In fact there have been no previous reports of slowly progressive FCMS associated with chronic viral infection.

In conclusion, this is the first report of a case of FCMS associated with chronic herpes simplex encephalitis. Further similar cases would establish this as a variant type of FCMS.

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Lesion responsible for WEMINO syndrome confirmed by magnetic resonance imaging

WEMINO (wall eyed monocular internuclear ophthalmoplegia) syndrome is a rare neurological impairment involving disconjugate ocular movements.[1] Neuroradiological findings of the lesion responsible for WEMINO syndrome have not been reported to date. We report a case of the syndrome in which cerebral magnetic resonance imaging (MRI) clearly showed a tiny isolated lesion causing this impairment.

The patient was a 61 year old Japanese man who had been admitted to hospital for surgery for mitral regurgitation. He had a two year history of mitral incompetence, and mitral valve plasty was completed successfully on 21 September 2000. There were no postoperative problems.

On the afternoon of 27 September, one week after the operation, he suddenly experienced double vision, and was found to have left exotropia without blepharoptosis. On neurological examination, adduction of left eye was disturbed and it could not move beyond the midline of orbit, although full abduction was possible. Bilateral upward nystagmus was noted on forward gaze. Right ocular movement was not disturbed in any direction, but horizontal nystagmus appeared on rightward gaze. There was deficiency of left convergence. No ptosis occurred at any time. His pupils showed isocoria and responded promptly to light. Vertical ocular movement was not disturbed in either eye (fig 1A). Other neurological findings were completely normal. His ocular symptoms were summarised as comprising a left internuclear ophthalmoplegia with ipsilateral exotropia; these findings have been termed WEMINO syndrome.[1]

Cerebral computed tomography, undertaken immediately after onset, did not show any abnormalities.

We considered that he might have had a cerebral embolus caused by microthromboembolism following the heart surgery, but echocardiography did not show any obvious thrombus. We speculated that the responsible lesion was isolated in the area that included the medial longitudinal fasciculus because his impairments were limited to the ocular symptoms described above. He had been given warfarin potassium since 25 September, but the anticoagulant effect was insufficient on the day of symptom onset. Thus heparin sodium was begun intravenously in a dose of 10 000 units/day, and the dose of warfarin was gradually increased.

MRI performed 20 hours after onset showed a tiny isolated lesion at the left paramedian pontine tegmentum just adjacent to the fourth ventricle on both fluid attenuated inversion recovery (FLAIR) imaging and diffusion weighted MRI (fig 1B). This corresponds to the anatomical area of the medial longitudinal fasciculus. The tiny lesion showed high signal intensity on FLAIR imaging and diffusion weighted MRI, and low signal intensity on T1 weighted MRI. These MRI findings are typical of an acute lesion resulting from cerebral infarction. Other parts of the brain showed no abnormalities. Cerebral magnetic resonance angiography showed neither stenosis nor occlusion of any of the major vessels.

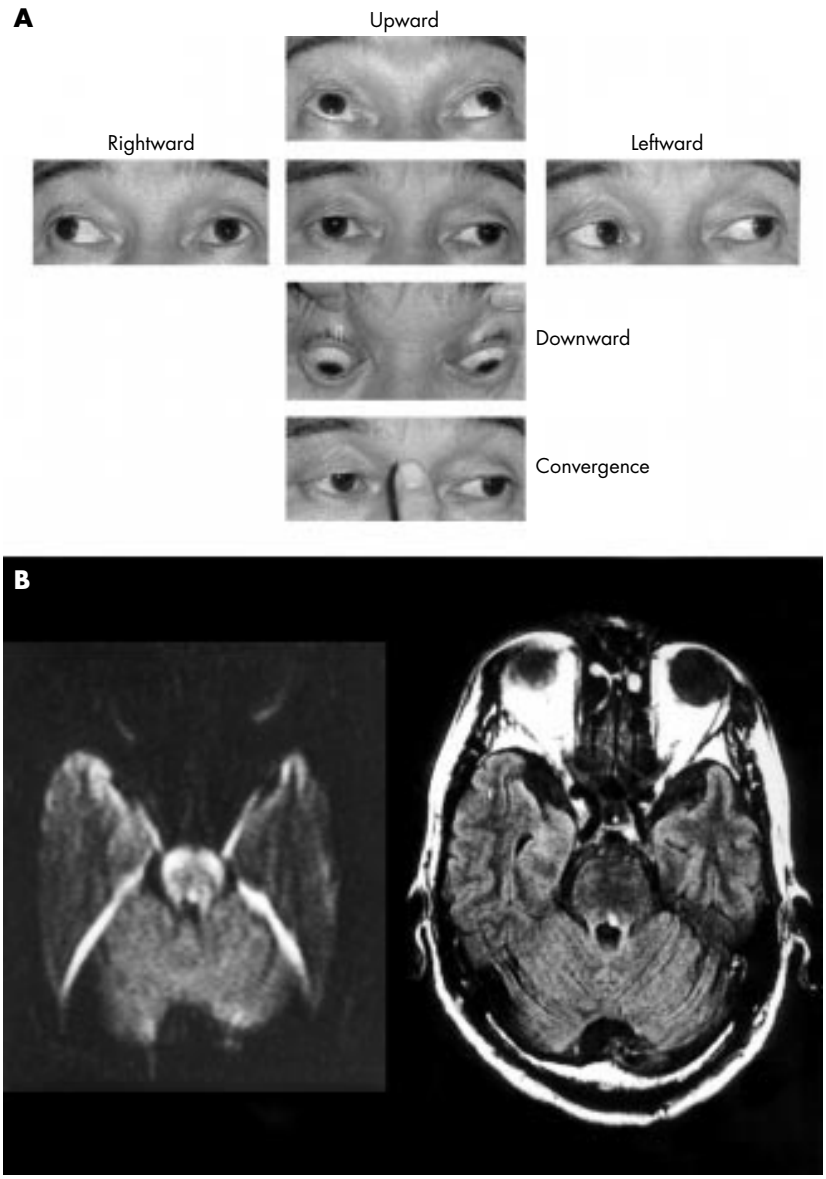

Figure 1 (A) Ocular impairment in the patient at the time of onset. Left exotropia was present on forward gaze without blepharoptosis. Adduction of left eye was disturbed and it never reached beyond the midline of the orbit, although full abduction was possible. Right ocular movement was not disturbed in any direction, but horizontal nystagmus appeared on rightward gaze. There was deficiency of left convergence. Vertical ocular movement of both eyes was undisturbed. (B) Cerebral magnetic resonance imaging (MRI): a tiny isolated lesion was present at the left paramedian pontine tegmentum just adjacent to the fourth ventricle on both axial fluid attenuated inversion recovery (FLAIR) imaging (right) and diffusion weighted MRI (left). The tiny lesion causing WEMINO syndrome showed high signal intensity on both MRI modes.

The ocular impairment began to improve by the third day after onset. On the seventh day, the left exotropia on forward gaze had disappeared, and the left internuclear ophthalmoplegia had begun to improve. By the 13th day, eye position and ocular movement were completely normal, and on the 14th day the high signal intensity on FLAIR MRI had diminished.

There are various syndromes that involve disconjugate ocular movement and eye position simultaneously. WEMINO syndrome consists of symptoms similar to internuclear ophthalmoplegia with ipsilateral exotropia.[1] There are two other syndromes supposedly involving a combination of injury to the medial longitudinal fasciculus and exotropia; these are paralytic pontine exotropia (PPE),[2 3] and non-paralytic pontine exotropia (NPPE).[4 5] However, WEMINO syndrome can be discriminated from both PPE and NPPE, because the latter show exotropia on the side contralateral to the injured medial longitudinal fasciculus. There have been few reports describing WEMINO syndrome, and up to