

Short report

Pontine lesion in opsoclonus-myoclonus syndrome shown by MRI

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SUMMARY Two patients with opsoclonus-myoclonus syndrome are reported whose magnetic resonance imaging (MRI) showed brain stem lesions. Both patients developed the opsoclonus-myoclonus syndrome after an upper respiratory illness. One case had visual hallucinations during the course of illness and MRI revealed a focal lesion in the pons involving the junction of basis and tegmentum. MRI of the second case showed a focal lesion at the upper pontine tegmentum.

Opsoclonus, originally described by Orzechowski¹ is a rapid, irregular and chaotic eye movement that occurs in all directions. Opsoclonus associated with generalised myoclonus is well known as the opsoclonus-myoclonus syndrome, which occurs in association with viral and bacterial infections of the central nervous system, postinfectious encephalitis, intracranial tumours, hydrocephalus, thalamic haemorrhage, multiple sclerosis, and toxic encephalopathies.² The site of the responsible lesion, however, has been a matter of controversy; cerebellum,³⁻⁵ midbrain,^{6,7} thalamus and midbrain,⁸ have been suggested, as well as a combination of several sites in the central nervous system.² We report two recent cases of opsoclonus-myoclonus syndrome whose magnetic resonance imaging (MRI) showed pontine tegmentum lesions. We will discuss the pathophysiology of opsoclonus and myoclonus based on the MRI findings. This appears to be the first report of MRI in patients with opsoclonus-myoclonus syndrome.

Case reports

Case 1: A 73 year old male, whose chief complaint was body tremulousness and oscillopsia. Past history and family history were unremarkable. On 12 March 1985 the patient

had a cough and diarrhoea. The following day he noted oscillopsia and body tremulousness, which had worsened and he had become unable to walk nor stay in the sitting position. He was admitted to the local hospital on 19 March 1985 and became slightly drowsy; because of body tremulousness he was unable to use chopsticks during meals so that he had to use a spoon. Oscillopsia was worse when changing visual fixation or during neck movement. For a few days at the beginning of April he had visual hallucinations before falling asleep. He saw a big rock or toy monsters moving in front of him. They were vivid, colourful, and non-threatening hallucinations. He was transferred to our hospital on 30 April.

Neurological examination on admission revealed that the patient was alert and there was no nuchal rigidity. He had abnormal bursts of eye movements. The eyes showed frequent rapid horizontal pendular oscillations but occasionally rapid conjugate vertical, rotatory or oblique movements. The abnormal eye movements were more prominent when changing fixation, closing eyes or during emotional stress but absent during sleep. The patient also had myoclonus of the neck, trunk and all the extremities which was initiated by movement, attempts at movement, and even the intention to move. The myoclonus was absent during relaxed recumbent posture or during sleep and induced by sudden noise, visual threat and pin prick stimuli. The myoclonus was more marked in the proximal rather than the distal limb muscles. He could stand but was unable to walk because of the myoclonus. The muscle tone in the resting posture and deep tendon reflexes of the four extremities were slightly decreased. Finger to nose and heel to knee tests showed mild to moderate oscillations due to myoclonus and incoordination. There was no palatal myoclonus. Sensory examination was normal.

Laboratory examination revealed that the peripheral blood count was normal except for mild leukocytosis.

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Received 25 March 1988
Accepted 20 June 1988

Erythrocyte sedimentation rate was 43/1h and CRP was 5+ but other routine blood and urine tests were normal. Serum viral titres for influenza A and B, mumps, adenovirus, measles, VB, mumps, adenovirus, measles, varicella, RS, cytomegalovirus, polio virus, herpes simplex virus, Epstein-Barr virus and Japanese encephalitis were all negative. Cerebrospinal fluid contained 6 mm³ (all lymphocyte) cell, 37/dl protein, 76 mg/dl glucose. The electroencephalogram showed mild diffuse slow abnormalities. Surface electromyography of the sternocleidomastoid, biceps brachii, triceps brachii, pectoralis major, quadriceps femoris and hamstrings revealed about 3–7 Hz asynchronous irregular repetitive group discharges with no apparent reciprocities (fig 1). Cranial computed tomography (GE CT/8800) showed mild enlargement of the third and lateral ventricles, and a small round area of low attenuation in the right putamen consistent with an old lacunar infarction but no abnormality in any other regions including the brain stem and cerebellum. MRI operating at 0.25 tesla, VISTA-MR, on the 75th day from the onset of the disease, with an axial T2 weighted spin echo (SE) image with a repetition time of 2.0 s and an echo time of 80 ms showed an area with increased signal in the right putamen (old lacunar infarction) and pons near the junction of basis and tegmentum (fig 2a). Axial T1 weighted inversion recovery (IR) MRI, however, demonstrated no decreased nor increased signal lesions in any other regions.

There was gradual spontaneous recovery of both abnormal eye movements and myoclonus, and the patient was able to walk by himself one month after admission and was then discharged.

Case 2: A 32 year old male complained of body tremulousness and oscillopsia. His past history and family history were unremarkable. On 3 June 1987 the patient had a sore throat and fever of 38.5°C. He was treated for tonsillitis. On 3 July he started to have an oscillopsia and body tremulousness which increased rapidly. On 6 July he was admitted to the local hospital, unable to stand or sit. He also developed

urinary retention. He was transferred to our hospital on 16 July, where neurological examination showed that the patient was alert, well oriented, without fever or nuchal rigidity. Abnormal conjugate agitation of the eyes was present in the primary position. There were mainly horizontal pendular oscillations, but occasionally vertical, rotatory or oblique movements were observed. The abnormal eye movements were increased by changing fixation, and emotional stimuli, and persisted even during eye closure. There was no palatal myoclonus but outstretched tongue showed myoclonic movements. The patient had myoclonus of the neck, trunk and all extremities during voluntary movement, attempts at movement, which was absent while in a relaxed recumbent posture, and during sleep. The myoclonus was more marked in the proximal than the distal muscles. Mild to moderate incoordination was noted in finger to nose and heel to shin tests. Walking was almost impossible because of the myoclonus. Muscle tone in resting posture, power, deep tendon reflexes and sensory examinations were normal. The patient had urinary retention with an indwelling catheter.

Laboratory examination revealed a peripheral white blood cell count of 8100/mm³. Erythrocyte sedimentation rate was 20 mm/lh. CRP was 1+. Other routine blood and urine tests were normal. Immunoglobulin was normal. Serological tests for syphilis were negative. Serum viral titres for Influenza A and B, mumps, Coxsack B, Epstein-Barr virus were normal. Cerebrospinal fluid examination on the 8th hospital day showed cells 13/mm³ and protein 94 mg/dl. Cranial computed tomography, electroencephalogram, auditory brain stem response and sensory cortical evoked response in the upper extremity were all normal. Electro-oculography showed continuous abnormal eye movements without intersaccadic latencies which was exaggerated by fixation, calculation and eye-closure. Surface electromyography on biceps brachii, triceps brachii, quadriceps femoris and hamstrings showed repetitive irregular group discharges with no apparent reciprocities. Blink reflex test showed reduced



Fig 1 Surface electromyography of case 1 during standing. Irregular repetitive group discharges were noted in sternocleidomastoid (SCM), biceps brachii, triceps brachii, pectoralis major, quadriceps femoris and hamstrings. There was no apparent reciprocal discharges between agonist and antagonist muscles.

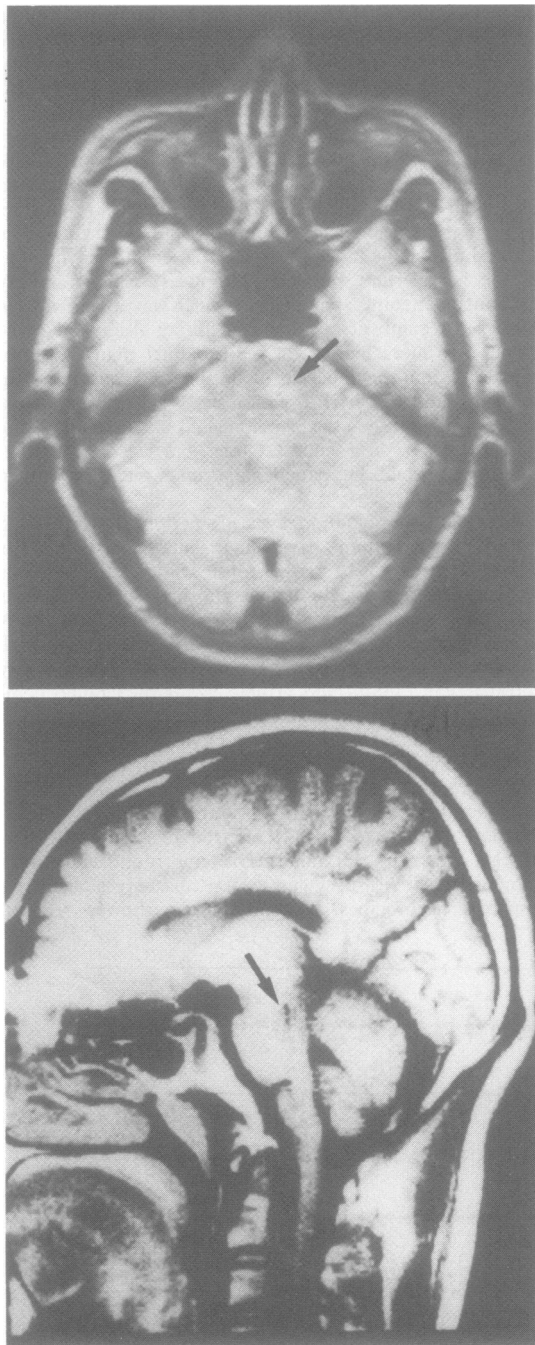


Fig 2 (a) Transverse T2 weighted spin echo MRI of case 1. Note increased signal intensity in the pons near the junction of basis and tegmentum (arrow). (b) Midline sagittal T1 weighted spin echo MRI of case 2. Note decreased signal intensity in the region of the tegmentum of upper pons (arrow).

appearance rate of R_1 but latencies of R_1 and R_2 were abnormal. Urodynamic study revealed detrusor-sphincter dyssynergia but normal cystometrogram. MRI on the 7th day from the onset of the disease, using T1 weighted SE MRI with a repetition time of 500 ms and an echo time of 50 ms showed a decreased signal lesion in the upper pontine tegmentum near the basis with no mass effect (fig 2b).

The patient showed gradual spontaneous recovery and began to urinate himself on the 5th hospital day. The abnormal eye movements appeared to respond to 1 mg clonazepam administration. The myoclonic movements also decreased and the patient was able to walk by himself on the 28th hospital day and was soon discharged.

Discussion

The abnormal eye movement of our patients which consisted of involuntary rapid conjugate movement in all directions without any definite rhythm and were exaggerated when changing fixation, persisted during eye closure and absent during sleep. These are consistent with the features of opsoclonus previously described.^{1,5,9} The anatomical basis of opsoclonus is still a matter of controversy. The frequent association of opsoclonus with cerebellar ataxia suggests that opsoclonus is a sign of cerebellar involvement.³⁻⁵ However, the pathological findings and known anatomical correlates of the control of saccadic eye movements make it difficult to correlate opsoclonus with cerebellum disorder.² According to Zee and Robinson¹⁰ three types of saccade-related neurons (burst cells, pause cells, and tonic cells) can be found within the pontine paramedian reticular formation (PPRF). Burst cells initiate saccades, and pause cells inhibit burst cells. The authors postulate that a disease of pause cells is responsible for flutter-like oscillation or opsoclonus. The pontine lesions of MRI in both our patients seem to include PPRF at least partially. Therefore their abnormal eye movements could well be explained by the theory of Zee and Robinson.¹⁰

The myoclonic movements of our patients were initiated by voluntary movement, attempts at movement and absent during relaxed recumbent posture or during sleep. These are the typical features of action or intention myoclonus. The anatomical basis of action myoclonus has not yet been established and the condition is usually associated with diffuse neuronal disease such as post-hypoxic encephalopathy, uraemia, and various forms of progressive myoclonic epilepsy.¹¹ The underlying disorder appears to be a loss of inhibitory mechanisms involving serotonin and possibly γ -aminobutyric acid.¹¹ The brain stem lesions in our patients seem to include brain stem serotonergic neurons, raphe nucleus, so that the action myoclonus of our patients could be caused by the lesions shown in MRI.

Visual hallucination in case 1 could have been a peduncular hallucination because it was of a vivid,

colourful, non-threatening nature. Peduncular hallucination is usually seen in midbrain lesions¹² but can also be seen in pontine tegmentum lesions.¹³ Therefore the brain stem lesions in our two cases could explain not only opsoclonus but also myoclonus and visual hallucination altogether.

The clinical as well as laboratory findings indicate that our patients suffered from post-infectious or benign encephalitis so that there may be more widespread neural dysfunctions other than the lesions shown by MRI, which may contribute to the production of opsoclonus-myoclonus syndrome. Dropcho *et al*² postulated that functional or structural disruption of several sites in the CNS can result in the clinical picture of opsoclonus. Our MRI findings, however, confirm that the pontine tegmentum lesion plays a definite key role in the production of opsoclonus-myoclonus syndrome at least in our cases.

We thank Dr K Munakata, Department of Neurosurgery, Maruyama Kinen Sogobyoin for referring the second patient.

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