Case Report

Ataxia and deafness in a young male: An unusual aetiology

Department of Medicine, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi - 2, India

We report here a case of 18 year old male with tremors of hands, deafness, tendency to fall while walking, drowsiness and double vision of total duration 1½ years. The tremors were bilateral, insidious in onset, gradually progressive, exacerbated on motion, interfered in his day-to-day activities. He also complained of deafness for one year. For last six months, he noticed a tendency to fall while walking, felt drowsy for most part of the day and had double vision. There was no history of associated lower cranial nerve palsy, no bowel/bladder involvement or similar history in the family. There was no history of trauma to neck/spine, fever, headache, vomitings.

On examination, vital examination was unremarkable. Detailed neurological examination revealed conscious oriented male with normal higher mental functions. Patient had internuclear ophthalmoplegia, with broken saccades and horizontal nystagmus to left. Pupillary reactions were normal and fundus examination did not reveal optic neuritis/atrophy or peripheral retinal degeneration. Jaw jerk was absent. On motor examination, patient had hypertonia and hyperreflexia in all four limbs with bilateral positive Babinski's and Hoffman's signs. Tests for coordination revealed intention tremors, past-pointing, dysdiakinesia, positive finger-nose and heel-shin tests on both sides. Patient had a drunken gait, was unable to perform tandem walking with increased tendency to fall but had no preferential direction of fall. There was no sensory neurological deficit. Patient did not have a short neck or low hair line, no restriction of neck movements, no signs of meningeal irritation or sensory neurological deficit were present. MRI head and cervical spine with gadolinium enhancement revealed demyelination as evident from multiple oblong foci isointense on T1-weighted images and hyperintense on T2-weighted and fluid attenuated inversion recovery sequences in corpus callosum, sub-cortical white matter, right thalamus, pons and periaqueductal region of midbrain. Ill-defined linear hyperintense signals were observed in cervical spinal cord. No skeletal abnormality was noted in the skull or cervical spine. Oligoclonal bands were present in the cerebrospinal fluid. Haematological, biochemical and metabolic parameters, electrocardiography and chest radiography were normal. Various radiological views of cervical spine did not reveal any craniovertebral junction anomaly. Enzyme-linked immunosorbent assay for HIV, VDRL, antinuclear antibody testing and connective tissue profile were negative. MRI head and cervical spine with gadolinium enhancement revealed multiple oblong foci isointense on T1-weighted images and hyperintense on T2-weighted and fluid attenuated inversion recovery sequences in corpus callosum with perivenular extension into deep white matter [Figure 1], sub-cortical white matter [Figure 2], right thalamus, pons and periaqueductal region of midbrain. Medulla, bilateral cerebellum and basal ganglia and the ventricular system were normal. Ill-defined linear hyperintense signals were also noted in cervical

Key words: Ataxia, deafness, internuclear ophthalmoplegia, primary progressive multiple sclerosis

Introduction

Multiple sclerosis (MS) was first reported in India in 1954.1 Recently, there has been a spurt in documentation of these cases with easy accessibility of magnetic resonance imaging (MRI) scans and electrophysiological studies. MS may have varied presentations and we report here an unusual presentation of MS in a young male.

Case Report

An 18 year old male mechanic, resident of Muzaffarnagar, Uttar Pradesh presented with tremors of hands for 1½ years. The tremors were bilateral, insidious in onset, gradually progressive, exacerbated on motion, interfered in his day-to-day activities. He also complained of deafness for one year. For last six months, he noticed a tendency to fall while walking, felt drowsy for most part of the day and had double vision. There was no history of associated lower cranial nerve palsy, no bowel/bladder involvement or similar history in the family. There was no history of trauma to neck/spine, fever, headache, vomitings.

On examination, vital examination was unremarkable. Detailed neurological examination revealed conscious oriented male with normal higher mental functions. Patient had internuclear ophthalmoplegia, with broken saccades and horizontal nystagmus to left. Pupillary reactions were normal and fundus examination did not reveal optic neuritis/atrophy or peripheral retinal degeneration. Jaw jerk was absent. On motor examination, patient had hypertonia and hyperreflexia in all four limbs with bilateral positive Babinski’s and Hoffman’s signs. Tests for coordination revealed intention tremors, past-pointing, dysdiakinesia, positive finger-nose and heel-shin tests on both sides. Patient had a drunken gait, was unable to perform tandem walking with increased tendency to fall but had no preferential direction of fall. There was no sensory neurological deficit. Patient did not have a short neck or low hair line, no restriction of neck movements, no signs of meningeal irritation or sensory neurological deficit were present. MRI head and cervical spine with gadolinium enhancement revealed demyelination as evident from multiple oblong foci isointense on T1-weighted images and hyperintense on T2-weighted and fluid attenuated inversion recovery sequences in corpus callosum with perivenular extension into deep white matter [Figure 1], sub-cortical white matter [Figure 2], right thalamus, pons and periaqueductal region of midbrain. Medulla, bilateral cerebellum and basal ganglia and the ventricular system were normal. Ill-defined linear hyperintense signals were also noted in cervical

Haematological, biochemical and metabolic parameters, electrocardiography and chest radiography were normal. Various radiological views of cervical spine did not reveal any craniovertebral junction anomaly. Enzyme-linked immunosorbent assay for HIV, VDRL, antinuclear antibody testing and connective tissue profile were negative. MRI head and cervical spine with gadolinium enhancement revealed multiple oblong foci isointense on T1-weighted images and hyperintense on T2-weighted and fluid attenuated inversion recovery sequences in corpus callosum with perivenular extension into deep white matter [Figure 1], sub-cortical white matter [Figure 2], right thalamus, pons and periaqueductal region of midbrain. Medulla, bilateral cerebellum and basal ganglia and the ventricular system were normal. Ill-defined linear hyperintense signals were also noted in cervical
Prakash A, et al.: Ataxia and deafness unusual aetiology

spinal cord opposite C2-C3 vertebral bodies. There was no skeletal abnormality noted in the skull or cervical spine. The imaging study was suggestive of a demyelinating disorder, multiple sclerosis. Cerebrospinal fluid analysis was normocellular with protein content- 40 mg/dl; glucose- 51 mg/dl, with oligoclonal bands; Cerebrospinal fluid (CSF) IgG index was not done. Brainstem auditory evoked potentials revealed increased interwave latency (LV wave) in both ears (5.35 milliseconds in the left and 5.53 milliseconds in the right). Visual evoked potentials were normal for both the eyes.

The clinical history and examination suggested a progressive disorder involving corticospinal and spino cerebellar tracts with internuclear opthalmoplegia and sensorineural deafness without any remissions. Investigations revealed abnormal brain-stem auditory evoked potentials, oligoclonal bands in the cerebrospinal fluid and MRI evidence of demyelinating plaques. Hence, a diagnosis of primary progressive multiple sclerosis (PPMS) was made.

**Discussion**

MS is a disorder of the central nervous system manifesting as acute focal inflammatory demyelination and axonal loss with limited remyelination, culminating in chronic multifocal sclerotic plaques from which the disease gets its name. It typically presents with intermittent episodes of neurologic dysfunction, so-called “relapsing-remitting” MS. In most patients, after a variable number of years, there follows a secondary progressive deterioration. PPMS is seen in 10% of multiple sclerosis patients and is characterized by gradual deterioration from the onset of disease. The consensus definition for PPMS in 1996 was gradual nearly continuously worsening disease progression from onset with occasional plateaus and temporary minor improvements allowed, but no distinct relapses. PPMS usually involves the spinal cord and less frequently the optic nerve, cerebrum or cerebellum.

In its typical form, multiple sclerosis is believed to have an immune-mediated inflammatory origin; however, inflammation is believed to have a less important role in PPMS. Because PPMS affects an older (predominantly male) population, has a less favourable prognosis and is associated with fewer radiological and histological inflammatory lesions, this type has been considered to be a separate disorder. It is believed that differences in the immunogenetic background of patients influence the susceptibility of developing either typical or primary progressive multiple sclerosis.

The characteristic clinical and paraclinical evidence for at least two demyelinating lesions, affecting different sites within the brain or spinal cord, separated in time; in a young patient qualifies for diagnosis of MS. The best known diagnostic criteria for MS are those of Schumacher and Poser. However, the criteria for diagnosis of PPMS are different because of its relentless progression without any relapses or remissions. The criteria for PPMS have recently been defined and three levels of characterization have been made—“Definite PPMS”, “Probable PPMS” and “Possible PPMS” [Table 1]. As per the criteria outlined, the present case had “Definite PPMS” in view of clinical progression for over one year, positive CSF evidence for oligoclonal bands and positive MRI evidence. Besides, our case did not have acute focal inflammatory demyelination and axonal loss with limited remyelination, culminating in chronic multifocal sclerotic plaques from which the disease gets its name.

It typically presents with intermittent episodes of neurologic dysfunction, so-called “relapsing-remitting” MS. In most patients, after a variable number of years, there follows a secondary progressive deterioration. PPMS is seen in 10% of multiple sclerosis patients and is characterized by gradual deterioration from the onset of disease. The consensus definition for PPMS in 1996 was gradual nearly continuously worsening disease progression from onset with occasional plateaus and temporary minor improvements allowed, but no distinct relapses. PPMS usually involves the spinal cord and less frequently the optic nerve, cerebrum or cerebellum.

In its typical form, multiple sclerosis is believed to have an immune-mediated inflammatory origin; however, inflammation is believed to have a less important role in PPMS. Because PPMS affects an older (predominantly male) population, has a less favourable prognosis and is associated with fewer radiological and histological inflammatory lesions, this type has been considered to be a separate disorder. It is believed that differences in the immunogenetic background of patients influence the susceptibility of developing either typical or primary progressive multiple sclerosis.

The characteristic clinical and paraclinical evidence for at least two demyelinating lesions, affecting different sites within the brain or spinal cord, separated in time; in a young patient qualifies for diagnosis of MS. The best known diagnostic criteria for MS are those of Schumacher and Poser. However, the criteria for diagnosis of PPMS are different because of its relentless progression without any relapses or remissions. The criteria for PPMS have recently been defined and three levels of characterization have been made—“Definite PPMS”, “Probable PPMS” and “Possible PPMS” [Table 1]. As per the criteria outlined, the present case had “Definite PPMS” in view of clinical progression for over one year, positive CSF evidence for oligoclonal bands and positive MRI evidence. Besides, our case did not have acute focal inflammatory demyelination and axonal loss with limited remyelination, culminating in chronic multifocal sclerotic plaques from which the disease gets its name.

It typically presents with intermittent episodes of neurologic dysfunction, so-called “relapsing-remitting” MS. In most patients, after a variable number of years, there follows a secondary progressive deterioration. PPMS is seen in 10% of multiple sclerosis patients and is characterized by gradual deterioration from the onset of disease. The consensus definition for PPMS in 1996 was gradual nearly continuously worsening disease progression from onset with occasional plateaus and temporary minor improvements allowed, but no distinct relapses. PPMS usually involves the spinal cord and less frequently the optic nerve, cerebrum or cerebellum.

In its typical form, multiple sclerosis is believed to have an immune-mediated inflammatory origin; however, inflammation is believed to have a less important role in PPMS. Because PPMS affects an older (predominantly male) population, has a less favourable prognosis and is associated with fewer radiological and histological inflammatory lesions, this type has been considered to be a separate disorder. It is believed that differences in the immunogenetic background of patients influence the susceptibility of developing either typical or primary progressive multiple sclerosis.

The characteristic clinical and paraclinical evidence for at least two demyelinating lesions, affecting different sites within the brain or spinal cord, separated in time; in a young patient qualifies for diagnosis of MS. The best known diagnostic criteria for MS are those of Schumacher and Poser. However, the criteria for diagnosis of PPMS are different because of its relentless progression without any relapses or remissions. The criteria for PPMS have recently been defined and three levels of characterization have been made—“Definite PPMS”, “Probable PPMS” and “Possible PPMS” [Table 1]. As per the criteria outlined, the present case had “Definite PPMS” in view of clinical progression for over one year, positive CSF evidence for oligoclonal bands and positive MRI evidence. Besides, our case did not have acute focal inflammatory demyelination and axonal loss with limited remyelination, culminating in chronic multifocal sclerotic plaques from which the disease gets its name.
any exacerbations or relapses and there was no clear remission of symptoms.

The present case has certain peculiarities. Firstly, the age of onset in our patient was 16 years. The criteria proposed by Thompson[7] were applicable to age between 25 and 65 years. They acknowledged that very rarely patients who fall outside this age range may also develop PPMS. Mean age at onset in PPMS is significantly higher than secondary progressive forms which in turn is higher than relapsing remitting forms; and one series reported it as $40.4 \pm 11.3$ years for PPMS.[8] Only 5% patients of multiple sclerosis present with disease onset before 16 years age[2] and another series reported the figure to be 10.9% for age of onset below 20 years.[9] The young age at onset of PPMS was intriguing, however, attempts to prove alternative diagnosis in this patient turned out to be futile. Eventually it appeared to be an unusual presentation of PPMS.

The most common presentation of PPMS is a slowly progressive spastic paraparesis seen in 83% of cases in a European study,[9] while 8% had progressive cerebellar and 1% had brainstem involvement. Our case had cerebellar symptoms since onset of disease followed by overt brainstem involvement for one year. Although he did had signs of spasticity but no paraparesis or quadriaparesis. The patient had drowsiness and internuclear ophthalmoplegia accompanied with demyelination of pons and midbrain suggesting possible involvement of reticular activating system and the brainstem connections. Additional proof of brainstem involvement was forthcoming in form of deafness co-existent with abnormal brain-stem auditory evoked potentials. Brainstem involvement early in the disease course of this patient is another unusual feature of this case.

Recently[10] it has been reported that brain MRI lesion activity and burden are low in PPMS, despite the presence of severe neurological impairment. In fact it is suggested that the severity of multiple sclerosis pathology in the cervical cord is one of the factors contributing to neurological impairment in PPMS. It is believed that ‘magnetization transfer imaging’ (MTI) scans and their further analysis aids in delineating both, the loss of fibres leading to MRI-visible cord atrophy and the microscopic tissue damage affecting the remaining cord parenchyma.[10,11] The present case had ill-defined lesions in the cervical cord, but no cord atrophy; although considerable neurological involvement was present; probably this can explain absence of paraparesis or quadriaparesis in our case, despite evidence of upper motor neuron signs in all four limbs. Since MTI scan was not done, the exact extent of tissue damage in the cervical cord could not be assessed solely on the basis of MRI scans.

Indian series reviewing MS exist,[12,13,14] however, documentation of primary progressive multiple progressive is lacking. This case of “Definite PPMS” presenting at a very early age of onset, with brainstem involvement, is a unique case report from India of such an entity, more so, after the new diagnostic criteria have been laid down.[7]

References


Accepted on 09-10-2006

Source of Support: Nil, Conflict of Interest: None declared.

414 Neurology India | December 2006 | Vol 54 | Issue 4