Hypersomnia and Bilateral Horner's as an Initial Presentation in Multiple Sclerosis

Vinit Suri, Sovietlana Dixit, Ruchi Rastogi, Rajender, Kunal Suri*

Abstract
Multiple Sclerosis is characterized by predominantly white matter pathology at least in the initial stages. Certain clinical features including optic neuritis, bilateral internuclear ophthalmoplegia and Lhermitte's phenomenon are considered characteristic. Certain other symptoms and signs e.g. aphasia, apraxia, ataxia, hemianopsias and symptoms related to involvement of deep grey matter nuclei are considered rare and should alert the clinician in considering an alternate diagnosis. Involvement of the deep grey matter structures including the basal ganglia, thalamus and hypothalamus are rare in Multiple Sclerosis. MRI evidence of these grey matter nuclei is considered as a red flag for the diagnosis of Multiple Sclerosis though clinical manifestations attributed to the involvement of these grey matter nuclei is even rarer and considered as a major red flag (1). When the deep grey matter nuclei are involved, the lesions are more often seen involving the thalamus and the caudate nucleus and involvement of the hypothalamus is the least common (2,3). Hypothalamic lesions can clinically present as periodic hyperthermia or hypothermia, amenorrhea, autonomic disturbances and disorders of arousal and sleep. We describe a rare presentation of Multiple Sclerosis where the patient presented with the first clinically isolated syndrome manifesting as acute onset hypersomnia with bilateral Horner's with MRI evidence of involvement of the bilateral hypothalamus.

Key Words
Hypersomnia, Horner's Syndrome, Hypothalamic Plaques

Introduction
Multiple Sclerosis is characterized by predominantly white matter pathology at least in the initial stages. Certain clinical features including optic neuritis, bilateral internuclear ophthalmoplegia and Lhermitte's phenomenon are considered characteristic. Certain other symptoms and signs e.g. aphasia, apraxia, ataxia, hemianopsias and symptoms related to involvement of deep grey matter nuclei are considered rare and should alert the clinician in considering an alternate diagnosis. Involvement of the deep grey matter structures including the basal ganglia, thalamus and hypothalamus are rare in Multiple Sclerosis. MRI evidence of these grey matter nuclei is considered as an intermediate red flag for the diagnosis of Multiple Sclerosis though clinical manifestations attributed to the involvement of these deep grey matter nuclei is even rarer and considered as a major red flag (1). When the deep grey matter nuclei are involved, the lesions are more often seen involving the thalamus and the caudate nucleus and involvement of the hypothalamus is the least common (2,3). Hypothalamic lesions can clinically present as periodic hyperthermia or hypothermia, amenorrhea, autonomic disturbances and disorders of arousal and sleep. We describe a rare presentation of Multiple Sclerosis where the patient presented with the first clinically isolated syndrome manifesting as acute onset hypersomnia with bilateral Horner's with MRI evidence of involvement of the bilateral hypothalamus.

Case Report
A 17 years old girl presented with hypersomnia of 3 weeks duration. Prior to this she had a normal sleep duration of 6-7 hours at night and attended school regularly. After the onset of hypersomnia she slept for more than 15-20 hours everyday with frequent daytime naps and had a tendency to fall asleep easily in the middle of a conversation or while eating. She woke up for brief periods during the day to eat and bathe and had frequent yawning during these wakeful periods. She was examined by a general physician and routine metabolic parameters and a CT scan (plain) head were within normal limits. She was prescribed Modafinil with a transient response in...
Hypersomnia for the first 2-3 days followed by recurrence of 18-20 hours of sleep every day. Patient developed subtle ptosis of both eyes 2 weeks after the onset of hypersomnia which was attributed to 'sleepy eyes' by the family (Fig 1). Subsequently she developed binocular diplopia with vertical separation of images following which she was referred for neurological evaluation. Neurological evaluation revealed a drowsy patient who could be easily aroused though with frequent yawning. Higher mental function assessment revealed impaired short term memory. Bilateral Horner's with bilateral pinpoint pupils were observed. Fundi were normal and external ocular movements were full and diplopia charting was indicative of left 3rd nerve palsy. No motor or sensory deficit was observed and plantars were bilaterally flexor. No hemispherical cerebellar signs nor any trunkal ataxia was observed. MRI brain (Fig 2) revealed multiple variable sized lesions which were hypointense to isointense on T1 and hyperintense on T2 and Flair involving callososseal interface, left centrum semiovale and bilateral thalamic ad hypothalamic regions with no enhancement post contrast. MRI of the entire spine did not reveal any spinal cord lesions. CSF examination revealed mild pleocytosis (20/ml) with negative oligoclonal bands but elevated IgG Levels. VER study revealed normal P-100 response in left eye (103 ms) with prolonged P-100 response in right eye (118 ms) suggestive of demyelination across the right optic nerve. BERA study revealed normal and symmetrical responses. Serum was negative for antiaquaporine antibody and vasculitic screen and angiotensin converting enzyme was normal. Patient was managed with Methylprednisolone infusion followed by oral steroids with a dramatic response of hypersomnia by the 3rd day and near complete recovery of bilateral Horner's by 10th day. Repeat MRI after 6 weeks revealed 2 new lesions in bilateral centrum semiovale with open ring enhancement.
Discussion

Our patient had clinically isolated syndrome manifested as acute onset hypersomnia, impaired short term memory and bilaterally Horner's syndrome. The initial MRI study fulfilled the McDonald's Criteria (4) for dissemination in space and the repeat MRI done at 6 weeks showed new lesions fulfilling the criteria for dissemination in time confirming a diagnosis of remitting and relapsing multiple sclerosis. Posterior lateral hypothalamus and the peri-aqueductal region in the midbrain has been recognized as the location of hypocretin neuronal cell bodies whose neurotransmitters are considered as arousal neuropeptides and the area itself has been called 'waking centre' (5). Horner's syndrome can result from lesions extending from the posterior lateral hypothalamus or involvement of first order, 2nd order or 3rd order sympathetic fibres supplying the iris dialater and Muller muscle leading to ptosis which is at the most 2 mm. Our patient had involvement of bilateral posterior hypothalamus resulting in this rare presentation of bilateral Horner's and acute hypersomnia. Various types of sleep disturbances have been described in patients with Multiple Sclerosis. These include difficulty in falling asleep, restless sleep, nonrestorative sleep, early morning awakenings and REM sleep behaviour disorder. Fatigue, tiredness and lack of energy may sometimes simulate hypersomnia. These sleep disorders have a multifactorial etiology involving both physical and psychological factors resulting from Multiple Sclerosis. Sleep disturbances especially hypersomnia due to direct involvement of the hypothalamus have been seen rarely in Multiple Sclerosis. Hypersomnia in MS has been reported earlier (6, 7, 8, 9). Isolated hypersomnia without Horner's has been described as the first presentation in a 16 year old girl (6). Low CSF hypocretin-1 levels have been described in MS patients showing hypersomnia with bilateral hypothalamic lesions (7 - 10) and treatment with steroid pulse has shown both clinical improvement and rise in hypocretin levels (7, 8).

Pathological MRI imaging studies are challenging the view of Multiple Sclerosis as a chronic inflammatory - demyelinating condition affecting solely the white matter of the central nervous system. Indeed there is a growing body of evidence showing that a significant portion of Multiple Sclerosis related damage affects the grey matter structures. Demyelination may be in the neocortex especially cingulated cortex, grey matter of thalamus, basal ganglia, hypothalamus, hippocampus cerebellum and spinal cord (11). Hypothalamic involvement in Multiple Sclerosis has also been described previously in a number of studies including a postmortem study (11, 12, 13,14) and on an MRI based study which found hypothalamic lesions in 13.3% of Multiple Sclerosis patients (13). Most of these patients presented with hypersomnia and one case report reported a presentation with hyperhydrosis (14). Grey matter involvement in early Multiple Sclerosis is a phenomenon which is being increasingly recognized. To the best of our knowledge this is the first reported case with acute hypersomnia with bilateral Horner's as the presenting manifestation of Multiple Sclerosis due to involvement of bilateral posterior hypothalamus.

References