

Familial Multiple Sclerosis

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Abstract: Multiple sclerosis (MS) is an important cause of neurological disability. Familial MS is uncommon in India and is seen mostly in the high prevalence countries like United States of America, Canada and New Zealand. In the present paper, two members of the same family were diagnosed as having MS. As the disease is uncommon, there was initial diagnostic difficulty in the first case. The clinical and radiological findings are described with a note on the treatment and follow up.
Keywords: Familial multiple sclerosis, Dawson’s fingers, Dimethyl fumarate.

INTRODUCTION

Multiple sclerosis (MS) is an important cause of neurological morbidity world over. MS is not a Mendelian inherited disease; only the susceptibility to the disease is inherited, the risk of MS being also related to environmental factors [1]. Its incidence and prevalence increase as the distance from equator increases being relatively common in New Zealand, Canada, United States of America and Northern Europe. Familial aggregation of MS patients is common in high prevalence areas of the world. Up to 20% of cases can be familial in some high prevalence communities; but is rare in a low prevalence country like India. The disease typically affects younger patients in their twenties and thirties.

Two members of a family were identified to have MS. Though the first case was difficult to diagnose at presentation, the second could be diagnosed with ease as there was a case already in the family.

Case-1

A 44 year old female patient was admitted with 2-days duration of acute onset of slurred speech, numbness of right hand and difficulty in holding objects with right hand on 23-06-2017. There was no walking difficulty, headache or fever. There was history of a similar illness 10 years ago, few months following her second delivery. She improved within 2-3 weeks at that time. She also had hypothyroidism for which she was receiving levothyroxine 100mcg daily as supplementation. There was no diabetes or hypertension.

Her examination showed normal vital signs, well oriented female patient with mild dysarthria of cerebellar type. Mild upper motor neuron right facial paresis was present. Other cranial nerves examination was normal. There was no relative afferent papillary defect. Right hand grip was weak at 80%. There were bilateral brisk deep tendon jerks and extensor plantar responses bilaterally. The laboratory parameters were normal including thyroid profile. The diffusion weighted magnetic resonance imaging (MRI) showed

restricted diffusion in left frontal cortex with reversal on corresponding Apparent Diffusion Coefficient (ADC) sequence (Fig-1).

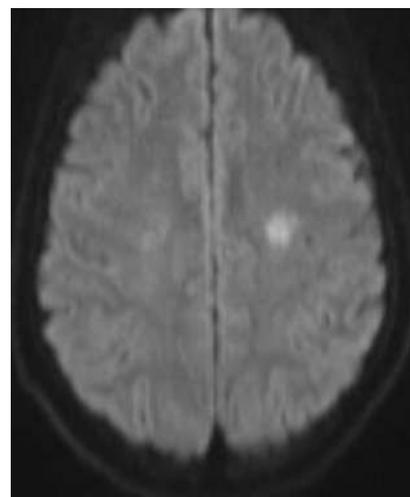


Fig-1: Diffusion weighted MRI in Case 1 showing acute left frontal lesion

As the clinical and radiological findings suggested an acute ischemic stroke she was started on aspirin and atorvastatin and routine stroke care. The work up for a cardiac source was negative. In the meantime the remaining MRI sequences were obtained which suggested that there were preexisting periventricular lesions (Fig-2), some of them in the form of Dawson's fingers – periventricular radiating signals. The T1 weighted image showed 'black holes' suggestive of permanent axonal loss (Fig-3). We performed a screening MRI of the spine also which suggested a lesion in the cervical spine. The cerebrospinal fluid (CSF) showed oligoclonal bands (OCBs) and a marginal rise in the protein content. Protein-62mg/dl Glucose -78mg/dl (corresponding blood glucose was 120mg/dl) Adenine deaminase (ADA) value -1 and Cell count-4 cells; all were lymphocytes. CSF oligoclonal bands (OCB) – Positive. Serum aquaporin antibody test to exclude neuromyelitis optica, was negative. So also serum angiotensin converting enzyme levels and collagen vascular disease profile were within normal levels. Viral markers were also negative.

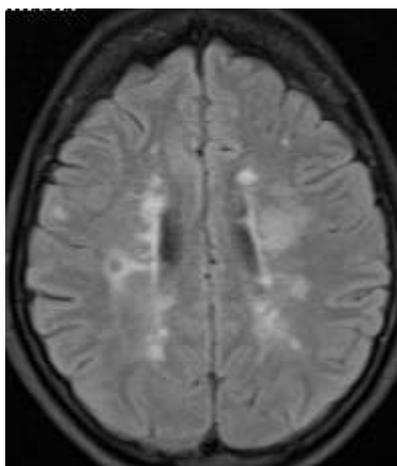


Fig-2: FLAIR MRI in Case 1 showing Dawson's fingers

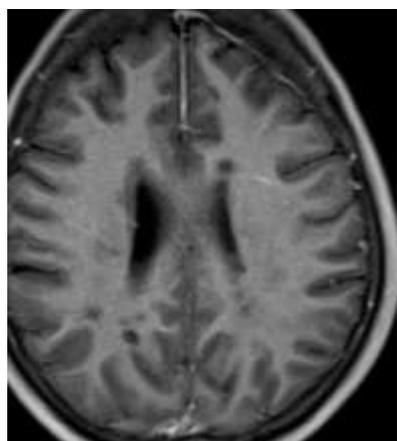


Fig-3: T1 weighted MRI image in Case 1 showing black holes

Aspirin and statins were discontinued and the patient was given five doses of methylprednisolone intravenously. Her right hemiparesis and speech deficit improved and she was discharged after a week in a stable condition.

Case-2

A 19-year old male patient, son of Case 1, was admitted one month later with history of diplopia about two months earlier. The diplopia improved within 4 days spontaneously. This time he was admitted for further evaluation of his neurological problem.

His clinical examination was mostly normal except for brisk deep tendon reflexes bilaterally. There were no ocular findings and fundi were normal. The laboratory evaluation showed normal blood parameters. The visual evoked potentials showed normal latencies; brainstem auditory evoked responses were abnormal on right suggesting a delayed wave V. The CSF analysis was normal and there were no OCBs. The cranial MRI scan was similar to the Case-1 showing periventricular radiating hyperintense signals (Fig 4 & 5), subcortical U-fibres getting affected (Fig-6) and showing black holes on T1 weighted images suggesting axonal loss.

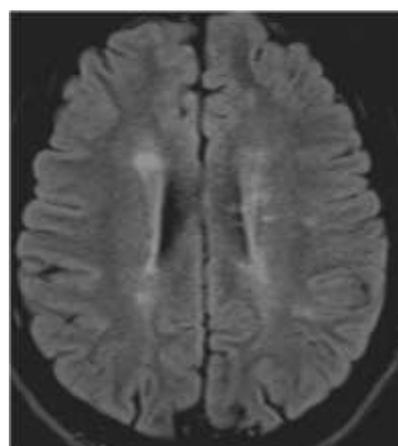


Fig-4: FLAIR MRI of case 2 periventricular lesions

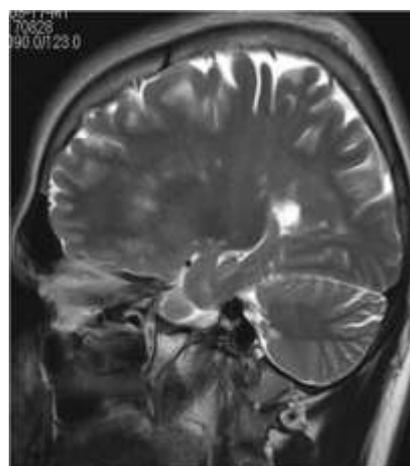


Fig-5: Sagittal T2 image of Case 2

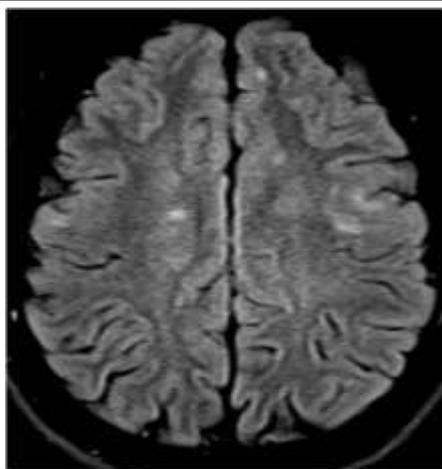


Fig-6: Axial FLAIR image of Case 2 showing subcortical U-fibres involvement

As there were no acute symptoms in Case 2, steroids were not given. Both the patients were started on oral Dimethyl fumarate Capsules 240 mg twice daily as prophylactic treatment to prevent further attacks of MS. At the time of last follow up 6 ago months both were doing well without any recurrence.

DISCUSSION

MS is an important cause of disability in the productive years of life. When the Expanded Disability Status Score exceeds 5, the subjects need assistance for ambulation and for many activities of daily living. The first episode mostly occurs in the second or third decade though occurrence of first episode in later years is not uncommon as can be seen in Case 1. Familial aggregation is commonly seen in high prevalence countries and is uncommon in Asian countries. The risk is significantly increased in first degree relatives [2, 3]. The risk of familial MS is 6-25 folds in children of MS subjects, and 12-38 folds in siblings. In general, first-degree relatives of probands have a risk that is 30-50 times greater than the 0.1% risk for the general population [4]. Sister-sister relationship is the highest risk factor for familial MS and lowest is between mother – son relationship, probably secondary to the fact that MS is more common in female subjects. Rima [5] had reported familial incidence of MS from India in one family wherein sister-sister relationship was involved in the disease process.

MS is a complex multifactorial disease where genetic, environmental factors and their interaction contribute to the disease risk and outcome. Relapsing-remitting MS is the most common variant, although the most disabling scenario would be a primary progressive variety of MS (PPMS). The treatment modalities and prevention strategies in PPMS are not yet defined.

CONCLUSION

Two family members of a family with multiple sclerosis were described. Both had RRMS like presentation and the first case responded to treatment.

Disclosure

There are no financial conflicts to disclose.

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