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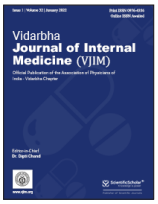

Case Report

Marburg Variant of Multiple Sclerosis: A Case Report

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ABSTRACT

Multiple sclerosis (MS) is a demyelinating disorder with central nervous system (CNS) involvement, leading to varied presentations. It is an autoimmune disease characterised by chronic inflammation, demyelination, gliosis (plaques or scarring) and neuronal loss with relapsing or progressive course. MS plaques typically develop at different times and in different CNS locations (i.e., MS is said to be disseminated in time and space). The clinical course is extremely variable, ranging from a relatively benign condition to a rapidly evolving and incapacitating disease requiring profound lifestyle adjustments. MacDonald's criteria are frequently used to diagnose MS. Rapidly, evolving severe forms of MS such as Marburg's variant and Balo's concentric sclerosis account for <4% of total incidence of MS. The clinical course is rapid and often fatal. The exact aetiology behind this malignant nature of Marburg's variant MS is unknown. In this case report, we will be discussing one such rare presentation of Marburg variant of MS.

Keywords: Multiple sclerosis, Marburg variant, Demyelinating disorder, Dawson fingers

INTRODUCTION

Multiple sclerosis (MS) is a demyelinating disorder with central nervous system (CNS) involvement, leading to varied presentations. It is an autoimmune disease characterised by chronic inflammation, demyelination, gliosis (plaques or scarring) and neuronal loss with relapsing or progressive course. MS plaques typically develop at different times and in different CNS locations (i.e., MS is said to be disseminated in time and space). More than 900,000 individuals in the United States and millions of individuals worldwide are affected. The clinical course is extremely variable, ranging from a relatively benign condition to a rapidly evolving and incapacitating disease requiring profound lifestyle adjustments.[1]

Symptoms of MS are varied and depend on the location and severity of lesions within the CNS. Symptoms could be sensory with Lhermitte's sign, weakness in limbs with spasticity, optic and facial weakness that may resemble idiopathic Bell's palsy, ataxia, vertigo, bladder involvement and epilepsy, to name a few.[1] MacDonald's criteria are frequently used to diagnose MS.

In this case report, we will be discussing one such rare presentation of a rapidly progressive demyelinating disorder.

CASE REPORT

A 52-year-old male with, known case of systemic hypertension with hypothyroidism, presented with urinary retention for 10 days, and progressive weakness of both lower limbs for 4–5 days. Weakness progressed to complete paralysis over 1–2 days. The patient had no history of fever or traumatic spine injury.

The patient was admitted 3 months back for drooping of the right eyelid and deviation of angle of mouth to the left side. The patient had been investigated and discharged on tapering doses of steroids. MRI Brain + Orbit done 3 months back was suggestive of multiple T2/FLAIR hyperintensities in multiple areas of brain with a normal orbit scan. CSF analysis showed mildly raised CSF proteins. ANA profile was positive with speckled pattern with antibodies Mi-2B and PM-Scl-100 weakly positive. The patient was given a pulse therapy of intravenous methylprednisolone followed by tapering doses of oral steroids on discharge. The patient improved clinically. After 2–3 weeks of discharge, the patient started having difficulty walking with multiple falls and weakness in both lower limbs. He also experienced shooting type of pain down his legs (left > right). He did not consult a doctor for his complaints and took some herbal medication from a local quack.

On examination, the patient was conscious and oriented to time place and person with grade 0 power in both lower limbs with grade 5 power in upper limbs. Sensory examination was normal. Bilateral plantar reflexes were extensor. Deep tendon reflexes were absent in lower limbs while present in upper

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limbs. The patient exhibited emotional liability in the form of frequent crying spells.

Renal function tests, liver function tests, serum LDH, serum CPKMB and complete blood count were within normal limits.

Repeat MRI (Brain + orbit + spinal cord) was suggestive of multiple T2/FLAIR hyperintensities involving bilateral gangliocapsular region (right > left), right centrum semiovale, periventricular region, callososeptal-interface, body and splenium of corpus callosum, right cerebral peduncle and ventral pons. That is, there was dissemination of lesions in both time and space, as shown in [Figures 1 and 2], respectively. Multiple asymmetrical peripheral diffuse T2W/STIR hyperintense ovoid lesions in brainstem, cervical, dorsal and lumbosacral spinal cord [as shown in Figures 3a-c] with mild post-contrast enhancement were seen along with the lesions seen in the brain parenchyma. The periventricular lesions are distributed perpendicular to the body of lateral ventricles giving 'Dawson fingers' appearance. MR spectroscopy shows increased choline, and lipid lactate peaks with reduced NAA peaks. The study of orbit showed no abnormality.

The study of CSF was done which showed an otherwise normal report with mild increase in CSF protein. Further studies showed a negative anti-neuromyelitis optica antibody panel (Aquaporin 4 and myelin oligodendrocyte glycoprotein 'MOG' antibodies) in serum. Oligoclonal bands were absent in serum.

Above investigations and the rapid course of progression of disease were suggestive of a progressive demyelinating disorder (Marburg/Malignant variant of MS). The patient was started on Methylprednisolone intravenous pulse therapy for 5 days, following which he was shifted to oral prednisolone in tapering doses. Within 3–4 days of starting corticosteroids, power in lower limbs was improved following which patient was discharged on tapering doses of oral prednisolone.

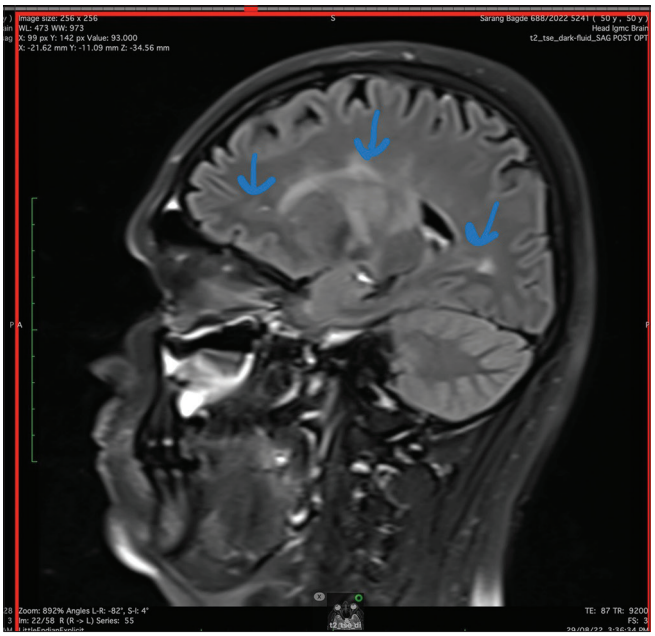

Figure 1: Figure 1 shows the T2 weighted MRI sagittal section (performed on 29 August, 2022) of brain showing hyperintensities involving multiple regions, especially periventricular lesions distributed to perpendicular to the body of lateral ventricle giving 'Dawson fingers' (blue arrows) appearance.

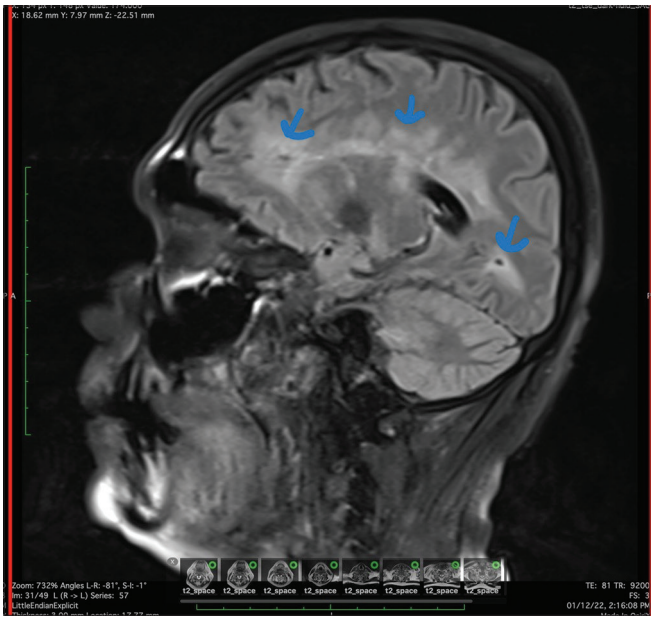

Figure 2: Figure 2 represents T2-weighted MRI scan on 1 December, 2022 with blue arrows showing the lesions disseminated in time and space as compared to August.

DISCUSSION

Rapidly evolving severe forms of MS like Marburg's variant and Balo's concentric sclerosis account for <4% of total incidence of MS. The clinical course is rapid and often fatal. The exact aetiology behind this malignant nature of Marburg's variant MS is unknown. This aggressive course can be due to involvement of vital areas like brainstem or due to an unusual aggressive immunological or pathological process.[2]

Our patient first presented with the right eye ptosis, which could be attributed to involvement of the right cerebral peduncle (possibly involving oculomotor nerve nucleus). Following which he developed Bell's palsy like symptoms which could be attributed to involvement of ventral pons, as MRI scan showed no involvement of cranial nerves. Repeat MRI scans and clinical presentation showed dissemination of disease in space as well as time. MRI shows demyelinating lesions with post-contrast enhancement. MR spectroscopy shows increased choline peak with reduced NAA peak. These were also present in this case.[3]

CSF study showed mild increase in proteins with minimal or no increase in cellularity. CSF oligoclonal bands were

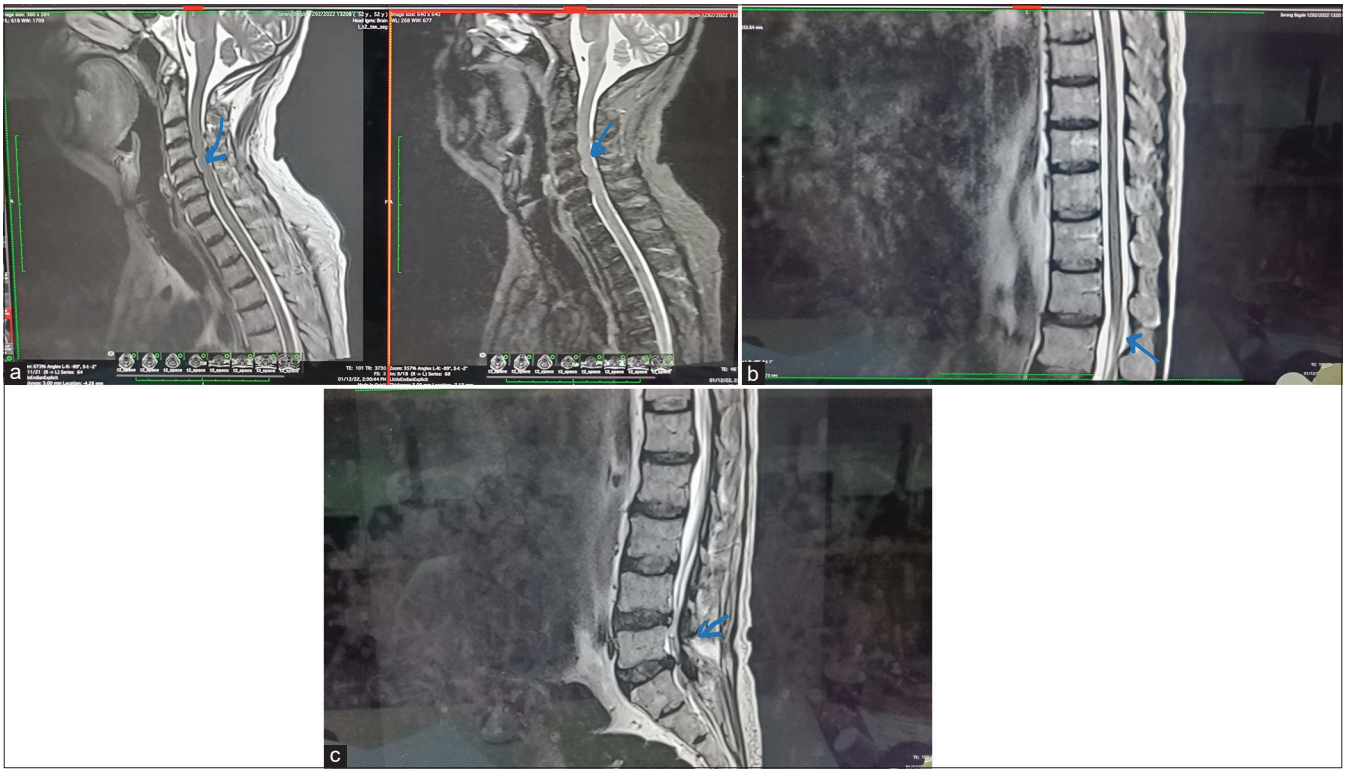

Figure 3: (a) Figure 3a shows T2-weighted MRI scan (done on 1 December, 2022) showing (blue arrow) dissemination of lesion at cervical level of spinal cord. (b) Figure 3b shows T2-weighted MRI scan (done on 1 December, 2022) showing (blue arrow) dissemination of lesion at dorsal level of spinal cord. (c) Figure 3c shows T2-weighted MRI scan (done on 1 December, 2022) showing (blue arrow) dissemination of lesion at lumbosacral level of spinal cord.

absent in our patient. As in other forms of MS, oligoclonal bands may be present in CSF, but less often in Marburg variant.[3]

Differentials include the widespread demyelinating disorders, such as Balo's concentric sclerosis, Schilder's diffuse sclerosis and acute demyelinating encephalomyelitis acute disseminated encephalomyelitis (ADEM).[2]

Balo's concentric sclerosis has a typical histological feature of alternating layers of myelin loss and myelin preservation or remyelination. This is seen as concentric rings in T2WI and T1WI contrast MRI.[4] Schilder's diffuse sclerosis is a very rare disease seen in children and MRI shows one or two large lesions, often bilateral involving the centrum semiovale with no significant peripheral oedema.[5] Our patient's MRI scan did not show any of these characteristics. ADEM is another fulminant demyelinating disease that progress over days and attains rapid remission. It occurs due to an autoimmune response to the MBP following an infection or immunisation, predominantly occurring in younger age groups. ADEM lesions extend into grey matter unlike other forms of MS.[6] ADEM has a stable disease process compared to other fulminant MS and serial MRI shows absence of any new lesions.[7] In our case, patient was an older adult with no history of any infection or vaccination and more importantly serial MRI showed new lesions. Our patient did not have any evidence of vascular pathology, with MRI brain showing no evidence of microangiopathy, nor did he have any history or features suggestive of any metabolic or infectious pathology.

Therefore, the diagnosis of Marburg variant of MS with a malignant course is most likely in this patient. First line of treatment is intravenous corticosteroids, which was tried in our patient with improvement in the clinical condition. In cases refractory to corticosteroids, intravenous immunoglobulins or plasmapheresis has been tried with positive responses.[8] Other therapies that can be used are immunosuppressants and immunomodulators like Mitoxantrone.[9] In patients where all these therapies fail, intense immunosuppression followed by autologous stem cell transplant can be tried as last resort.[3]

CONCLUSION

The data in literature on Marburg's variant of MS is limited due to its rarity. The exact incidence of this condition is unknown. Currently consensus is lacking on diagnostic criteria of Marburg's variant of MS. There was marked improvement in our patient following IV methylprednisolone, but adjunct therapy is to be considered in long run.

Declaration of patient's consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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