Case study

High Dose Methylprednisolone in Fulminant Progressive Quadriparesis With Optic Neurites: The Marburg Variant

ABSTRACT

Marburg described an acute variant of Multiple Sclerosis (MS) which was rare with a fulminant demyelinating progressive course with multiple lesions, predominantly in young adults, leading to severe disability and death within a yearof onset. The disease was associated with an Antibody-mediated process, acute fulminant course and typical MRI findings whichare diagnosticof the disease. High-dose glucocorticoids, cyclophosphamide and mitoxantrone have shown good response to treatment. The malignant form of MS accounts for less than 4% of the incidence. Here the patient had no history or sign of infectious, metabolic, or vascular pathologyand thus the diagnosis of Marburg's variant was made by exclusion. The Marburg variant is rare and needs a high index of suspicion. In the future, studies of patients with tumefactive demyelinating lesions are necessaryfor early diagnosis, greater understanding of the disease and for the development of therapeutic strategies.

Keywords: Multiple Sclerosis, Marburg Variant, Methylprednisolone

1. INTRODUCTION

Acute MS is a rare and fulminant demyelinating process with multiple lesions involving cerebral hemispheres, brainstem and optic nerves. It occurs predominantly in young adults and has a rapid progressive course without remission leading to death and severe disability within a year(1). Marburg first described it in 1906 with three cases of fulminant demyelinating disease (2). The disease does not seem to follow infection or previous vaccination. It is associated with Antibody-mediated processes and genetically predisposed persons (3). Acute fulminant features, rapidly progressive course and typical malignant MRI findings are diagnostic in many cases (4). Treatment with high-dose glucocorticoids, cyclophosphamide and mitoxantrone have shown good response with respect to outcome however no long term studies and randomized controlled trials have been performed so far(5,6).

2. PRESENTATION OF CASE

A 36-year male presented in the emergency department with a complaint of numbness in left upper limb for 7 days, which was acute in onset, progressive in nature and was relief on its own in a span of 1 week. There was a history of acute progressive asymmetric quadriparesis for the past 10 days and painless progressive diminution of vision in the left eye for the past 2 weeks. There was no history of girdle-like sensation suggesting radiculopathy, no history of sensory involvement and no history suggestive of autonomic nervous system

involvement.There was no history of recent headache, projectile vomiting, fever and abnormal limb movement suggestive of infectious etiology. There was no history of similar complaints in the past as per the patient. There was no history suggestive of chronic conditions like diabetes mellitus, hypertension or history of recent vaccination noted.

On neurological examination, the patient was conscious and oriented at presentation. The second cranial nerve examination was performed and the patient had visual acuity of 6/18 in the left eye and 6/9 in the right eye. On performing swinging light reflex Relative Afferent Pupillary Defect (RAPD) was observed in the left eye and on direct ophthalmoscopic examination the optic nerve was normal in both eyes. On performing the motor examination tone was increased in flexor group of the muscles in upper limb and in extensor group muscles in lower limb with left side of the body more involved than right side of body. On examining power, power of 1/5 was observed in the patients left shoulder in all groups of the muscles and power of 4/5 was observed in the patient`s right shoulder joint predominantly in flexor group of muscles, power of 3/5 was observed in left elbow joint in both flexor and extensor groups of muscles and 5/5 in right elbow joint in both flexor and extensor groups. In the lower limb power at the left hip was 1/5 in all groups of muscles (flexor, extensor, abductor, adductor, internal and external rotators) and power at right hip was 4/5. Similarly, power at left knee joint was 1/5 in both flexor and extensor groups of muscles and 4/5 at right knee joint in both the groups of muscles. Coordination couldn't be assessed due to spasticity. On deep tendon reflex examination bilateral biceps, triceps quadriceps femoris and ankle reflexes were exaggerated. On performing superficial reflex examination abdominal reflex was absent and the bilateral Babinski sign was positive.

On performing Visual Evoked Potential (VEP) test, prolonged peak and p100 latency was observed in the left eye which was more significant than the right eye. CSF analysis was also performed and normal cells, protein and glucose levels without oligoclonal bands were observed. Hemogram, serum creatinine and serum electrolytes (sodium, potassium, calcium, phosphorus) were normal range of limit and serum for HIV antibody, HBV antigen and HCV antibody was non-reactive. Serology for autoantibodies like ANA, MOG IgG and Aquaporin-4 were also performed and were absent. Serum vitamin B12 and vitamin D3 were within normal range and a normal vasculitis workup was also observed (Table 1) (Figure 1a,1b,2a,2b).

Based on the clinical, radiological and biochemical analysis and excluding other causes of tumefactive demyelinating lesion (TDL) a diagnosis of Marburg variant of MS was made. The patient was started on high-dose methylprednisolone 1000mg/day for 3 days and was kept on oral prednisolone 40mg/day which was gradually tapered over a duration of 2 weeks. Follow-up MRI was also planned after 6 weeks of pulse therapy. Clinical improvement was observed after 6th day of treatment initiation.

Table 1: Investigations done

CSF Analysis	*Cells*	6
	Protein	40
	Glucose	78
	Oligoclonal band	Absent
Serology	*Hemogram*	Hb-13.4 TLC-3400 PLT-146000
	RFT *Electrolytes (Na, K, Ca, P)*	BUN-10 S.Cr-0.7 S.Na-135 S.K-4.2

		S.Ca-9.9 S.Po4-3.8
	HIV 1&2 antibody, HCV &HbsAg Elisa	NR
	S Vitamin D-3	96
	S. Vitamin B-12	564
	Serum Folate	10.6
	AQUAPORIN 4 IgG antibody	Negative
	ANA(IFA), ANCA(IFA)	Negative
VEP	B/L optic neuritis	
CE MRI cervical spine with WSS	No significant abnormality	
CE MRI B/L optic nerve	Post-contrast enhancement of bilateral optic nerve right more than left with perioptic fat stranding	
CE MRI BRIAN	Bilateral asymmetrical large confluent areas of altered signal intensity in B/L periventricular and juxtacortical white matter (R>L) in B/L frontal, parietal, occipital, & part of temporal lobe with post-contrast enhancement of lesion on edges (Figure 1a,1b,2a,2b).	

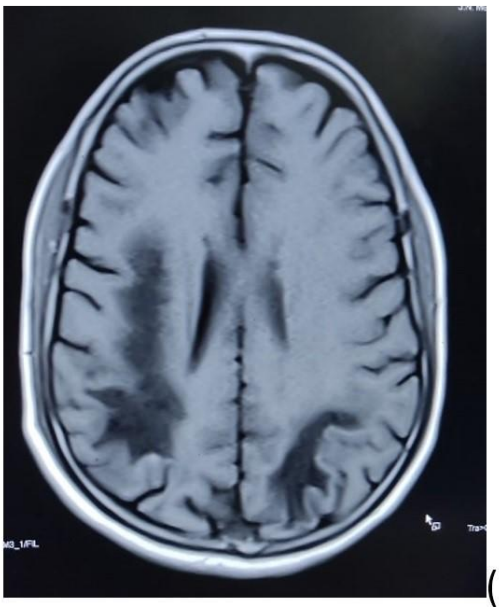
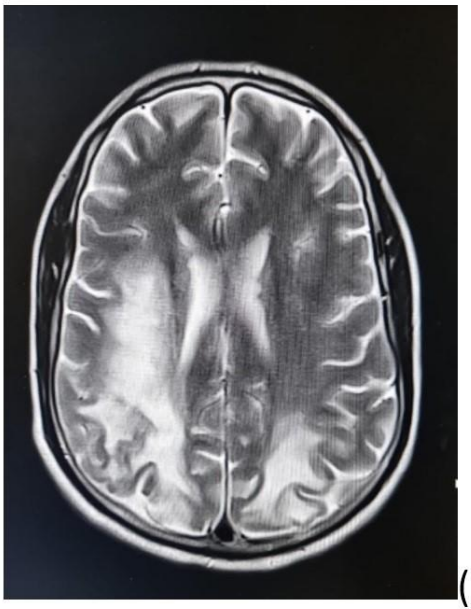

(1a)

(1b)

Figure 1a and 1b: CE(Contrast Enhanced) MRI brain suggestive of Bilateral asymmetrical large confluent areas of altered signal intensity in B/L periventricular and juxtacortical white matter (R>L) in B/L frontal, parietal, occipital, & part of temporal lobe with post-contrast enhancement of lesion on edges.

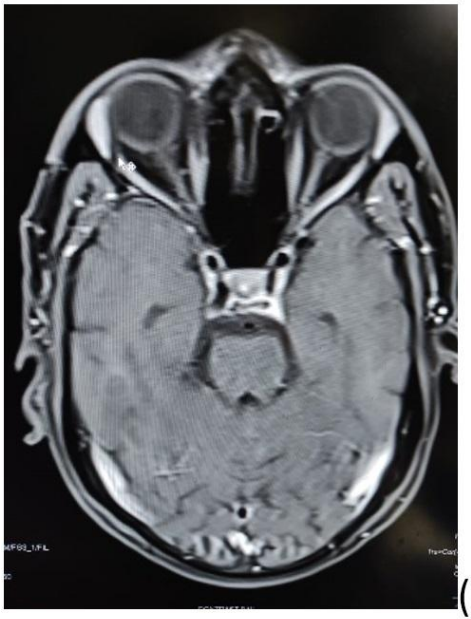
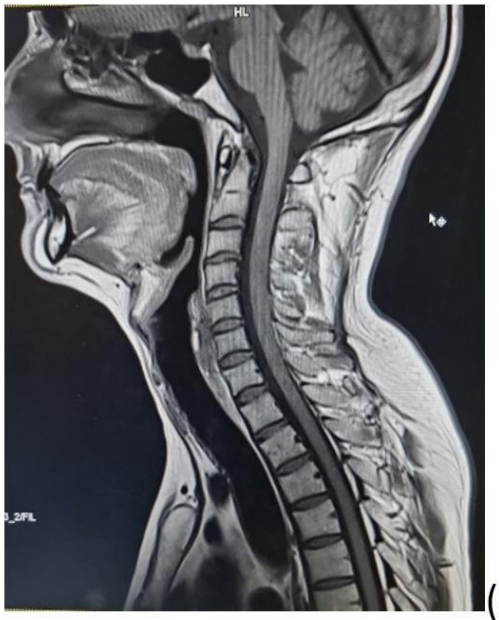

(2a)

(2b)

Figure 2a: CE MRI of bilateral optic nerve suggestive of post-contrast enhancement of bilateral optic nerve right more than left with perioptic fat stranding. 2b: CE MRI cervical spine with whole spine screening suggestive of no significant abnormality.

3. DISCUSSION

Malignant forms of MS like Marburg and Balo's concentric sclerosis account for less than 4 percent incidence of MS(7), this is because of its rarity it remains incompletely characterized. On performing MRIbrain and spinal cord the distribution of demyelinating lesions is usually indistinguishable from classical multiple sclerosis, but unlike classical MS, they occur simultaneously in all affected areas. The patient had persistent disabling symptoms and MRI brain was suggestive of disseminated demyelinating plaque of the same hyperintensity in both hemisphere supratentorial areas like periventricular and juxtacortical which are consistent sites for MS but in some cases sub tentorial involvement is also seen (2). MR spectroscopy showed an increased peak of choline and a decrease of N-acetyl-aspartate which are observed in demyelinating lesions. The CSF examination suggested normal protein, cells and absent oligoclonal band which may be present in some cases but are less often (8). The Differential diagnosis includes Neuromyelitis Optica Spectrum Disorder (NMOSD), multifocal brain tumor, a toxic and metabolic disorder like vitamin B-12 deficiency and acute demyelinating encephalomyelitis (ADEM)(9,10). To make a diagnosis of NMOSD without aquaporin4 IgG antibody at least two core clinical characteristics is required(11).The patient had only optic neuritis and MRI brain and spinal findings were not consistent with NMOSD. Extensive involvement of white matter on MRI is common in both MS & ADEM but neurological symptoms should precede by febrile illness and vaccination. The patient had no history or sign of infectious, metabolic, or vascular pathology. Hence a diagnosis of Marburg's variant of MS was made by exclusion.

4. CONCLUSION

Marburg variant of MS is a rare disease that needs a high index of suspicion, diagnosis should be made by excluding other causes of tumefactive demyelinating lesions. Clinical and radiological feature and the acute course of the disease is diagnostic in most case of Marburg disease. In the future, studies of patients with TDL lesions are necessary for a better understanding of these diseases and generation of therapeutic approaches.

CONSENT

As per international standard or university standard, parental(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The protocol of the study was approved by the Institutional Ethical Committee and the study was conducted as per the standards of Good Clinical Practice and the Helsinki Declaration.

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