Case study

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

ABSTRACT

Marburg described an acute 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 year; associated with an Antibody-mediated process. Acute fulminant course and typical MRI findings are diagnostic. High-dose glucocorticoids, cyclophosphamide, and mitoxantrone seem to be beneficial. The malignant form of MS accounts for less than 4% of the incidence. Our patient had no history or sign of infectious, metabolic, or vascular pathology. So, 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 necessary.

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. Occurs predominantly in young adults. It 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). It doesn't seem to follow infection or vaccination. Usually, it is associated with Antibody-mediated processes and genetically predisposed persons. Acute fulminant features and rapidly progressive course and typical malignant MRI findings are diagnostic in many cases (3). High-dose glucocorticoids, cyclophosphamide, and mitoxantrone seem to be beneficial(4,5).

2. PRESENTATION OF CASE

A 36-year male presented in the emergency department with a complaint of numbness in his left upper limb for 7 days, which was gradual, progressive, and relief on its own in a span of 1 week. There was a history of acute progressive asymmetric quadriparesis for 10 days and painless progressive diminution of vision in the left eye for 2 weeks. No history of girdle-like sensation, neck pain, sensory, bowel & bladder involvement. No history of headache, projectile vomiting, fever, and abnormal movement. No history of similar complaints in the past, no history of chronic conditions like diabetes mellitus, hypertension, and preceding vaccination or viral infection noted. On neurological examination, the patient was conscious and oriented. The second cranial nerve examination visual acuity was 6/18 in the left eye and 6/9 in the right eye. On swinging light reflex RAPD was present in the left eye, on direct

ophthalmoscope optic nerve was normal in both eyes. In the motor examination tone was increased in all four-limb left more than right. Power was 1/5 and 4/5 in the left and right shoulder joint respectively, 3/5 and 5/5 in the left and right elbow in all range of motion. In the lower limb power at the hip and knee joint was 1/5 and 4/5 in left and right respectively, in all ranges of motion. Coordination couldn't be assessed due to spasticity. Deep tendon reflexes were exaggerated in all four limbs, superficial reflexes were absent, and the bilateral Babinski sign was positive.

On VEP showed prolonged peak p100 latency left more than right. CSF analysis suggested normal cells, protein, and glucose levels without oligoclonal bands. Blood examination of hemogram, creatinine, and electrolytes (sodium, potassium, calcium, phosphorus) was normal, and serum for HIV antibody, HBV antigen, and HCV antibody was non-reactive. Serology for autoantibodies like ANA, MOG IgG, and Aquaporin-4 were absent. Serum vitamin B12 and vitamin D3 were normal. Vasculitis workup were normal (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 kept on oral prednisolone 40mg/day and gradually tapered over 2 weeks. Follow-up MRI is planned after 6 weeks of pulse therapy. Clinical improvement was observed after 6th day.

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).	

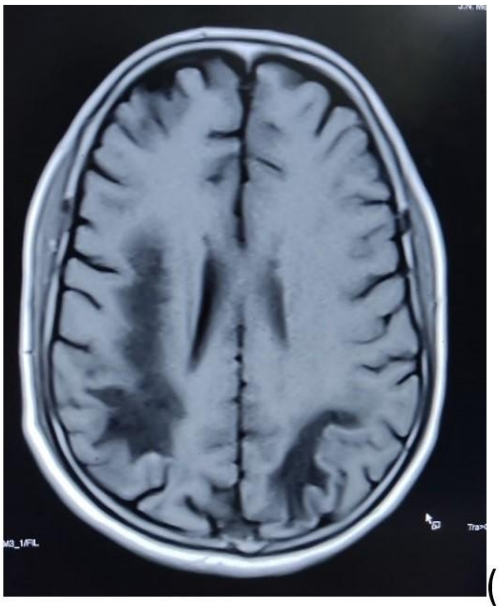
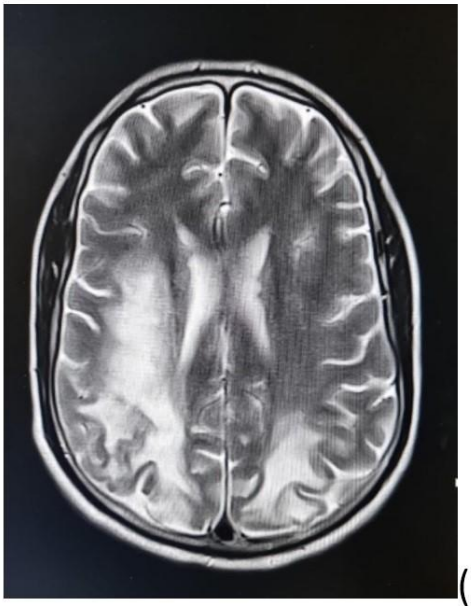

(1a)

(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.

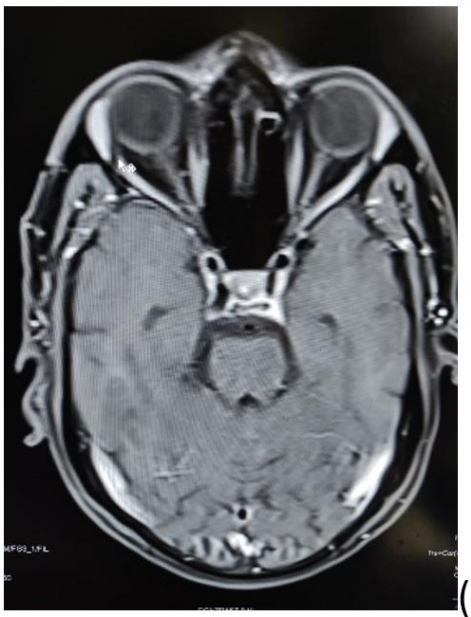
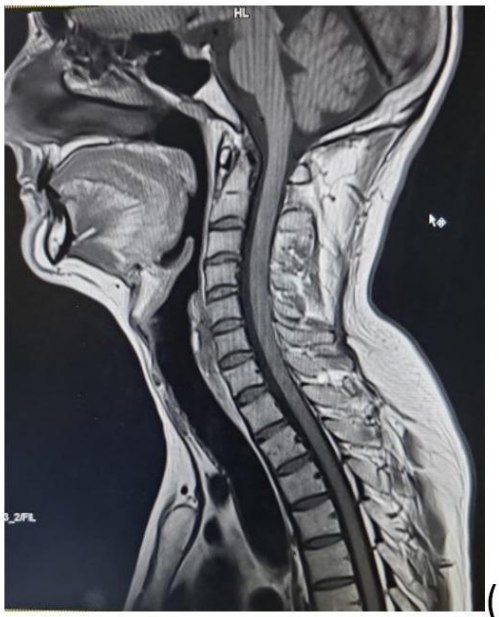

(2a)

(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 % incidence of MS(6), because of its rarity it remains incompletely characterized. On MRI distribution of demyelinating lesions is usually indistinguishable from classical multiple sclerosis, but unlike classical MS, they occur simultaneously in all affected areas. In our patient, persistent disabling symptoms, and MRI 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 is seen in demyelinating lesions. CSF examination suggested normal protein, cells, and absent oligoclonal band which may be present in some cases but are less often (3). 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). Diagnosis of NMOSD without aquaporin4 IgG antibody needs at least two core clinical characteristics(7), in our patient only optic neuritis is there, and MRI brain and spinal findings are 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. Our 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.

REFERENCES

1. Johnson MD, Lavin P, Whetsell WO. Fulminant monophasic multiple sclerosis, Marburg's type. J Neurol Neurosurg Psychiatry. 1990 Oct 1;53(10):918–21.
2. Ludwig A. Marburg's Variant of Multiple Sclerosis with Extensive Brain Lesions: An Autopsy Case Report. Int J Neurol Neurother [Internet]. 2015 Jun 30 [cited 2023 Aug 19];2(1). Available from: https://clinmedjournals.org/articles/ijnn/ijnn-2-027.php?jid=ijnn
3. Walid MS, Sanoufa M. The diagnosis of Marburg Disease is course-dependent. GMS Ger Med Sci 8Doc06 ISSN 1612-3174 [Internet]. 2010 [cited 2023 Aug 19]; Available from: http://www.egms.de/en/gms/2010-8/000095.shtml

4. Nozaki K, Abou-Fayssal N. High dose cyclophosphamide treatment in Marburg variant multiple sclerosis. J Neurol Sci. 2010 Sep;296(1–2):121–3.
5. Manuel A, Vasudevan MC. A Case of Marburg's Variant of Multiple Sclerosis Successfully Treated with IVIg and Mitoxantrone. Ann Indian Acad Neurol. 2021;24(1):92–4.
6. Capello E, Mancardi GL. Marburg type and Balo`s concentric sclerosis: rare and acute variants of multiple sclerosis. Neurol Sci. 2004 Nov;25(S4):s361–3.
7. Borisow N, Mori M, Kuwabara S, Scheel M, Paul F. Diagnosis and Treatment of NMO Spectrum Disorder and MOG-Encephalomyelitis. Front Neurol. 2018;9:888.