A Case Report of Marburg Multiple Sclerosis responding to Mitoxantrone

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Background

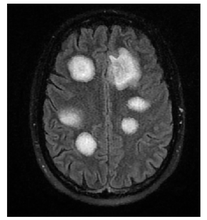
Marburg variant of Multiple Sclerosis (MS) is an aggressive and rare form of MS that can be devastating due to rapid progression to severe disability. It must be recognized quickly to initiate appropriate treatment. This type of MS was originally described by Otto Marburg in 1906[1] who coined the name Marburg Disease. Incidence is <4% of cases of MS[2] and prevalence is 6-12% of patients with MS[3]. Definitive diagnosis is based on pathology findings but indicative factors include rapid progression of clinical findings and confluent large lesions on imaging, especially in the brainstem. Mitoxantrone is a drug that was initially developed and approved for acute myelogenous leukemia in 1986. In 1997 trials were published on its use in MS[4]. Currently it is not commonly used in most types of MS but there have been a handful of case reports describing its use in aggressive cases of MS. We will describe a patient with Marburg-variant MS who had a favorable response to Mitoxantrone.

Presentation

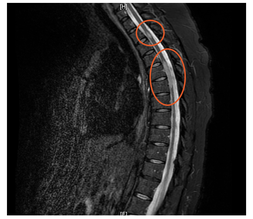
Patient initially presented to medical care with lower extremity weakness and urinary incontinence, was diagnosed with Tumefactive MS, received high dose steroids and was discharged with a steroid taper and Neurology follow up. She was initially improving, but 17 days after her initial symptoms, just after her steroid taper ended, she developed new expressive aphasia, disorientation, right visual field cut, and lower extremity paralysis (strength 0/5). At this point she returned to the hospital, where she had further workup with Magnetic Resonance Imaging (MRI) and cerebrospinal fluid (CSF) studies. Initially Plasma Exchange (PLEX) was chosen as it is a known treatment for MS and other demyelinating disorders and the patient had not responded to steroids. As she continued to rapidly decline in the hospital despite PLEX, more effective treatment was needed. Other standard MS therapies (i.e. natalizumab, ocrelizumab), immunomodulators and chemotherapeutic agents were considered including rituximab, cyclophosphamide, and cladribine. Mitoxantrone became the best choice as it was potent enough for her symptoms, had a quick onset of action, with relatively acceptable side effects and is FDA-approved for MS. Additionally, considering the pathology of Marburg variant is heavily macrophage-predominant[5], we choose a cytotoxic therapy (versus a humoral-mediated agent). One dose was administered soon after readmission, and patient later received high dose steroids and additional rounds of PLEX. Her repeat MRI brain after Mitoxantrone showed decreased peripheral enhancement and diffusion restriction of the initial lesions. She slowly improved until she was completely oriented and had ⅗ strength on her lower extremities so was discharged. Post hospital stay, patient was in inpatient rehab for two weeks, after which she continued from home. She was able to improve until she could walk with a cane. At the time of this report, her mental status is almost to her baseline, with slight word-finding difficulties. Her visual field cut is mostly resolved and she was cleared

Imaging

Initial Imaging on Admission



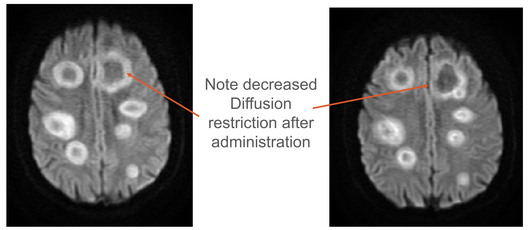
MRI Brain with and without contrast (w/wo) Axial T2 FLAIR



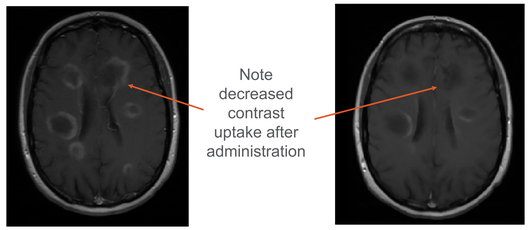
MRI Thoracic Spine w/wo Sagittal STIR

Prior to Mitoxantrone Administration

After Mitoxantrone Administration



MRI Brain w/wo Axial Diffusion Weighted Imaging



MRI Brain w/wo Axial T1 with Contrast

Studies

CSF:

RBC 1/ WBC 3/ Glucose 55/ Protein 36.8

Absent Oligoclonal Bands

Serum:

Aquaporin 4 Antibody (Ab) and Myelin Oligodendrocyte Glycoprotein Ab negative

MRI Brain w/wo

Multifocal (up to 12) T2 white matter hyperintense lesions with peripheral enhancement and diffusion restriction throughout the bilateral hemispheres, the right cerebellum, left lateral pons and middle cerebellar peduncle.

Post-Mitoxantrone imaging showed decreased restricted diffusion and enhancement.

Presentation, Cont.

to drive by her Neuro-Ophthalmologist. She was started on Ocrelizumab for disease modifying treatment by her outpatient Neurologist and repeat MRI Brain and Spine 5 months after her hospital stay showed no new lesions. She has made multiple diet and exercise changes which she felt have amplified her improvements.

Discussion

This patient had rapidly progressing demyelinating disease with an incomplete response to high dose steroids, but a strong response to Mitoxantrone, typical of Marburg disease. On review of literature, this case was similar to other cases as there were rapidly progressive neurological deficits which were unresponsive to steroids. It differed from some others in that there was no brainstem involvement, there were less numerous, larger, confluent lesions, and there was not a high level of CSF protein[6]. When diagnosing MS, it is important to be aware of this variant which confers an aggressive course that does not respond to steroids, but may be responsive to Mitoxantrone.

Conclusion

Mitoxantrone is an option when considering treatments for Marburg MS. First steps include identifying Marburg disease, which is recognized as MS with a rapidly deteriorating clinical course, suboptimal response to conventional treatment and large, confluent FLAIR hyperintense lesions on MRI, frequently including the brainstem. It would be prudent to consider Mitoxantrone with the above findings after a poor response to, or quick relapse after steroids or PLEX treatments. Factors to consider before administering Mitoxantrone include cardiac health, surveilled with a baseline echocardiogram, and baseline platelet counts, especially to be monitored 10-14 days after administration, when the nadir would be expected.

As this is a very aggressive form of the disease without an established treatment strategy, it is important to keep good follow up with the patient, as they may require repeat treatments of Mitoxantrone or alternative treatment such as stem cell transfers, which have been described in case reports.

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