Clinical And Radiographic Improvement Of An Acutely Aggressive Case Of Multiple Sclerosis Treated With Cyclophosphamide

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Introduction

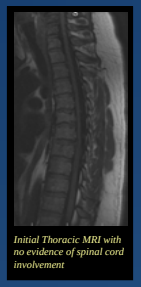
Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system, which partially responds to immune based therapies. There are patients who do not respond to the currently approved treatments and continue to have relapses and gadolinium enhancing lesions on MRI scans. For these patients a new direction in therapy is necessary.

Case Report

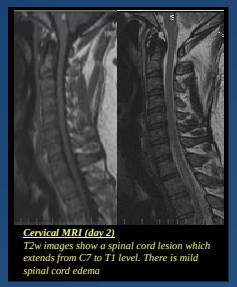
46 year old man with no past medical history, who developed genital sensory disturbances 2 weeks before admission. Symptoms progressed to numbness and weakness in lower extremities, with loss of sphincter control. He received oral steroids with no improvement.

He rapidly worsened in the next few days. Initial thoracic MRI did not show spinal cord lesions.CSF demonstrated high IgG synthesis rate (16.8) and IgG index (0.66), and more than 5 oligoclonal bands. Lyme antibodies, HIV test, rheumatologic profile were all negative.

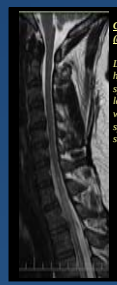
He received IV dexamethasone with minimal clinical response and was then transferred to our care. On arrival he was alert and orientated with fluent speech. Visual acuity and funduscopic examination was unrevealing. His eye movements were intact with minimal nystagmus on central and end gaze. Remaining cranial nerves were intact. Motor exam revealed 2/5 in right leg and 0/5 in the left lower extremity. There was decrease of all sensory modalities in both legs with a T12 sensory level. Deep tendon reflexes were 2+ in upper extremities and 3+ in lower with flexor plantar reflexes. One gram of IV methylprednisolone was given for 5 days followed by 60 mg of oral prednisone. Plasmapheresis was initiated every other day. Visual evoked potentials were normal. No improvement of symptoms was noted. After 4 days he began to notice decreased vision which rapidly worsened. At that time he had 20/70 vision in left eye, 20/40 in right eye and prominent horizontal nystagmus, bilateral dysmetria and dysdiadochokinesia. There was decrease of all sensation modalities with a T10 level. A new brain MRI showed a lesion in the right medulla and a new course of IV Solumedrol was given for 3 days. He worsened in the next 72 hrs. His vision was now 20/200 in left eye and 20/70 in right, with normal fundus. A new brain MRI showed increasing areas of T2 hyperintensity in the left posterior lateral midbrain plus areas of enhancement in the upper anterior pons and left middle medulla. An orbital MRI showed optic nerve enhancement. A second lumbar puncture was performed obtaining 3 WBC, 5 RBC, protein 111, glucose 79, and IgG index of 1.96, Lyme, ACE negative.



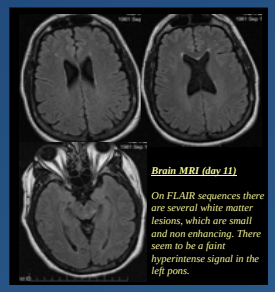
Initial Thoracic MRI with no evidence of spinal cord involvement



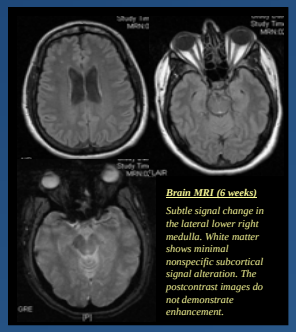
Cervical MRI (day 2)
T2w images show a spinal cord lesion which extends from C7 to T1 level. There is mild spinal cord edema



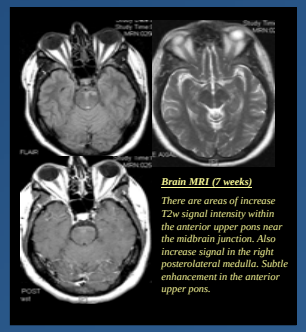
Cervical MRI (day 11)
Large hyperintense spinal cord lesion (C7 to T3) with significant spinal cord swelling.



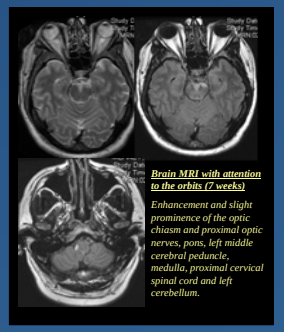
Brain MRI (day 11)
On FLAIR sequences there are several white matter lesions, which are small and non enhancing. There seem to be a faint hyperintense signal in the left pons.



Brain MRI (6 weeks)
Subtle signal change in the lateral lower right medulla. White matter shows minimal nonspecific subcortical signal alteration. The postcontrast images do not demonstrate enhancement.



Brain MRI (7 weeks)
There are areas of increase T2w signal intensity within the anterior upper pons near the midbrain junction. Also increase signal in the right posterolateral medulla. Subtle enhancement in the anterior upper pons.

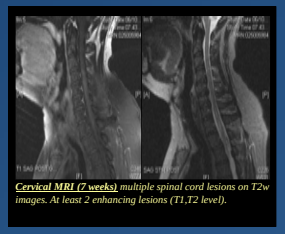


Brain MRI with attention to the orbits (7 weeks)
Enhancement and slight prominence of the optic chiasm and proximal optic nerves, pons, left middle cerebral peduncle, medulla, proximal cervical spinal cord and left cerebellum.

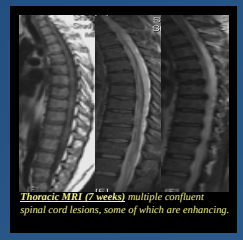
NMO antibodies were negative. He continued with plasmapheresis completing 10 exchanges. A follow up brain MRI was performed which showed increased enhancing lesions. At this point we decided to begin treatment with cyclophosphamide 750 mg/m2. He tolerated the medication and was transferred to the rehabilitation unit on 80 mg of oral prednisone daily which we began to taper. He slowly began to improve; he has currently received 6 monthly doses of cyclophosphamide. His vision has improved to 20/20 in both eyes, motor was 5/5 in upper extremities and 4/5 in lower extremities. Mild decrease in light touch and temperature in left leg, vibration is diminished in both, there is no sensory level at present time. He is standing by himself and walking with assistance. Follow up brain and spinal MRI show significant improvement of white matter lesions with no enhancement after contrast administration.

Conclusion

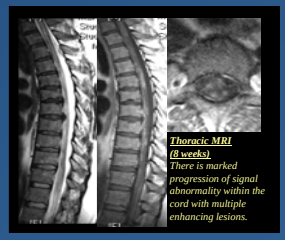
The use of induction therapy with cyclophosphamide and other immunosuppressant agents for the initial episode of aggressive MS with negative prognostic factors has been reported to have short and long lasting beneficial effects. The only limitations are the safety concerns.
One of the main concerns with the use of cyclophosphamide is the risk of bladder cancer. Such a risk must be balanced by the existence of bad prognostic factors, such as very high disease activity or very poor recovery from attacks.
Cyclophosphamide is an alkylating chemotherapeutic drug that can be used in aggressive cases of MS and in patients that are unresponsive to other MS treatments.



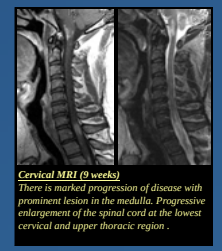
Cervical MRI (7 weeks) *multiple spinal cord lesions on T2w images. At least 2 enhancing lesions (T1,T2 level).*



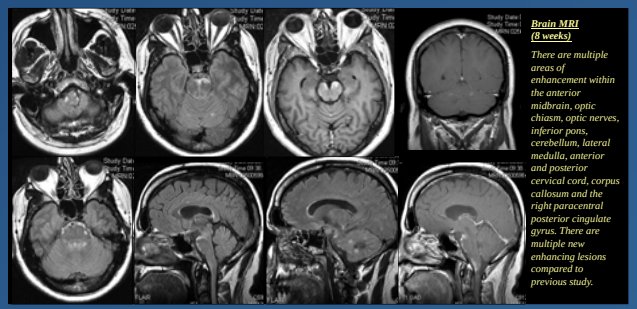
Thoracic MRI (7 weeks) *multiple confluent spinal cord lesions, some of which are enhancing.*



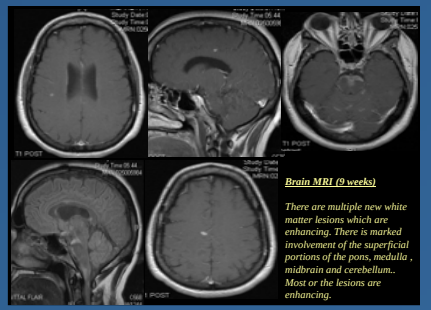
Thoracic MRI (8 weeks)
There is marked progression of signal abnormality within the cord with multiple enhancing lesions.



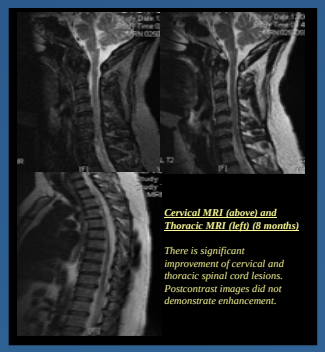
Cervical MRI (9 weeks)
There is marked progression of disease with prominent lesion in the medulla. Progressive enlargement of the spinal cord at the lowest cervical and upper thoracic region .



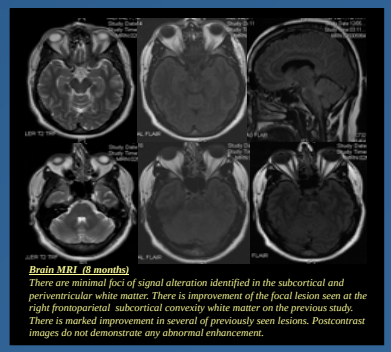
Brain MRI (8 weeks)
There are multiple areas of enhancement within the anterior midbrain, optic chiasm, optic nerves, inferior pons, cerebellum, lateral medulla, anterior and posterior cervical cord, corpus callosum and the right paracentral posterior cingulate gyrus. There are multiple new enhancing lesions compared to previous study.



Brain MRI (9 weeks)
There are multiple new white matter lesions which are enhancing. There is marked involvement of the superficial portions of the pons, medulla , midbrain and cerebellum.. Most or the lesions are enhancing.



Cervical MRI (above) and Thoracic MRI (left) (8 months)
There is significant improvement of cervical and thoracic spinal cord lesions. Postcontrast images did not demonstrate enhancement.



Brain MRI (8 months)
There are minimal foci of signal alteration identified in the subcortical and periventricular white matter. There is improvement of the focal lesion seen at the right frontoparietal subcortical convexity white matter on the previous study. There is marked improvement in several of previously seen lesions. Postcontrast images do not demonstrate any abnormal enhancement.

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