AN UNUSUAL PRESENTATION OF NEUROMYELITIS OPTICA (NMO)

MURTHY TV THIMANNAGOWDA
Department of Neurology,
CHRISTIAN MEDICAL COLLEGE

Abstract:
We are reporting atypical presentation of Neuromyelitis Optica in 18 year old female patient

Keyword: NMO, TB, MS, AQP4

Neuromyelitis optica (NMO) is a devastating demyelinating disease of the central Nervous system affecting the optic nerves and the spinal cord. NMO is characterized by the presence of pathogenic specific IgG anti- aquaporin4 antibodies (AQP4). Aquaporin-4 (AQP4) is a specific biomarker of the disease and its targeted antigen. NMO has relapsing and remitting course. NMO would lead to severe neurological disability if not treated early. We are reporting a case of an 18 year old female patient presented with headache, low grade fever, hiccups, vomiting and spastic quadriplegia. Initially she was treated as Tubercular meningomyelitis, later the cause was found to be NMO by clinical features, neuroimaging and laboratory features.

CASE REPORT:
18 year old female patient presented with history of headache, intermittent low grade fever and recurrent hiccups for two weeks. Headache was insidious in onset, started in the occipital region then became holocranial, aching in character, continuous and moderate in intensity. Headache was associated with hiccup, occasional vomiting and photophobia. One week following onset of headache, she developed acute onset of weakness of lower limbs followed by upper limbs with decreased sensations of all modalities below the neck with bladder involvement. The onset to peak of weakness was 3 days. There was no history of disturbance in consciousness. No history of visual disturbances like dimness of vision, double vision. No history of nasal twang in speech, nasal regurgitation, coughing while eating or drinking. No history suggestive of cranial nerve deficits. No previous history of tuberculosis (either pulmonary or extra pulmonary). No significant past medical history of optic neuritis or myelitis. On examination patient was conscious and well oriented. The cranial nerves were normal. The fundus was normal. She had quadriplegia with 1 power (MRC grade) in both upper and lower limbs with exaggerated deep tendon reflexes and bilateral extensor planter response.
She had decreased sensations for all modalities below C4 level. She had neck stiffness. Overall features suggestive of Meningomyelitis. The etiological possibilities considered were of infective (tuberculosis/ viral causes/ inflammatory disorders (Neuromyelitis optica, Sjogren’s syndrome, Neurosarcoïdosis, Neuro Behcets disease) and neoplastic disorders. MRI brain and spine showed long segment T2 hyper intensities involving entire length of spinal cord up to the cauda equina with few skip regions. MRI also showed mild enhancement noted in the cervical cord and the cauda equina region suggesting active disease. There were white matter T2 hyperintensities in the genu of corpus callosum and surrounding periventricular white matter with associated gliosis. The optic nerves were normal. Her complete blood counts, Liver function tests, Renal function tests were normal. ESR was elevated (73mm/1st hour). CSF analysis showed 130 cells with lymphocytic predominance (99%). CSF protein was 282mg/dl and sugar was 54mg/dl (Concurrent RBS of 110mg). CSF viral multiplex PCR was negative. CSF cultures including bacterial, viral and fungus were negative. CSF cytospin showed lymphocytosis. All the vasculitic markers were negative. CT thorax and abdomen was non-contributory. VEP (visual evoked potential) was normal. SSEP tibial and median showed features of dorsal column dysfunction. A probable diagnosis of Meningomyelitis of probable Tubercular etiology was considered in view of acute presentation, of headache, hiccup, spastic quadriaparesis, elevated ESR, MRI brain and spine changes (involvement of long segment of cord with thickened cauda equina roots and enhancement). CSF features of lymphocytic pleocytosis with elevated proteins with borderline sugars. She was started on first line 4 drugs ATT (anti-tubercular drugs) with oral dexamethasone. She noticed improvement in weakness, headache and hiccups. The improvement was noticed within one week after starting medicines (ATT with steroids). She was able to walk with one person support and able to feed herself. She was discharged. She continued to take ATT but stopped oral Dexamethasone after 3 weeks of starting. Within a week of following stopping steroids, she developed holocranial headache, bilateral vision loss and progressive worsening of weakness of all 4 limbs. This was followed by progressive altered sensorium. These symptoms progressed over 2 weeks prior to readmission. There was no history of seizures. On admission, she was in altered sensorium with flaccid quadriaparesis with hypo reflexia suggestive of a necrotic myelopathy. The fundus showed bilateral disc pallor. She was evaluated for Inter current causes of worsening such as sepsis and metabolic derangements which was excluded. Repeat MRI brain and spine showed new T2 hyper intense lesion seen in the midbrain and upper part of the pons also involving the superior cerebellar peduncle and the medial aspect of the middle cerebellar peduncle with mild patchy enhancement. There were no areas of restricted diffusion/hemorrhage. Her CBC, LFT, RFT and electrolytes were normal. Repeat CSF analysis showed 15 cells with lymphocytic predominance, protein of 97mg/dl and sugar of 68mg/dl (concurrent RBS 100). CSF cultures were negative for TB and fungus. CSF multiplex PCR was also negative. HIV status was negative. Other infective workup was negative. CSF Oligoclonal bands were present. Anti-aquaporin 4 antibodies were strongly present (2+) in the blood. VEP showed bilateral anterior optic pathway dysfunction.
Her diagnosis was revised in view of dramatic improvement in her symptoms within a week of starting steroids and relapse within a week following stopping steroids. So she was responded to steroid than the ATT. She was diagnosed as Neuromyelitis optica based on history, examination, characteristic neuroimaging findings involvement of dorsal brainstem, periaqueductal region, hypothalamus, long cord segment involvement more than 3 segments and the presence of specific Aquaporin4 antibodies. Her altered sensorium was due to involvement of the brainstem reticular activating system and hypothalamus. She was started on Immunomodulation with pulse methyl prednisolone (1gram daily for 5 days followed by weekly tapering schedule) and pulse Cyclophosphamide. ATT was discontinued. During hospital stay she started improving within a week of starting steroids (pulse methylprednisolone, Cyclophosphamide) with improvement in sensorium and she started sitting with support and power in the upper and lower limbs improved to grade 3. Repeat MRI imaging showed significant resolution of T2 hyper intensities in the brain stem and the cord. She then underwent rigorous Physiotherapy and occupational therapy during her stay. At time of discharge (5 weeks of admission), she was able to walk with single person support. She could eat with her hands. She had residual visual impairment bilaterally and spasticity in the limbs.

**Fig.1: MRI BRAIN and SPINE during 1st admission**

A. T2 FLAIR showing hyper intensities involving the periventricular white matter in the frontal region  
B. T2 FLAIR axial image showing hyper intensities in the dorsal medulla  
C. T1 Sagittal image showing T1 hypointense lesion extending from medulla down the cauda equine with few skip lesions  
D. T2 sagittal spine showing hyper intensities extending from brain stem to cauda equina  
E and F Gado images showing contrast enhancement of the cervicomedullary lesion.

**Fig.2: MRI BRAIN and SPINE during 2nd admission**

A and B; T2 axial FLAIR images showing hyper intensities involving the brainstem, pons, midbrain, periaqueductal region and hypothalamus  
C; T1 Sagittal image showing the T1 hypointense lesion extending from the brainstem to cervical cord  
D; No areas of restriction  
E and F showed mild enhancement of brainstem and cord lesions.
Fig.3: MRI BRAIN and SPINE following treatment with Immunomodulation A,B. Decrease in hyper intense lesions in the mid-brain and pons C,D. Decrease in hyper intense signals in brainstem and cord but with mild cord thinning. E,F. Contrast images showing no enhancement.

DISCUSSION:
Neuromyelitis Optica is an autoimmune inflammatory disorder of CNS. Prior to the detection of Anti-aquaporin-4 antibodies, NMO was considered a variant of Multiple sclerosis. Now is being considered as a separate entity(1,2,3). In MS involvement is asymmetric in nature(1). MS causes optic neuritis which is usually unilateral and it had good recovery either spontaneously or with steroids. MS involves only peripheral segment of the cord and its less than 3 segments(2)(3). The Neurological disability due to cord involvement is minimal. In brain MS involves the sub cortical white matter mainly pericentral(Dawson’s fingers). CSF analysis shows the presence of Oligoclonal Bands IgG (OCBS) with normal cellularity, normal sugar and normal or mildly elevated csf proteins(3)

(4) NMO is common in females (8:1) presenting commonly in 3rd to 4th decade. The incidence of NMO worldwide is 1 in 1akh population. In India, NMO contributes about 10 to 20% of the demyelinating diseases(7). Anti-aquaporin 4 antibodies are specific for NMO and are absent in MS(5). Anti-aquaporin4 antibodies are present in up to 80% of NMO cases, 5 to 27% of relapsing optic neuritis and 25 to 60% in long extensive transverse myelitis(8). Presence of AntiAQP4 antibodies common in females than males. The severity of the disease correlates with the antibodies titres. Relapse is common in females than males (9). NMO presents with relapsing episodes of Optic Neuritis, Myelitis or both in more than 90% of the patients(4,10). Remaining 10% of the patients presents with simultaneous optic neuritis with myelitis and monophasic course. NMO patients with Optic neuritis and myelitis have more disabilities when compared to MS patients(3,11). So if not treated early will left with severe neurological disability(1). Early introduction of the strong immunosuppressive therapy will reduce the morbidity, mortality and chances of relapses(12). The chances of developing blindness was reported to be >50% of patients with optic neuritis over a period of 6 to 7years(8). The mortality over 5 years reach 2.9% to 25%(11) (13). NMO can present with uncommon clinical features like seizures, intractable hiccoughs, vomiting, cranial nerve palsies, recurrent coma, PRESS$posterior reversible encephalopathy syndrome), and SIADH. NMO and spectrum disorders associated with autoimmune diseases like SLE, Sjogren’s syndrome, Myasthenia Gravis, Hypothyroidism. Such an association is not seen with MS(5)(14). CSF analysis in NMO will be abnormal.
in 50 to 70% of the patients. The cellularity usually 20 /cm and can go up to 500 cells/cm(6)(7). The predominant cell type is lymphocytes along with neutrophils and eosinophils during relapse(15)(10)(9). The CSF protein is often elevated due to damage to blood brain barrier. CSF OCB are present in 18% in Antiaquaporin antibody positive NMO patients and in 90% of MS patients(6). There is no difference in CSF finding is seropositive or seronegative aquaporin antibody status(16). MRI features includes, long cord lesions extending over three or more vertebral segments, often with patchy and inhomogeneous contrast enhancement over weeks or even months, or, less frequently central necrosis and cavitation seen which are characteristic features and highly suggestive of an NMO(1)(15)(17). Brain lesions tend to be located at sites of high aquaporin-4 expression such as the diencephalon, hypothalamus, area postrema and periaqueductal region (5)(16)(18) . Contrast enhancement on brain MRI with a cloudlike shape and pencil-thin ependymal enhancement were reported to be typical of NMO. severe inflammation may cause irreversible cord atrophy, which may be a negative predictive factor for response to plasma exchange/Immunotherapy in case of subsequent attacks(19)(13).

In the diagnosis of neuromyelitis optica, the absolute criteria is that optic neuritis and acute myelitis exist, and the support criteria is that 2 or more of the following is satisfied: negative brain MRI at disease onset, spinal cord MRI with contiguous T2-weighted signal abnormality extending over 3 or more vertebral segments, and NMO-IgG seropositive status(14)(15). In our case, she had presented with acute onset of headache, hiccoughs, vomiting followed by spastic quadripareisis with bladder involvement. MRI showed involvement of the entire length with cord and mild thickening of cauda-equina roots. There was mild enhancement of the lesions. CSF analysis showed significant lymphocytic pleocytosis with low CSF sugars and elevated CSF proteins. She was treated as Tubercular meningomyelitis due to acute presentation and a common scenario in countries like India. MRI didn’t showed much brain stem lesions during first admission. She was started on first line 4drug ATT with oral steroids. She showed dramatic improvement within a week of starting steroids. She stopped steroids 3weeks later due to non compliance and continue ATT. Within a week of stopping steroids, she developed progressive worsening of symptoms like headache, reduced visual acuity and worsening of weakness of the limbs with altered sensorium over a period of next 2 weeks. She was readmitted and neuroimaging repeated which showed worsening of findings when compared to first admission imaging. The MRI showed increased extension of involvement of brainstem up to midbrain, involvement of hypothalamus with necrotising myelopathy involving the cervical thoracic cord. These are the classical aquaporin receptor sites which are not seen in tuberculosis(4,16). There was minimal enhancement of the lesions. There were no features of hydrocephalus or raised ICT. CSF analysis showed mild pleocytosis with normal sugars and mildly elevated CSF proteins. NMO patients will have elevated csf counts ranging from 20 to 500cells/micro litre, lymphocytic predominance with elevated proteins(6,7). Anti aquaporin 4 antibodies were strongly positive in the blood. These antibodies are specific to NMO and not seen in any other disorder(6).
VEP showed bilateral anterior optic pathway dysfunction. The Symptomatology, strong clinical response to steroids and relapse following stopping of steroids, MRI finding of involvement of classical aquaporin4 receptor areas, bilateral optic nerve involvement, positive Anti-aquaporin 4 antibodies were in favour of Neuromyelitis optica. The points against the tubercular etiology there was no features of raised ICT, hydrocephalus, adhesive arachnoiditis, atypical, no basilar meningitis or papilloedema even after 8 weeks of onset of disease. She was diagnosed Neuromyelitis optica and started on intensive immunosuppression with pulse methylprednisolone and steroid sparing pulse Cyclophosphamide. The ATT was stopped. She showed dramatic improvement within a week of starting treatment (pulse methylprednisolone and Cyclophosphamide). Her sensorium improved. She started sitting with support and power in the upper and lower limbs improved to grade 3. She was able to feed herself. She had residual visual impairment and spasticity in the limbs. Repeat imaging after 8 weeks showed significant resolution of the lesions. In conclusion, whenever a patient presents with atypical features like hiccoughs, vomiting, headache, low-grade fever, brainstem involvement and long segment myelitis, we must consider Neuromyelitis optica as important differential. Since delay in diagnosis and treatment will lead to reduced morbidity and mortality.

References:


