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ANTI-MOG ASSOCIATED ENCEPHALITIS MASQUERADING AS AN ACUTE MANIC EPISODE RESPONDED TO RITUXIMAB.

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ABSTRACT Myelin Oligodendrocyte Glycoprotein (MOG), encoded by MOG gene present in chromosome no. 6, is found exclusively in the CNS, where it is localized on the surface of myelin and oligodendrocyte cytoplasmic membranes helping in myelination of nerves and serves as an important adhesion molecule. In the last two decades many MOG-opathies have been discovered and enlisted in the category of inflammatory demyelinating diseases. Anti-MOG associated encephalitis has varied presentations. Seldom they present as neuropsychiatric syndromes and may be therefore misdiagnosed for a primary psychiatric illness. Again, this can be prevented with high index of suspicion, and accurate early diagnosis with proper serologic testing. And early institution of therapy is life-saving.
We hereby report a case of anti-MOG encephalitis which presented with cardinal manifestations of an acute manic episode hiding the catastrophe underneath.

KEYWORDS : myelin oligodendrocyte glycoprotein, psychiatric illness, inflammatory demyelinating diseases

INTRODUCTION:

Anti-myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) have been reported in different inflammatory demyelination diseases such as acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorders (NMOSD), idiopathic optic neuritis, idiopathic myelitis, and atypical multiple sclerosis [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13]. However, the whole spectrum of clinical phenotypes associated with MOG-Abs-related disorders has yet to be distinctly defined. Here, we present a patient with MOG-Abs associated encephalitis resembling clinical picture of acute mania as a possible new clinical phenotype associated with MOG-opathies.

CASE REPORT:

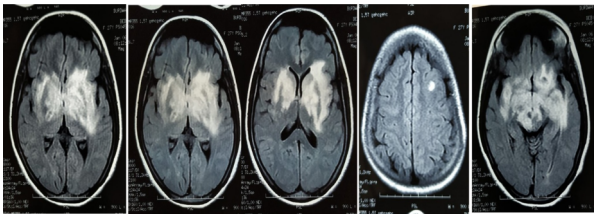
A 27-year-old female patient was referred from the psychiatry OPD to emergency department of medicine due to recent onset altered level of consciousness and a single episode of focal seizure with dyscognitive features. She visited the psychiatry OPD only one week ago due to threatening behavior, irritability, and inability to take personal care. During the initial psychiatric visit she was hyper verbal with pressured speech and a tangential thought process. Her mood was elated with a labile affect with inapt bursts of tearfulness. She also gave history of decreased need for sleep over the past 2 weeks. She endorsed hearing strange noises and voices around her apartment. Her family members complained that she kept on dancing after midnight for the last three days in spite of all prohibitions. They also strongly denied any history of fever, drug ingestion, addictions, jaundice and taking oral contraceptive pills and thyroid pills.

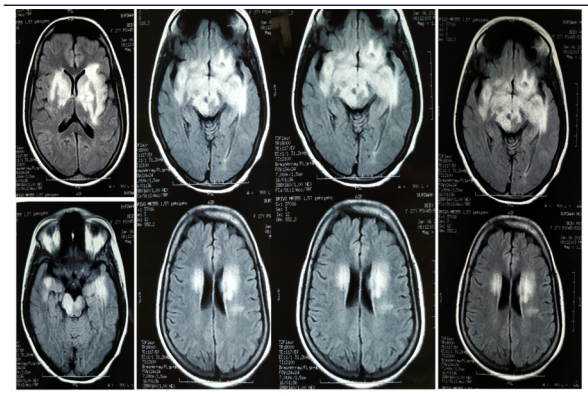
Her past medical record was insignificant for any psychiatric illness and substance abuse. A plain CT scan of brain revealed no abnormality. Using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria she was diagnosed with having an acute manic episode and treatment was started with lithium, aripiprazole and divalproex to which she did not respond at all. Again, condition got worse when she attended this time at the OPD with a history of seizure and altered mental status and hence referred to general medicine emergency.

On examination, patient was having active focal seizure of entire left side of the body with dyscognitive features. She was tachycardic, tachypnoeic, afebrile, normotensive and nondiabetic. On neurological examination, she was drowsy, disoriented to time, place and person (GCS score: E2V3M5) without any sign of meningeal irritation. Both pupils were equally and sluggishly reacting to light without any demonstrable relative afferent papillary defect. All her deep tendon reflexes were depressed. Plantar responses were bilaterally extensor. Fundoscopy did not show any papilloedema. A detailed neurological examination could not be done at that time because of her poor mentation.

Based on this history and clinical findings, a list of differential diagnoses were made: ADEM (Acute Disseminated Encephalo myelitis), Infective meningoencephalitis, Hashimoto's encephalopathy, Autoimmune Encephalitis, anti-MOG associated encephalitis, Metabolic encephalopathy, Cerebral venous thrombosis, PRES (Posterior Reversible Encephalopathy Syndrome), Space occupying Lesion with acute hemorrhagic transformation, Vascular malformations with its rupture related complications, and deposition disorders. We put her on intravenous antiepileptic, antibiotics and antiviral and sent her for a Magnetic Resonance Imaging of brain with contrast and then performed lumber puncture for CSF analysis.

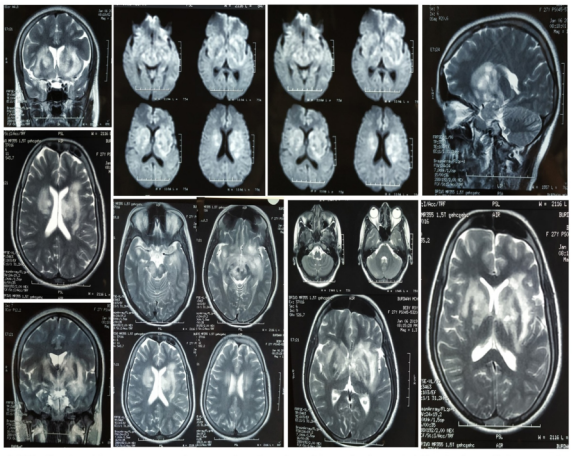
MRI of brain with Contrast revealed fluid attenuated inversion recovery (FLAIR) and T2 diffuse hyper intensities involving brainstem, bilateral thalamus, basal ganglia, internal capsule, medial temporal and frontal lobes associated with small hyper intensities in the subcortical, periventricular and cortical regions minus any contrast enhancement. Again, diffusion weighted images (DWI) displayed mild restrictive pattern of the aforesaid affected regions which exhibited medium apparent diffusion coefficient (ADC) values and with core having low ADC values plausible for inflammatory process (Images below). MRI of spinal cord divulged no abnormal intensity changes.





MRI of brain with contrast reveals non-enhancing altered intensity hyper in T2 FLAIR at both medial temporal, basal ganglia, peri-ventricular and in brain stem and both frontal area.

Comprehensive metabolic panel, lipid profile and thyroid profile including anti-TPO were unremarkable. CSF studies eliminated possibilities of an infective etiology and showed presence of 4-10 oligoclonal bands. A comprehensive workup for viral encephalitis including polymerase chain reaction for *Enterovirus, Herpes simplex virus 1, 2, HHV-6, Epstein-Barr virus, Cytomegalovirus, Varicella Zoster virus, Dengue, Chikungunya, and Japanese encephalitis* including cultures for bacteria and fungi resulted negative. CSF CBNAAT (for MTB), VDRL (CSF and serum) were negative too. Serum and CSF for NMOSD panel tests and VEP (Visual Evoked Potential) test were absolutely non-contributory. Serum Ceruloplasmin and 24 hours urinary copper excretion levels were within the normal range. Connective tissue disorder profiles, autoimmune encephalitis profile, APLA profile, Vasculitis screen came out to be negative. Serologies for Hepatitis B, Hepatitis C, and HIV were non reactive. Thrombophilia Panel, Coagulation Profile and MR Venogram of cerebral veins exhibited no abnormality.



MRI of brain with contrast reveals non-enhancing altered intensity hyper in T2 at both medial temporal, basal ganglia, peri-ventricular and in brain stem and both frontal area.

Diffusion weighted images (DWI) displayed mild restrictive pattern of the aforesaid affected regions which exhibited medium apparent diffusion
coefficient (ADC) values and with core having low ADC values plausible for inflammatory process.

However special investigation done for Anti-MOG antibody came strongly positive sealing the diagnosis. The patient was treated with Intravenous methylprednisolone and Rituximab with an almost complete clinical recovery in a few days. On follow-up MRI examination after 2 weeks a noticeable improvement of pre-existing lesion was observed only the persistence of slight unsteady gait was noted at the last clinical evaluation 2 weeks after the onset.

DISCUSSION:

We are broadcasting an atypical presentation of MOG-Abs associated encephalitis which presented as an acute manic episode followed by an encephalopathy with prompt response to IV methylprednisolone and Rituximab. Since the patient presented with subacute onset of altered mental status, new focal central nervous system findings in absence of alternative causes, she also met the revised diagnostic criteria for possible autoimmune encephalitis recently proposed [14]. However, the absence of ant-NMDR, AMPA-GluR1, 2, VGKC (LG1 and Caspr2) and GABA-B receptor antibodies both in serum and CSF made the diagnosis refutable. In this case reported, some features, as the multiple supratentorial lesions of the white matter, basal ganglia, thalamus and brainstem, simulate those observed in ADEM but MRI was not totally compatible due to the type of gray and periventricular involvement and the absence of spinal cord lesions. Since criteria for ADEM have been clearly established only for pediatric cases [15] and the diagnosis in adults, also with MOG-Abs, remain challenging [14].

Diagnosis and management of MOG-opathies remains a path yet to be paved. Anti-MOG associated encephalitis is exquisitely rare. Less than ten cases of encephalitis with MOG-Abs have been reported so far to the best of our literature review [16, 17]. Again, our case did not have any features of optic neuritis that would have made diagnosis of neuromyelitis optica spectrum disorder (NMOSD) and MOG-opathies more credible. Added to it, this particular case presented with characteristic manic psychotic symptoms making the diagnosis even more arduous. Our case confirms that anti-MOG antibody test should be asked for ad rem and anti-MOG encephalitis is a separate clinical entity amongst the spectrum of inflammatory demyelinating disorders of central nervous system. Again, with apt diagnosis and expedient treatment lives can be salvaged.

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