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Case Report

Neuromyelitis Optica Spectrum Disorder (NMOSD) with Sjogren's Syndrome: A Case Report

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ABSTRACT

Neuromyelitis Optica (NMO) is an infrequently encountered autoimmune demyelinating condition that predominantly affects central nervous system. NMO is often found to be associated with Sjogren's syndrome (SS) which is a chronic autoimmune disease characterized by lymphocytic infiltration of exocrine glands.

Here we report a case of 45 years old female who suffered from recurrent nausea and vomiting. She consulted multiple gastroenterologists for her complaints and even underwent cholecystectomy. But there was no relief in her symptoms. She later developed quadriparesis and MRI showed demyelinating changes suggestive of Neuromyelitis Optica. She was screened for ANA profile which was positive for SSa/ Anti-Ro, confirmatory for Sjögren's syndrome, despite having no glandular symptoms.

KEYWORDS: Multiple sclerosis, Demyelinating disorder, Aquaporin 4, IgG antibody

INTRODUCTION

Neuromyelitis Optica (NMO) also known as Devics disease, is a clinical condition characterized by recurrent episodes of optic neuritis and transverse myelitis. NMO transpires via formation of IgG autoantibodies to aquaporin 4 (AQP4) which is the most prevalent water-channel protein concentrated in the astrocytic foot processes in the central nervous system[1]. It is quite evident from the literature survey that individuals who are seronegative for AQP4-IgG antibodies have been found positive for IgG antibodies against myelin oligodendrocyte glycoprotein; one of the most common structural protein in the outer myelin sheath of neurons[2,3]. This relapsing demyelinating disease involving optical nerve and spinal cord, had signs of hypothalamic and hypophyseal dysfunction and a common association with other systemic autoimmune conditions such as Sjogren syndrome (SS), Systemic Lupus Erythematosus (SLE) and Rheumatoid Artheritis[4-9].

Sjögren's syndrome (SS) is a chronic systemic disease characterized by inflammation and dysfunction of exocrine glands. According to literature SS is one of the most recurrent entities seen in conjunction with NMO among various other autoimmune disorders[10,11]. Here in we are reporting a case of middle-aged female who presented to Neurology department and was eventually diagnosed as a case of NMO with secondary association of SS.

CASE PRESENTATION

A 45-year-old female first presented in Gastroenterology Outpatient Department of PMCH with complaints of recurrent vomiting, retching & dyspepsia for 4 months. Earlier she had consulted multiple gastrophysicians for the same complaint but had no relief in her symptoms. On evaluation, she was found to have cholelithiasis and she underwent surgery. Her symptoms did not subside even after the surgery.

After one month, patient presented to the Neurology clinic with symptoms of increased sleep and weakness in lower limbs along with the previous complaint. MRI brain was done which revealed T2/ FLAIR hyperintense lesion involving lower part of dorsal medulla in bilateral paramedian location giving impression of demyelinating lesion and possibility of Neuromyelitis Optica with Area Postrema syndrome was kept. Haematological investigations showed normal CBC, normal renal and liver function tests. Serum electrolytes were normal. CSF examination showed normal protein, cell counts but elevated glucose level (87mg/dl). On further evaluation of the patient, Antinuclear antibody (ANA) by immunofluorescence was positive (1:100 dilution). ANA (Immunoblot) showed positivity for SSA/ Ro52. Anti dsDNA, Antineutrophil cytoplasmic antibody (p-ANCA & c-ANCA) and antiphospholipid antibodies were negative. AQP4-IgG antibody (cell-based assay) came out to be positive and she was diagnosed as a case of NMOSD.

Patient was started on oral steroid therapy and responded to the treatment. Immunotherapy was advised to her but she postponed the therapy and even stopped taking medication on her own.

After a month the patient had a severe bout of relapse when she presented with quadriparesis and suffered cardiac arrest. She was revived by CPR and was kept on mechanical ventilation. On repeat MRI, her demyelination progressed erratically. There was abnormal signal intensity appearing hyperintense on T2 & FLAIR and hypointense on T1 with patchy areas of diffusion involving more than 3/4th of medulla. (Figure 1) The patient was treated with intravenous methylprednisolone (1gm/day) for five days followed by oral prednisolone. Patient responded well to the treatment with no further episodes. She was adviced to receive Rituximab therapy after appropriate preparation (Varicella Zoster, Pneumococcal and Influenza vaccines, measurement of CD-19 levels and HbcAg).

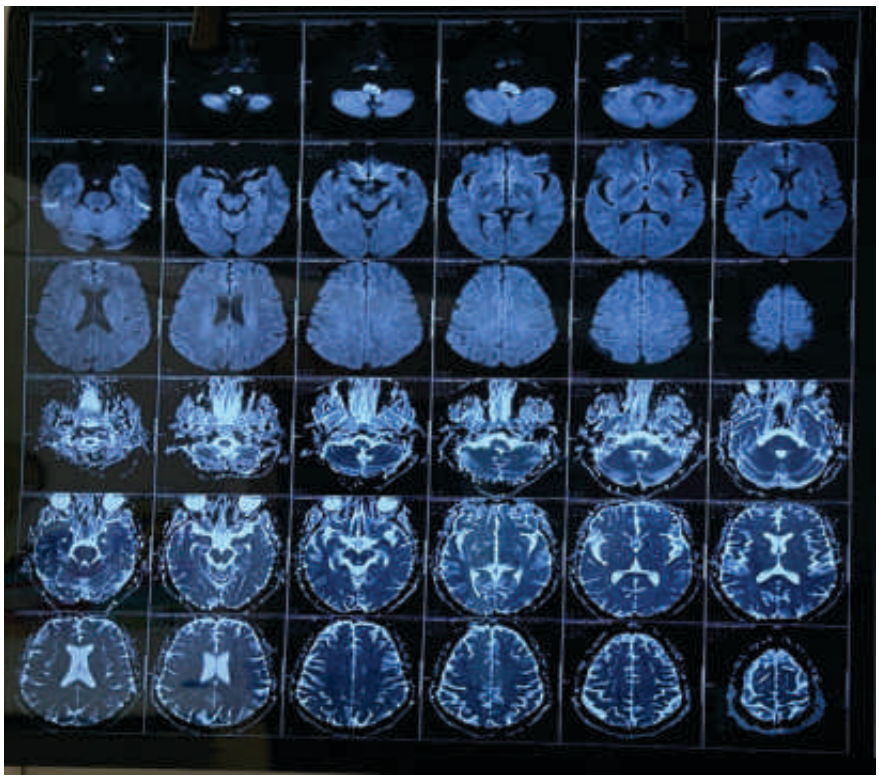

Figure 1: MRI Brain showing demyelination appearing hyperintense on T2 & FLAIR and hypointense on T1 with patchy areas of diffusion involving more than 3/4th of medulla

DISCUSSION

NMO is an inflammatory, demyelinating disease primarily involving the spinal cord and the optic nerves in the nervous system. Wide spectrum of neurological abnormalities are present in NMOSD, which include asymptomatic brain lesions on MRI to symptomatic brain lesions, meningitis, myelopathy, cranial neuropathy, sensorimotor polyneuropathy and mononeuritis multiplex[12]. In 2006, Wingerchuk et al developed definitive criteria for diagnosis of NMO as 1. Optic neuritis, 2. Transverse myelitis and two of the following: (a) A large lesion that exceeds 3 spinal cord segments (LETM); (b) Cranial MRI examination to be atypical for MS (not fulfilling the McDonalds criteria), (c) AQP4-IgG positivity and the cases that do not fulfill these criteria were defined as the NMO spectrum disorders (NMOSD)[13]. These criteria were revised again in 2015 which described NMO and the spectrum disorders as a single entity, and named as NMOSD. According to this new criteria, for cases with AQP4- IgG positivity, one main clinical finding is enough for the definitive diagnosis, the other possible diagnoses must be excluded. The main clinical findings are: 1. Optic neuritis 2. Acute myelitis 3. Area postrema syndrome 4. Acute brainstem syndrome 5. Symptomatic narcolepsy or acute diencephalic clinical syndrome 6. Symptomatic cerebral syndrome that includes typical brain lesions for NMOSD[14]. Our case was fulfilling the diagnostic criteria.

The present case represented an overlapping pattern of autoimmune disease confirmed through clinical, serologic, CSF and neuroimaging. As per the documented literature Sjogren's Syndrome (SS) and Systemic Lupus Erythematosus (SLE) are the most commonly associated autoimmune diseases with NMOSD[15]. Similar to our case, a retrospective blinded serological survey also support the evidence of coexisting NMOSD (AQP-4Ab+) occurring with SSa seropositivity without any glandular & sicca symptoms[16].

SS is an autoimmune disorder with whole mark manifestations of sicca syndrome secondary to salivary and lacrimal gland autoimmune lymphocytic infiltration[17]. Peripheral neuropathy is considered the most common neurologic manifestation[18]. Although other CNS involvements as transverse myelitis (TM) and optic neuritis are less common, however, it is still one of the reported complications[19,20]. Recently, there are increasing reports of patients with SS with NMOSD manifestations and were seropositive for AQP4 antibodies, and other cases fulfilled the clinical and radiological NMOSD criteria and seronegative for AQP4 antibodies[21,22]. Recently, it has been deduced that in 60–80% cases of NMO, highly specific serum autoantibodies -AQP4 antibodies (AQP4-Ab) were positive[23]. Our case has also shown the similar finding.

Present case initially came with the chief complaint of recurrent voming, retching and dyspepsia for which the patient consulted in Gastroenterology department. Patients who present with vomiting as the first and isolated symptom of NMO are usually evaluated by gastroenterologists and are oftently overlooked in context of NMO[24]. However, these are characteristic symptoms of NMO medullary involvement[24-26]. The neuropathology of NMO lesions involving the area postrema and the medullary floor of the fourth ventricle leads to intractable, but reversible, nausea. Popescu et al demonstrated pathologic abnormalities in the caudal medullae at the floor of the fourth ventricle and area postrema in 40% of patients with NMO that corresponded to the incidence of clinical episodes of intractable nausea/vomiting/hiccups in NMO[27].

Even though our patient was seropositive for SSA/ Ro52, she denied of any sicca symptoms. A retrospective review suggested that up to 33% of patients who presented with primary SS involving the CNS did not have sicca symptoms at the time of presentation but developed them over a period of 5 years[28].

CONCLUSION

Although NMO is a rare demyelinating disorder and initial non specific symptoms are usually overlooked by physicians and are attributed to other causes like GI & hepatobilliary diseases, High degree of suspicion is the key to delineate and identify the disorder at the erstwhile eventually managing appropriatelyand timely.Current evidence supports the hypothesis that SS and NMOSD can coexist. We should recognize this association to ensure complete clinical and serological evaluations of these patients. Systematic prospective studies of patients with the association of NMOSD and SS may better define this relationship.

CONFLICT OF INTEREST: None

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