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CASE REPORT

NEUROMYELITIS OPTICA SPECTRUM DISORDER (DEVIC'S DISEASE): - A CASE REPORT OF FULL RECOVERY WITH CORTICOSTEROIDS, THERAPEUTIC PLASMAPHERESIS AND IMMUNOTHERAPY

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ABSTRACT

Neuromyelitis Optica is a severely disabling inflammatory disorder of autoimmune etiology of the central nervous system, mainly affecting the optic nerves and spinal cord. Here, we present a case report of neuromyelitis optica in a 28-year-old Indian woman who presented with sudden painless loss of vision with tingling followed by weakness of all four limbs with bowel involvement that developed over a period of one week, with a significant history of recent vaccination with COVISHIELD (ChAdOx1 nCoV- 19) vaccine. Clinical evaluation showed diminished vision in both eyes, which progressed to loss of power across all major muscle groups in all limbs and bowel involvement. Magnetic resonance imaging of brain with contrast was done which showed T2W/FLAIR hyperintense non-enhancing signal in bilateral thalami extending caudally in mid brain on left side and in midline anterior medulla with subtle T2 hyperintense signal in body of corpus callosum, similar foci are seen in bilateral frontoparietal white matter suggestive of ADEM or demyelination. Also, T2 hyperintense signal in both optic nerves [left> right] in posterior part of orbit suggestive of optic neuritis. MRI whole spine showed multiple patchy hyperintense signals on T2 and hypo intensity on T1 all over cervical and dorsal vertebrae through whole segment in contiguous manner. The patient was immediately started on intravenous methylprednisolone pulse therapy followed by plasmapheresis and immunomodulator therapy. The diagnosis of neuromyelitis Optica was later confirmed with strongly positive neuromyelitis optica immunoglobulin G. Since, treatment was started early patient responded very well and made full recovery. Hence, early initiation of aggressive immunosuppressive treatment is essential in such cases.

KEYWORDS: Neuromyelitis Optica Spectrum Disorder, Anti NMO Antibody, Aquaporin 4(AQP 4), Device's Disease, Plasmapheresis, Optic Neuritis.

INTRODUCTION

Neuromyelitis Optica (NMO) is a severe inflammatory disorder of the central nervous system (CNS) mainly affecting the optic nerves and spinal cord, being autoimmune in etiology [1]. NMO cases are rare and reported from around the world, although the disease prevalence has been found to be higher in areas with black, Asian, and Indian population [2]. Diagnosis of NMO is made based on the presence of core clinical characteristics like optic neuritis, area postrema syndrome, acute brainstem syndrome, acute myelitis, symptomatic narcolepsy, or acute diencephalic clinical syndrome with neuromyelitis optica spectrum disorder-(NMOSD-) typical diencephalic magnetic resonance imaging (MRI) lesions and symptomatic cerebral syndrome with NMOSD-typical brain lesions with or without NMO Immunoglobulin G (NMO-IgG) [3].

There has always been a controversy whether NMO is a subset of multiple sclerosis (MS) or can be classified as a distinct entity. However, clinical and laboratory evidences suggest NMO to be distinct from MS and that the pathogenesis of NMO is humoral mechanism [4]. We present a case of 28-year-old female with a history of sudden onset, painless diminution of vision and tingling followed by weakness of all four limbs and bowel involvement, who was eventually diagnosed to have

NMO. With timely diagnosis and aggressive treatment, she made a full recovery and thus the low anticipation of such diseases in our country, coupled with challenges in diagnosis, often leads to misdiagnosis and worse outcomes in patients that could have benefited from readily available treatment.

CASE REPORT

Patient 28 year married Indian female presented to hospital with complaints of severe frontal headache with VAS (Visual Analogue Scale) of 6/10; insidious in onset. It was associated with high grade fever, 2-3 episodes of chills and rigors 15 days back. There was associated low back pain aggravated with physical activity and straining like coughing & sneezing. There was no history of joint pains, vomiting, altered sensorium, seizures or neurological deficit. Patient was taken to local hospital where she was found to have low blood pressure; she was given antipyretics, IV fluids and supportive treatment. Her BP stabilized and fever subsided but headache persisted.

Then on 7-8th day of illness, she noted painless diminution of vision in left eye noted on waking up from sleep which progressed over 1 week with inability to even appreciate light. During this week color vision loss was associated with color desaturation.

She then developed bilateral trickling of knees while walking, associated with tremulousness while walking (left>right side). This was insidious in onset and progressed over 4 days with inability to turn in bed along with urinary incontinence/bed wetting for 1-2 days. All these symptoms were associated with progressive sensory loss with decreased appreciation of temperature sensation.

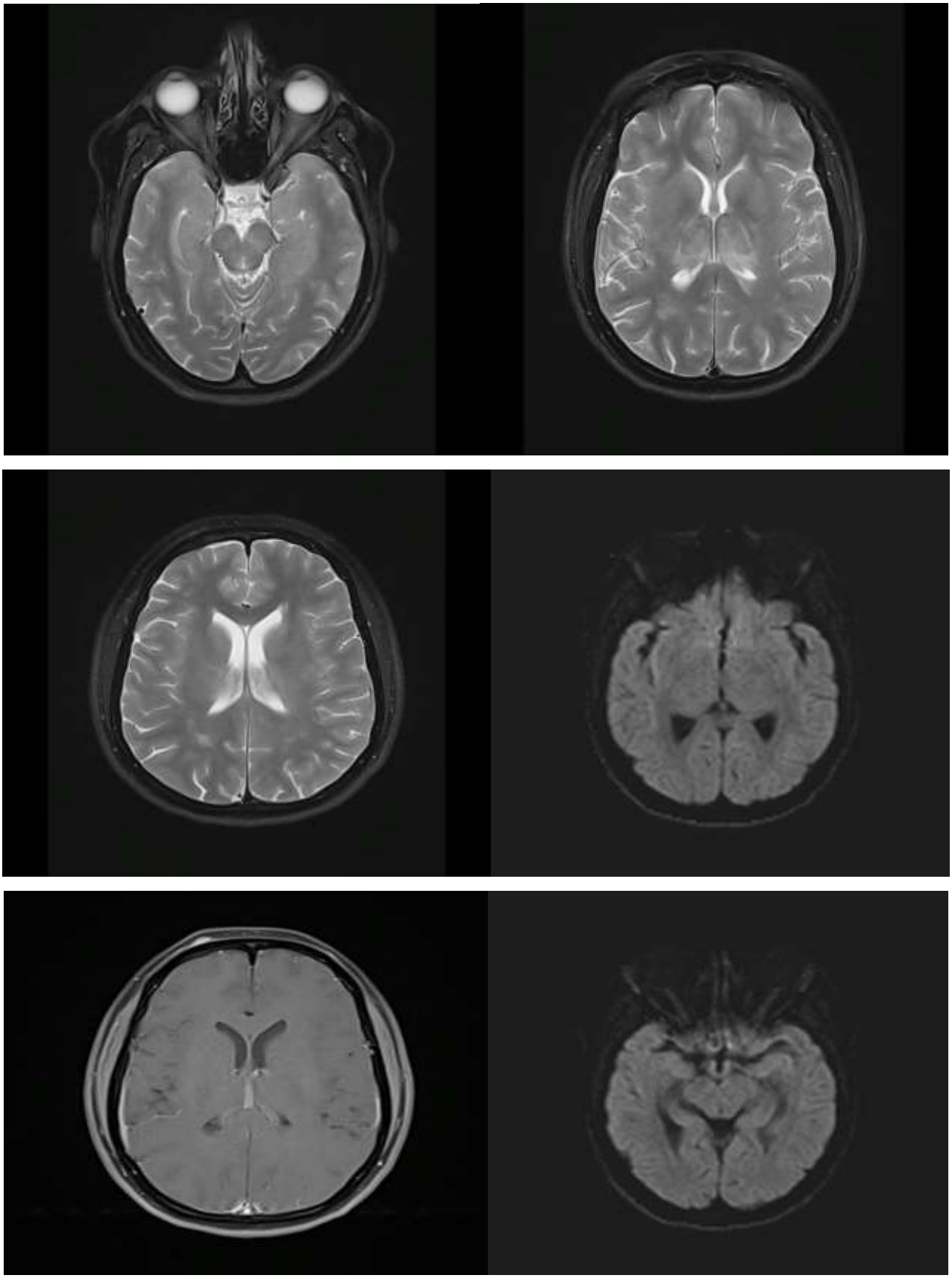
No history of involvement of upper limbs, vomiting, stiffness, heaviness of limbs, seizures, drooping of eyelids, squint, numbness over face or loss of sensation, excessive perspiration, difficulty in speaking or chewing, deviation on angle of mouth, hearing loss, vertigo, difficulty in swallowing, no memory, language or visuospatial disturbances, no dry eyes, mouth rash, joint pains, genital ulcers, no drooping of saliva, hoarseness of voice with regurgitation of feeds.

She has history of oral ulcers 1.5 months back which healed spontaneously. She was vaccinated with COVID 19 vaccine COVISHIELD on 20 days back with the 1st dose. She had no significant family or past history. Menstrual cycles are normal, nulliparous, no history of intrauterine device or oral contraceptive pills, vegetarian, no addictions, normal bowel/bladder habits before present illness.

On examination her vitals were stable; conscious and oriented to time, place and person. Her systemic examination was within normal limits.

On nervous system examination she was found to be lethargic, MMSE (mini mental state examination) 16/30, EDSS (expanded disability status scale) of 8, restricted to bed/wheelchair. Visual acuity bilateral eyes up to finger counting. Fundus examination revealed temporal pallor and rest normal. Ptosis of right eye more than left eye was found; extraocular muscle movements were normal and no diplopia. All other cranial nerves examination was within normal limits. Motor examination showed decreased power of 1/5 in all muscle groups, normal muscle mass in all four limbs but increased tone (spasticity) in all four limbs. All deep tendon reflexes were exaggerated. Bilateral plantar reflex was extensor. Touch, pain and temperature sensations were absent on big toes, feet till the mid-thigh anteriorly, laterally and posteriorly. Gait couldn't be assessed as patient was not able to stand and walk.

She was started on conservative treatment and urethral catheterization was done. NCCT head revealed no abnormality so MRI brain with contrast was done which showed T2W/FLAIR hyperintense non-enhancing signal in bilateral thalami extending caudally in mid brain on left side and in midline anterior medulla with subtle T2 hyperintense signal in body of corpus callosum, similar foci are seen in bilateral frontoparietal white matter suggestive of ADEM or demyelination (fig. 1). Also, T2 hyperintense signal in both optic nerves [left> right] in posterior part of orbit suggestive of optic neuritis. MRI whole spine showed multiple patchy hyperintense signals on T2 and hypo intensity on T1 all over cervical and dorsal vertebrae through whole segment in contiguous manner.



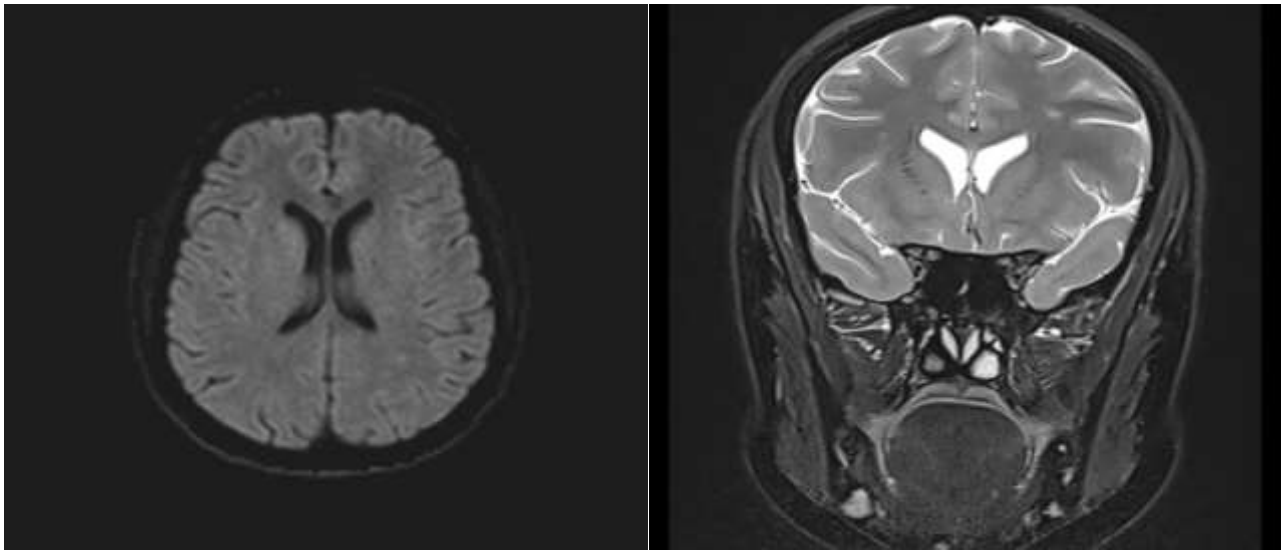


FIGURE 1- MRI: *Magnetic resonance imaging of brain with contrast was done which showed T2W/FLAIR hyperintense non-enhancing signal in bilateral thalami extending caudally in mid brain on left side and in midline anterior medulla with subtle T2 hyperintense signal in body of corpus callosum, similar foci are seen in bilateral frontoparietal white matter suggestive of ADEM or demyelination. Also, T2 hyperintense signal in both optic nerves [left> right] in posterior part of orbit suggestive of optic neuritis.*

Differential diagnosis considered for further workup were NMOSD (neuromyelitis optica spectrum diseases), MS (multiple sclerosis), Acute disseminated encephalomyelitis (ADEM), SLE, Acute idiopathic myelitis tranversalis (ATM).

CSF analysis was done; pressure was normal with cytology, sugar and protein values within normal limits, no albumin-cytological dissociation or oligoclonal bands. Serological tests were negative for syphilis, HIV, TB, varicella. Aquaporin-4 IgG NMO antibody titer was found positive. Thus, by IPND criteria fulfilment, a diagnosis of Neuromyelitis optica was made with bilateral optic neuritis, longitudinally extensive transverse myelitis and diencephalic syndrome.

Her CBC, LFT, KFT, CHEST XRAY were within normal limits and her ANA titer was positive [1:80] speckled type with anti SSA+; slightly decreased serum complements factor C4 levels (9.8 mg/dL; normal range, 10−40 mg/dL), low normal C3 levels (94.1 mg/dL; normal range, 90−180 mg/dL), as well as seropositivity for anti-Sm and anti-RNP. Antibodies to double-stranded DNA, SS-A, SS-B, and cardiolipin were undetectable. Schirmer test was done which was normal [15mm in both eyes]. VEP was done which showed bilateral prolonged latency on P100. BAER was normal with normal central auditory pathway. All other investigations were within normal limit and sepsis or any infections were ruled out.

After taking Neurologist opinion, she was started on Inj. Methylprednisolone pulse therapy [1gm iv once a day for 7 days] along with Inj Vit B complex, Gabapentin 200mg thrice a day orally. She was closely monitored and her vision improved significantly to 6/60 in left eye and 6/36 in right eye but no improvement in motor and sensory loss and bowel control; so, after ruling out any active and latent infections, further 5 cycles of plasmapheresis were done after which over next 5 days her vision returned to 6/6 in left eye and 6/9 in right eye. She became alert and started ambulation. She regained her bladder control and with physiotherapy she became completely self-mobile. On 7th day she developed high spiking fever during course of hospitalization after the plasma exchange. Further investigations revealed leucocytosis with thrombocytopenia. Fever profile workup was done and she was started on Inj Ceftriaxone 2gm iv BD and Inj linezolid 600mg iv BD. Peripheral smear showed toxic granules and neutrophilic leucocytosis and urine & blood cultures were found sterile. Patient responded well to antibiotics. Patient was vaccinated for pneumococcal and influenza vaccine.

She was discharged on 28th day of admission with 6/6 vision in both eyes, normal eye movements, no ptosis.

She regained complete sensations with normal superficial and deep tendon reflexes with no neurological deficit. She was prescribed tab prednisolone 60mg OD, calcium, vit B complex, gabapentin along with regular physiotherapy and supportive treatment.

She was reviewed one month later in OPD with no recurrence of symptoms and no neurologic deficit with routine investigation done and found within normal limits. She was given inj. Rituximab 1gm infusion 2 weeks later. On further follow up she had no relapses and low dose steroids were continued with advice for Inj Rituximab 6 months later. On further follow up she is doing well with no relapses or neurological deficit. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

DISCUSSION

NMOSD diagnostic criteria for adult patients: - IPND
Diagnostic criteria for NMOSD with AQP4-IgG
1. At least 1 core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnosis
Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status
1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome
b. Dissemination in space (2 or more different core clinical characteristics)
c. Fulfilment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses
Core clinical characteristics
1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions (figure 3)
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status
1. Acute optic neuritis: requires brain MRI showing
a. Normal findings or only nonspecific white matter lesions, OR
b. Optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium enhancing lesion extending over .1/2 optic nerve length or involving optic chiasm
2. Acute myelitis: requires associated intramedullary MRI lesion extending over 3 contiguous segments (LETM) OR >3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis
3. Area postrema syndrome: requires associated dorsal medulla/area postrema lesions
4. Acute brainstem syndrome: requires associated peri ependymal brainstem lesions
Abbreviations: AQP4 5 aquaporin-4; IgG 5 immunoglobulin G; LETM 5 longitudinally extensive

NMO is a demyelinating, inflammatory disease that primarily involves the spinal cord and the optic nerves in the nervous system. The ocular involvement includes optic or retrobulbar neuritis. Spinal cord may be involved as transverse myelopathy presenting as sensory loss below the lesion, motor power loss and sphincter defects (5)

The autoantibody developed against Aquaporin 4, a water channel protein, and intensively present at the astrocytic protrusions, was suggested to be responsible from the pathogenesis of the disease (6). The binding of these antibodies to the aquaporin 4 channel protein, occurs hyperpermeability at the blood brain barrier, followed by perivascular inflammation, astrocyte damage and

inflammation at the spinal cord with or without demyelination and cavitation at the optic nerve (5). Lennon et al. reported that the AQP4-IgG positivity shows 73% sensitivity and 91% specificity in patients with clinically NMO suspected patients. In the other autoimmune disease, however, the presence of NMO IgG couldn't be demonstrated (7). The AQP4-IgG antibody was also positive in our case. The most important data showing the role of autoimmunity in NMO, is the association of NMO with other autoimmune diseases such as SLE, antiphospholipid syndrome, Sjögren syndrome, Hashimoto's thyroiditis, rheumatoid arthritis, sarcoidosis, ulcerative colitis, pernicious anemia and myasthenia gravis (8,9) but in our case, however, neither clinical nor laboratory findings have been detected as a finding of such an association. Cerebrospinal fluid (CSF) findings are must for the diagnosis and ruling out MS. In MS patients, the number of cells per cubic millimeter are below 50 (usually below 20) and there are only mononuclear cells, protein is normal or slightly increased, and in more than 90% of the patients, there are oligoclonal bands that prove the synthesis of intrathecal IgG which were absent in our case. However, in NMO patients, the number of cells may be above 50 and polymorphs may be seen, protein may be increased, and the oligoclonal band positivity is seen in about 1/5 of the patients, and may be temporary. The CSF examination of our cases was consistent with NMO, with the oligoclonal band negativity and the IgG index negativity. NMO is a disease with a course with severe sequelae; for this reason, both the acute and maintenance therapies are important. In the acute period, very good results may be obtained with pulse steroid therapy. If the response to treatment is not good, plasmapheresis and IVIG and cytostatic drugs may be used (10). In addition, Rituximab, which is a monoclonal antibody against B lymphocytes is recommended (11). In our case, clinical improvement was observed with 7 day pulse steroid treatment in the acute period, and the patient was followed with 1 gr/day steroid each month (for 6 months), plasmapheresis and rituximab maintanence treatment. The primary and secondary treatment strategies for NMOSDs are defined by study groups. Oral prednisolone combined with azathioprine and rituximab are recommended as first line treatment, while cyclophosphamide, mitoxantrone and mycophenolate mofetil are recommended as the secondary treatment (5).

CONCLUSION

In conclusion we emphasize the importance of the early and right diagnosis of NMO, and the management of the treatment of both acute and chronic phases which results in good prognosis of the patient with reduced morbidity.

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