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NEUROMYELITIS OPTICA (NMO); A Case Report:

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ABSTRACT:

Devic's disease or syndrome also known as Neuromyelitis optica (NMO) which is a demyelinating central nervous system (immune-mediated) ailment that predominantly targets the optic nerves and spinal cord. NMO-IgG seropositivity & longitudinally extensive spinal-cord lesions typically represents the Devic's disease & differentiates it from Multiple Sclerosis (MS).Treatment for NMO is based upon its presentation such as for acute phase(steroids, IVIG etc), prevention of relapse (steroid sparing immunosuppression etc) and symptom based therapy (e.g spasticity etc). Here, we present a case of NMO in a young female (26 years old), married patient who presented to us with total vision loss, urinary & fecal incontinence & paraplegia. She was being treated as a case of Multiple Sclerosis (MS) several years ago but we further investigated & found NMO-IgG seropositivity and other findings in the history that conforms the diagnostic criteria of NMOSD for this patient. Furthermore, the patient was treated with IV glucocorticoids for its acute phase of disease & sent home when symptoms of transverse myelitis improved.

KEYWORDS: Neuromyelitis optica (NMO), Multiple Sclerosis (MS), Neuromyelitis optica-immunoglobulinG(NMO-IgG), aquaporin-4 antibody(AQP4-Ab), Cranial nerve(CN)

INTRODUCTION:

Neuromyelitis optica (a demyelinating disease of central nervous system)[1]was described by Albutt in 1870 and after two decades Devic narrated its clinical features i.e. acute transverse myelitis &optic neuritis. The incidence &prevalence of NMO is quite low as it is a rare disease to be found in general population. The worldwide incidence of this disease is 0.053 to 0.40 per 100,000, while the prevalence is ranged from 0.52 to 4.4 per 100,000[2] .This disease (NMO) is more to be found among Asians, Blacks & Indian populations & it is estimated that the prevalence in Northwest of England is approximately 0.72 per 100,000[3] & in Japan is 14 per 100,000[4,5] While the mean age for NMO is 40 years(approx.) but it could be present among young ones[6,7] & there is a female predominance with a female to male ratio of3:1. Neuromyelitis optica-immunoglobulin is a highly specific & sensitive auto antibody for diagnosis of NMO which binds to the aquaporin-4 (AQP4); channels that regulate water homeostasis in the CNS[4,7,8].

CASE REPORT:

A 26 year old female, married having two children (a girl & boy) presented to us with bilateral vision loss (total blindness) for the last 6 years(2012-18), paraplegia for the last 2 months(2018) with urinary & fecal incontinence (on/off). There was sudden loss of vision in the right eye with extreme pain 9 years ago(2010), followed by other eye vision loss after 3 years of the previous one but this time it was a gradual loss of sight over 2-3 months. In the same year she had her first episode of leg weakness (left) & urinary incontinence which was gradual & slow in nature but improved after 1 month of hospital treatment (drugs included steroids). After 3 years(2013) she felt moderate weakness in both upper limbs and left leg weakness with urinary & fecal incontinence. It was gradual in onset & power was much reduced according to the patient. It took almost 6 months to improve back to normal again after a hospital treatment (diagnosed as MS patient about 7 years ago & was treated in hospital as accordingly but not recovered according to patient's history). Now, she presented to us with the above stated symptoms for the last 2 months which

are worsening each day. There was no other significant medical history of any other disease previously but she had 2 cesarean sections for both of her deliveries. In her personal history she denied of taking any kind of drugs, smoking or alcohol intake. Her sleep is normal but appetite is decreased & there is urinary & fecal incontinence.Her family history was normal and insignificant regarding neurological diseases. Her physical examination revealed normal vitals state(Pulse80/min, B.P130/70, Temp98.6F & there was no lyphmadenophathy, jaundice, edema or cyanosis in body). The Mental state examination was evaluated & found completely normal as she was alert, attentive, and oriented in time, place & person. Speech was clear and fluent with good repetition, comprehension, and naming.Eye examination showed bilateral optic disc atrophy & there was no light perception(fixed dilated pupils) but movements were normal & there was no sign of ptosisor deviation of eyes. CN V examination showed facial sensation was intact to pinprick in all 3 divisions bilaterally & corneal responses were intact. Similarly,

TABLE NO.1 EXAMIANTION OF MOTOR SYSTEM

PARAMETERS	UPPER LIMB			LOWER LIMB		
	RIGHT		LEFT	RIGHT		LEFT
POWER	5/5		5/5	0/5		0/5
TONE	NORMAL		NORMAL	AVERAGE		AVERAGE
REFLEXES	BRACHIORADIALIS	Normal	Normal	ANKLE JERK	+4	+4
				KNEE JERK	+3	+3
	BICEPS	Normal	Normal	PLANTERS	Extensor	Extensor
	TRICEPS	Normal	Normal	ANKLE CLONUS:	Present	Present
				PATELLAR CLONUS:	Not present	Not present

All other systems including cardiovascular, respiratory & abdominal were normal & there was no clinical symptomatology /findings found related to these systems (except urinary incontinence). Her lab investigations showed leucocytosis (12500/mm3), raised ESR levels(70mm/hr) & CRP levels(4.5mg/l). Other investigations like renal function tests, liver function tests, serum electrolytes & serum glucose were in normal limits. ECG & Echocardiography was done and it was also normal showed nothing of peculiar importance. MRI brain & spine(with contrast) was advised to the patient for Bilteral optic neuritis and TM which favors NMO more than MS but MRI brain was unequivocal & showed no lesions in brain infact there was Longitudinally extensive transverse myelitis (large area of abnormal signals noted in the spinal cord at the level of T2 through T6 vertebrae with unrestricted diffusion & cord thinning).In our patient, a MRI done 5-6 years back had lesion around 3rd ventricle that are totally vanished now (normal MRI Brain). This led to the diagnosis of NMO as she was meeting the diagnostic criteria of NMO[table.2]1 so, the aquaporin-4 antibody(AQP4-Ab) was sent for the confirmation of Devic's disease & it came back positive(1385.5U/ml)ref range(0.0-0.3U/ml). Thus this established our diagnosis of NMO as per its criteria (100%) over Multiple Sclerosis1. As, she presented to us with an acute phase of NMO so we started her on IV glucocorticoids (methyl-prednisolone) 500mg diluted once a day for 7 days, injection Enoxaparin sodium(40mg) once a day for the prophylaxis of deep venous thrombosis, injection ceftrioxone 1gm(for leucocytosis) & IV proton pump inhibitors. She remained admitted in hospital for 8 days and then was discharged on immunosuppressive drug (tab. Azathioprine) for the prevention of future relapses of this disease. The displaying side effects were very little enhanced aside from urinary/fecal incontinence and she was likewise exhorted physiotherapy (for development of leg weakness) & she requested line up following multi month with 2 weekly rehashing of renal and liver capacity tests.

DISCUSSION:

Devic's disease or Neuromyelitis optica is an inflammatory & demyelinating disease of central nervous system1 having typical cardinal clinical characteristics i.e. Longitudinally extensive transverse myelitis & optic neuritis. The previously stated features can be present at the same time or can be separated by many years. Diseases like multiple sclerosis ,malignancy , neurosarcoidosis, infections, inflammation, idiopathic optic neuritis, idiopathic transverse myelitis or vascular diseases can mimic NMOSD by involving optic nerve or spinal cord. NMO and MS share some phenotypic features & it should be differentiated from each other as they have different treatment modalities.(Table no.3)9.So optic involvement, no MRI brain lesions, spinal cord lesions >3segments and positive AQP4-Ab, were all Confirmatory of NMO. Differentiation of NMO from MS is important as interferons, fingolimod and natalizumab are ineffective or may aggravate NMO10. Idiopathic optic neuritis is excluded from differentials because it is usually unilateral with impaired

color vision but improvement of visual acuity with 3 weeks to 1year11.In our case, relapsing disease course,bilateral optic nerve involvement, poor visual outcome & transverse myelitis causing paraplegia with urinary incontinence are the prominent features.

Table2 International consensus diagnostic criteria for Neuromyelitis Optica(2015) [1]

➢ **Diagnostic criteria for NMOSD with AQP4-IgG:**
▪ At least 1 core clinical characteristic
▪ Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
▪ Exclusion of alternative diagnoses
➢ **Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status:**
▪ 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 5 longitudinally extensive transverse myelitis lesions, or area postrema syndrome ▪ b. Dissemination in space (2 or more different core clinical characteristics) ▪ c. Fulfillment of additional MRI requirements, as applicable
▪ Negative tests for AQP4-IgG using best available detection method, or testing unavailable
▪ Exclusion of alternative diagnoses
➢ **Core clinical characteristics:**
▪ Optic neuritis
▪ Acute myelitis
▪ Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
▪ Acute brainstem syndrome
▪ Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
▪ Symptomatic cerebral syndrome with NMOSD-typical brain lesions
➢ **Symptomatic cerebral syndrome with NMOSD-typical brain lesions:**
▪ 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
▪ 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
▪ Area postrema syndrome: requires associated dorsal medulla/area postrema lesions
▪ Acute brainstem syndrome: requires associated periependymal brainstem lesions

Table3 Comparison between MS & NMO[9] .

Features		MS	NMO
Optic neuritis(visual field defects and severe visual loss)		Less common	Common
On MRI spinal cord:	Longitudinally extensive spinal cord lesions< 3segments	Adults : <5% Pediatric : 14%	Adults : 94% Pediatrics : 100%
	Location of spinal lesions on axial image	Asymmetric and peripheral involvement	Central grey matter involvement
On MRI brain:	Lesions perpendicular to lateral ventricle(Dawson fingers)	common	Rare
	Lesions adjacent to lateral ventricle & inferior temporal lobes)	Common	Rare
	Cortical & juxtacortical lesions	Common	Rare
	Optic chiasmal involvement	Rare	Relatively common
Pattern of CNS atrophy:		Significant atrophy of brain	Significant atrophy of spinal cord
Serology: Serum AQP4-		Not present	Common
CSF study:	Pleocytosis	Mild-moderate	Can be severe(upto 1,000mm^3)
	Oligoclonal bands	97%,rarely disappear on follow-up sampling	33-43% mostly disappear on follow-up sampling
Prognosis	Secondary progressive course	Common	Rare
	Rate of disability progression	Relatively slow	Can be fast
	Mortality	Can be low(life expectancy reduced by 7-14 years as compared to general population)	Can be high(five year survival can ba as low as 68%)

According to the International consensus diagnostic criteria for Neuromyelitis Optica (2015)[table no.2]1 our patient has positive aquaporin-4 antibody(AQP4-Ab) and has 2 core clinical characteristics which confirms the diagnosis. NMO can be monophasic i.e. a single episode with permanent remission or it can result in a relapsing disease which is present in 85-90% of the cases. The characteristics of both monophasic & relapsing NMO have quite dissimilarities.[table no.4][6]

Table 4 Characteristics of monophasic and relapsing Neuromyelitis optica[6]

	Monophasic	Relapsing
• Frequency (%)	➢ Less common (20)	➢ More common (80)
• Age of onset(year; median	➢ 29	➢ 39
• Sex ratio of female (%)	➢ 50	➢ 80-90
• History of autoimmune diseases	➢ Uncommon	➢ 50%(approx)
• Optic neuritis or myelitis (%)	➢ 48	➢ 90
• Bilateral Optic neuritis (%)	➢ 17	➢ 8
• Simultaneous ON+ myelitis	➢ 31	➢ 0
• Respiratory failure	➢ Rare	➢ 1/3(approx)
• 5-yr mortality rate (%)	➢ 10	➢ 32
• Recovery	➢ Good	➢ Fair

Identification of NMO is by neurological examination, blood test(positive anti AQP4-Ab),MRI,CSF findings .Here auto-antibodies develop against aquaporin 4(water channel protein) and there is disruption of blood–brain barrier, glutamate homeostasis impairment and induction of necrotic cell death by AQP4-Ab-positive serum10.this leads to astrocyte damage, perivascular and spinal cord inflammation and cavitations of optic nerve12.AQP4-IgG is 73%sensitive and 91% specific in NMO12.NMO is a disease with severe sequelae so acute and maintenance therapy both are very important. In acute cases, pulse steroid therapy is given. If response is not good, IVIG and plasmapheresis may play a role12for long term relapse prevention, Azathioprine with oral steroids and mycophenolate mofetil with oral steroids are given13.For refractory cases, Rituximab and mitoxantrone show some efficacy13.There is no role of interferons10.In our case patient showed improvement with 7 days IV steroids and then discharged on Azathioprine as maintenance therapy. As we had advised patient for follow up & she came with same presentation at which she was discahrged after 1 month. We ran all her baseline investigations(Cbc, Rft, Lft, Serum electrolytes & urine/RE) & they came in normal parameters. To sum up, 5 year survival of NMO is as low as 68%13.

CONCLUSION:

After all this inferencing we emphasize early and right diagnosis with management of acute and chronic phase as damage & disability is slowly cumulative by recurrent attacks that damage new areas of myelin. we also need attention to significance of strict patient-physician collaboration in follow-up-periods.

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Saad Waheed; concept, data collection, data analysis, manuscript writing, manuscript review
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Aqsa Shehzadi: data analysis, manuscript writing, manuscript review