Case Report

The Expanding Spectrum of Anti-IgLON5 Disease: A Case Series from an Indian Cohort

Avinash Ganapule, Divyani Garg, Ayush Agarwal, Anu Gupta, Roopa Rajan, Soaham Desai[1], Mitesh Chandarana[2], Sidharth S, Madhavi Tripathi[3], Ajay Garg[4], Divya M Radhakrishnan, Achal Kumar Srivastava

Departments of Neurology, [3]Nuclear Medicine and [4]Neuroimaging and Interventional Neuroradiology, All India Institute of Medical Sciences, New Delhi, [1]Department of Neurology, Shree Krishna Hospital and Pramukhswami Medical College and Shree Krishna Hospital, Karamsad, Anand, Gujarat, [2]Department of Neurology, Marengo Care Institute of Medical Sciences Hospital, Ahmedabad, Gujarat, India

Abstract

Anti-IgLON5 disease is an evolving entity that lies at the confluence of autoimmunity and neurodegeneration. Reports from India remain sparse. In this series, we describe seven Indian patients with anti-IgLON5–related disease. Patients presented across the fifth to eighth decades with a mean duration of illness of 16 months. All had movement disorders, which included gait ataxia, parkinsonism, and chorea. Six patients had sleep disturbances. Five had a frontal dysexecutive dementia phenotype. Two had epilepsy. Bulbar involvement was present in four, and one had amyotrophic lateral sclerosis (ALS)-like features. Magnetic resonance imaging was abnormal in two cases. Positron emission tomography of the brain also contributed to diagnosis. Combination immunotherapies were used in most of the patients, with three showing a sustained response and two deaths reported due to sepsis-related complications. It is important to recognize the increasing spectrum of IgLON5-related disease to enable timely initiation of immunotherapy before marked degeneration occurs.

Keywords: Autoimmune, dementia, chorea

Introduction

Anti-IgLON5 disease is a distinctive autoimmune syndrome that bridges the gap between autoimmunity and neurodegeneration. While sleep abnormalities are a hallmark feature, other prominent clinical syndromes[1] include a bulbar syndrome, as well as myriad movement disorders. Recognition of cognitive decline and neuromuscular involvement has further expanded the spectrum.[2] We present the largest series of seven cases from India. Other cases reported from India[3-9] have been reviewed, highlighting variability in presentation, including predominant sleep abnormalities,[4] hyperkinetic movement disorders,[5-8] and atypical parkinsonism.[8-10]

Case Series

A summary of the clinical description, treatment, and outcome of all cases is provided in Supplementary Table 1. The study was conducted over a period of 3 years, and cases were provided by four centers. Institutional ethical clearance was obtained as per local regulations of each center.

Case 1

A 49-year-old female presented with a 1-year history of bilateral tonic–clonic seizures of unknown onset (four episodes), along with cognitive decline primarily affecting her recent and working memory. Over the past 4 months, she also noted reduced movement on the left side of her body. She had hypertension, for which she had been on irregular medication for the past 3 years. On examination, her Mini-Mental Status Examination (MMSE) score was 9/30, and detailed lobar assessment revealed significant deficits in frontal and temporal lobe functions. She had gait ataxia. She had asymmetrical parkinsonism (left more than right). Magnetic resonance imaging (MRI) revealed mild to moderate generalized atrophy of the cerebral and cerebellar regions. In addition, microhemorrhages were observed in the bilateral basal ganglia, thalami, and right temporal subcortical white matter. The splenium of the corpus callosum showed increased hyperintensity on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences. She had mild orthostatic hypotension. Positron emission tomography (PET) scan demonstrated bilateral temporal hypometabolism and basal ganglia hypermetabolism, suggestive of an autoimmune etiology [Figure 1]. Cerebrospinal fluid (CSF) analysis showed 2 cells/mm^3 (all lymphocytes), elevated protein (150 mg/dL), and normal glucose. Her serum tested strongly positive for anti-IgLON5 antibodies by indirect immunofluorescence

Address for correspondence: Dr. Divyani Garg, Room 705, CN Center, All India Institute of Medical Sciences, New Delhi - 110 029, India.
E-mail: divyanig@gmail.com

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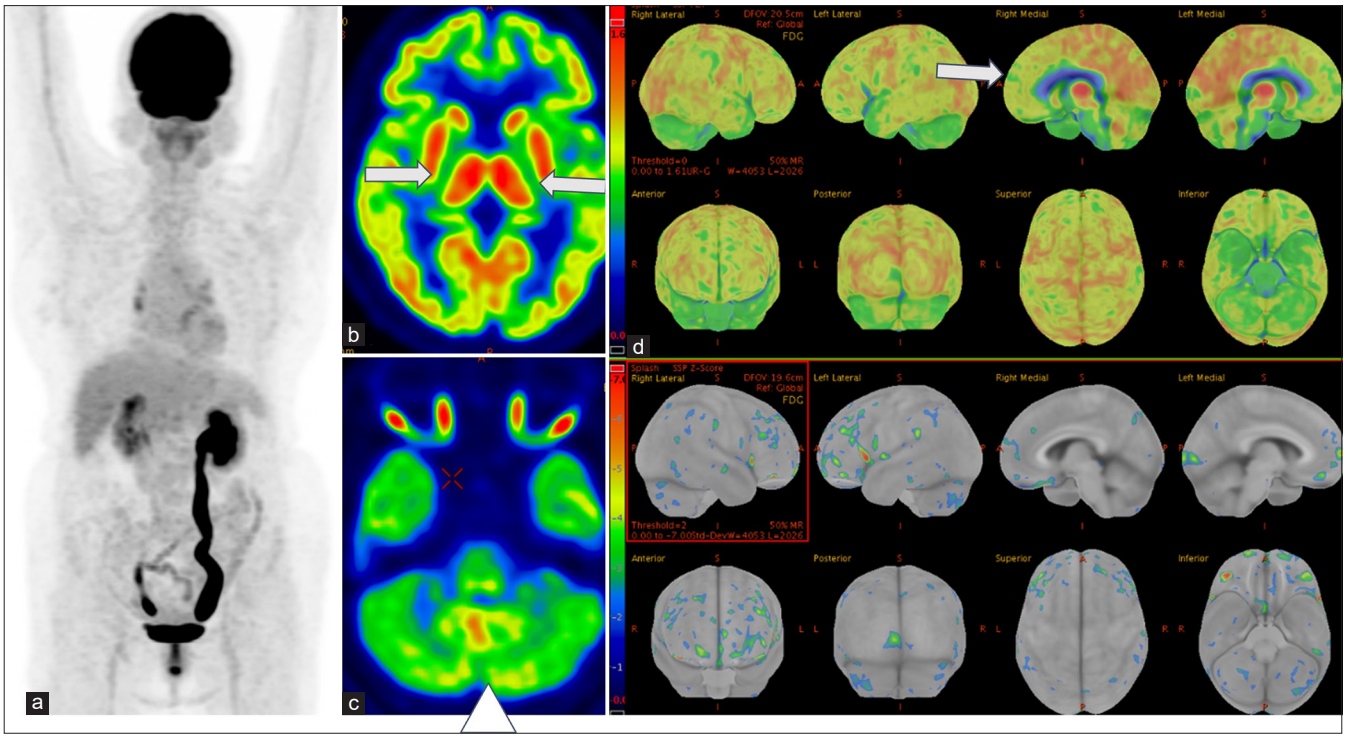

Figure 1: F-18 FDG PET maximum intensity projection image shows that (a) no focal metabolically active lesion has been identified. Transaxial plain FDG PET image of the brain (b) at the level of BG reveals BG hypermetabolism and (c) occipital hypometabolism. Cortex ID maps showing minimal prefrontal hypometabolism (d). BG: basal ganglia, PET: positron emission tomography, ID: identification, FDG: fluorodeoxyglucose

(IIF). Other autoimmune markers and paraneoplastic panel were negative. Routine blood tests, thyroid function test, and viral markers were negative. She was treated initially with pulse methylprednisolone (1000 mg/day for 5 days), followed by rituximab (1000 mg infusion each given 2 weeks apart), which resulted in improvement in her cognitive function and gait. Her seizures remain well controlled with levetiracetam and clobazam at 1 year of follow-up.

Case 2

A 64-year-old male with a 10-year history of diabetes, hypothyroidism, and recently diagnosed hypertension presented with a 6-month history of forgetfulness and behavioral changes, including difficulty with working memory and recognizing familiar faces or names. He experienced significant challenges with executive functions, struggling with daily activities such as eating and bathing. Over the past month, he exhibited increased sleep duration and Rapid eye movement (REM) sleep behavior disorder (RBD). His MMSE score was 24/30, with frontal lobe impairment. He had restricted vertical eye movements. MRI revealed mild cerebral atrophy. CSF analysis was acellular with elevated proteins (229 mg/dL) and normal glucose (105 mg/dL). PET imaging indicated brainstem and putamen hypermetabolism, with bilateral occipital and precuneus hypometabolism [Figure 2]. The diagnosis of anti-IgLON5 disease was confirmed with serum antibody testing by IIF. Autoimmune and paraneoplastic panels, anti-thyroid peroxidase (TPO) antibodies, viral markers, and serum Venereal Diseases Research Laboratory (VDRL) were negative. He was treated with pulse methylprednisolone (1000 mg/day for 5 days), intravenous immunoglobulin (IVIg) therapy (2 g/kg over 5 days), and rituximab (two doses of 1000 mg given 2 weeks apart). The patient had mild improvement in sleep disturbances, but other features did not improve.

Case 3

A 62-year-old hypertensive male presented with a 16-month history of progressive gait difficulty, seizures, sleep disturbances, and bulbar dysfunction. His gait issues included features of parkinsonism and cerebellar ataxia. He also had pronounced RBD, stridor, and bulbar palsy, which eventually necessitated intubation and tracheostomy. His MMSE was 21/30 with a frontal assessment battery score of 6/18. Polysomnography revealed reduced mean sleep latency with obstructive sleep apnea (OSA) and RBD. MRI of the brain and PET scan were normal. CSF analysis showed elevated proteins (86 mg/dL) with normal glucose (80 mg/dL) and 10 cells (lymphocytes). His CSF tested positive for anti-IgLON5 antibodies by IIF. He was treated with pulse methylprednisolone, IVIg, and then transitioned to maintenance steroids and mycophenolate mofetil (MMF). He kept having frequent aspiration pneumonia and was tracheostomized. However, 3 years into the illness, he again developed pneumonia and sepsis, and ultimately succumbed to the illness.

Case 4

A 75-year-old male with a history of diabetes, hypertension, and coronary artery disease presented with a 2.5-year history of behavioral and memory issues, predominantly affecting

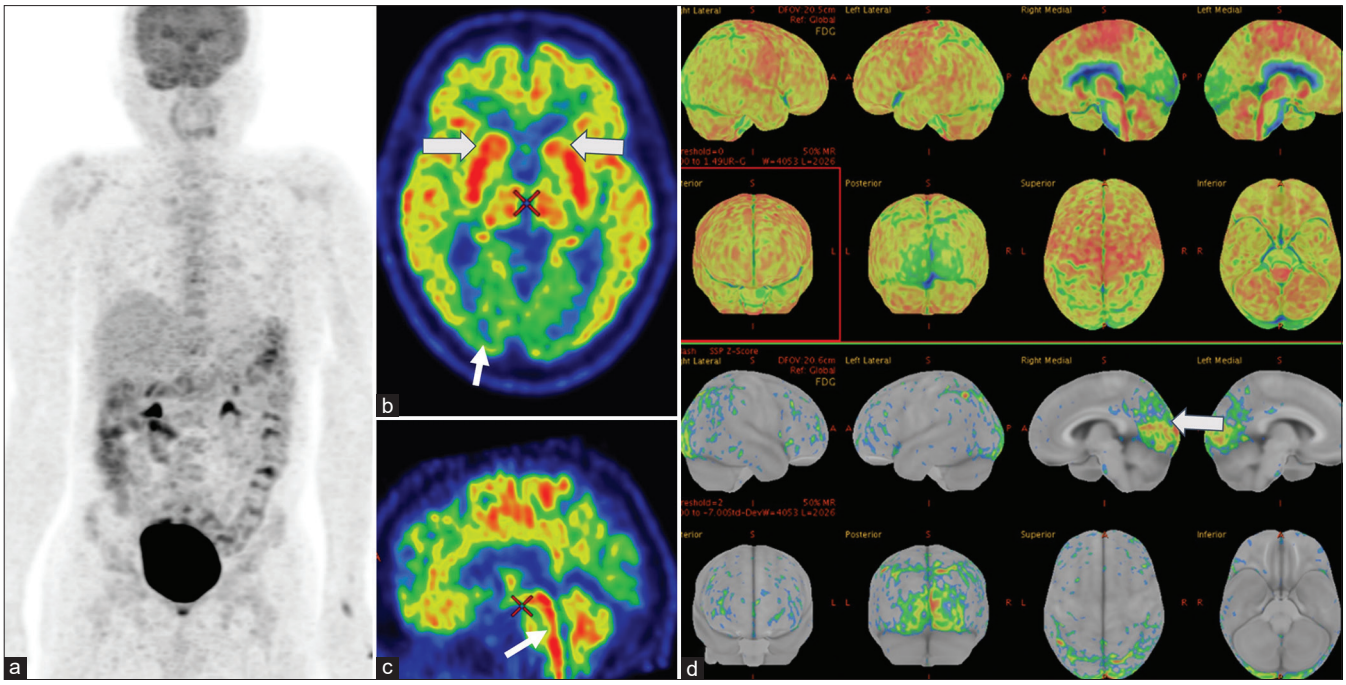

Figure 2: F-18 FDG PET maximum intensity projection image shows that (a) no focal metabolically active lesion has been identified. Transaxial plain FDG PET image of the brain (b) at the level of BG reveals BG hypermetabolism and occipital hypometabolism (white arrow). Sagittal plain FDG PET image shows brainstem hypermetabolism (c, white arrow). Cortex id maps showing significant hypometabolism in the occipital lobe (d). BG: basal ganglia, PET: positron emission tomography, F-18 FDG: 18-fluorodeoxyglucose

working memory and executive functions, later progressing to recent memory impairment. He also had gait difficulties with frequent falls and RBD. Examination revealed restricted vertical eye movements, bulbar palsy, gait ataxia, and bilateral muscle wasting with fasciculations in hands. Nerve conduction studies/electromyography confirmed neurogenic involvement in the bulbar and cervical segments. MRI and PET were normal, and CSF showed 12 cells/mm^3 (all lymphocytes), elevated proteins (118 mg/dL), and normal glucose levels. Serum anti-IgLON5 antibodies were positive by IIF. Viral markers, parathyroid levels, creatine phosphokinase, and routine blood tests were normal. He was treated with pulse steroids, but succumbed to respiratory infection and sepsis before further immunosuppression could be initiated.

Case 5

A 60-year-old female presented with a 1-year history of choreiform movements initially involving the face, followed by bilateral upper limbs, and eventually lower limbs, leading to walking difficulty. She also had complaints of insomnia. On examination, there were slow horizontal and vertical saccades and restricted downgaze. Her MRI and PET scan were both normal. Her serum tested positive for anti-IgLON5 antibody (IIF), and she was started on pulse methylprednisolone 1000 mg/day for 5 days, followed by IVIg 2 g/kg for 5 days. However, she did not have any marked improvement. She is being followed up with symptomatic management for chorea along with rituximab (two doses of 1 g 14 days apart followed by (f/b) two six-monthly doses) and has shown mild improvement in symptoms.

Case 6

A 72-year-old woman presented with a 2-year history of marked sleep disturbances and cognitive impairment (Addenbrooke's Cognitive Examination-III score 64/100). She reported excessive daytime somnolence (Epworth score 20/24), snoring, and frequent dream enactment. Over 6 months, she developed slow movements, forward truncal bending, and balance difficulties. She also exhibited intermittent left eyelid closure and repetitive throat clearing. Examination revealed slow vertical saccades, parkinsonism, cerebellar signs [Video 1], and intermittent exotropia of the left eye with diplopia. MRI demonstrated multiple foci of non-specific T2/FLAIR-hyperintense signal abnormalities within the white matter. CSF analysis revealed normal findings. Serum anti-IgLON5 antibodies were strongly positive (IIF). Polysomnography confirmed OSA and RBD, and laryngoscopy showed normal vocal cord function without stridor or aspiration. Autonomic function tests showed severe orthostatic hypotension and impaired heart rate variability. Serum and CSF autoimmune and paraneoplastic panels were negative. She was treated with five cycles of plasma exchange (200 mL/kg) followed by IVIg (2 g/kg over 5 days), which resulted in improvements in sleep and gait, and resolution of her eyelid closure and vocalizations after 6 months.

Case 7

A 52-year-old hypertensive woman presented with a 1-year history of choreiform movements, along with sleep issues and mild dysarthria. The chorea affected the upper limbs, neck, and head, and was associated with facial myokymia [Video 2]. MRI

of the brain revealed mild generalized cerebral atrophy, and a PET scan showed hypermetabolism in bilateral basal ganglia, thalamus, brainstem, and cerebellum. CSF analysis revealed 10 cells/mm^3 with normal protein and glucose. Anti-IgLON5 antibodies were positive in both serum and CSF (IIF). She was started on pulse methylprednisolone for 5 days, which led to almost complete resolution of the chorea. Scale for the Assessment and Rating of Ataxia score improved from 24 to 18. She is on maintenance therapy with oral steroids.

Discussion

Anti-IgLON5 disease is an emerging syndrome with a wide array of neurological manifestations, bridging autoimmunity and neurodegeneration.[11,12] This disease, associated with antibodies against the immunoglobulin-like cell adhesion molecule (IgLON5), has been linked to five classical syndromes including sleep disorders, a progressive supranuclear palsy (PSP)-like syndrome, amyotrophic lateral sclerosis (ALS)-like presentation, bulbar dysfunction, and cognitive decline, sometimes accompanied by chorea.[1] Despite its growing recognition, the pathophysiology remains poorly understood. We have summarized current and previously published Indian cases in Supplementary Tables 1-3.

Movement disorders are the initial reason for consultation in over 57% of cases. At diagnosis, around 87% of patients exhibit movement disorders.[10] Restricted vertical eye movements, seen in three patients in our cohort, are another notable feature of anti-IgLON5 disease. Apart from a semblance to PSP, gait ataxia combined with parkinsonism and dysautonomia may mimic multiple system atrophy (MSA). Indeed, the radiological "hot cross bun" appearance, mimicking multiple system atrophy-cerebellar (MSA-C), has been described with IgLON5.[9] In anti-IgLON5 disease, chorea affecting the limbs, trunk, or face is reported in approximately 33% of cases.[10] Bradykinesia and dystonia[6] each occur in about 27%, with tremors, predominantly affecting upper limbs, and have been reported in 21% of patients. Other less-predominant features include myoclonus, akathisia, myorhythmia,[5] tics,[7] and myokymia. Two other cases from India have previously reported chorea as a presenting feature.[3,4]

Sleep-related movement disorders including RBD and periodic limb movements in sleep often serve as clues to diagnosis. The presence of sleep disturbances (seen in six of our cases), which eventually develop in most patients, is further supportive.[1] These disturbances, which include RBD, OSA, stridor, insomnia, and excessive daytime sleepiness, reinforce the importance of sleep studies in the diagnostic process.[17]

Another important consideration is the role of anti-IgLON5 disease in rapidly progressive dementia, particularly in cases with a dysexecutive phenotype. In our series, five patients had frontal-dysexecutive dementia, which was a primary reason for consultation in three. Other cases reported from India also had a Dementia with Lewy Bodies (DLB)-like presentation with prominent visual hallucinations.[8] A notable feature in our series was the occurrence of seizures in two patients. Seizures are relatively uncommon in anti-IgLON5 disease, occurring in only about 5% of patients.[13]

Neuroimaging findings in anti-IgLON5 disease are varied and usually non-specific, but PET imaging can provide useful clues. In general, nearly 80% of patients with autoimmune encephalitis harbor basal ganglia hypermetabolism due to active ongoing inflammation as seen on PET and 13% have been noted to have occipital hypometabolism. Basal ganglia and brainstem hypermetabolism has also been noted in a previous series, with the hypothesis that these areas have a predilection to be affected by tauopathies, as in IgLON5 disease.[14] In our series, brainstem involvement on PET imaging was seen in PSP-like presentations, while basal ganglia, temporal lobe, and frontoparietal network abnormalities were noted across the cases. The current literature suggests testing both serum and CSF for anti-IgLON5 antibodies. The sensitivity and specificity of antibody testing are very high and almost equal for serum and CSF (ranging from 95% to 100%). Even with the neuropathological criteria outlined,[15] antibody testing is mandatory for a definite diagnosis.

Immunotherapy remains the cornerstone of treatment in IgLON5 disease. In a systematic review assessing treatment response in anti-IgLON5 disease, the response rates to plasma exchange (PLEX) (46%) were higher than to steroids (34.2%) or IVIg (42.8%). Furthermore, combination therapy had a better response rate (66.6%) compared to monotherapy (31.8%). Non-classical presentations and cognitive phenotypes had a better response.[16] Our patients were treated with a combination of pulse methylprednisolone, IVIg, rituximab, PLEX, and MMF. While the response to treatment is often modest, with improvement reported in about one-third of cases, three of our patients showed significant improvement.

Conclusion

We report the largest series of anti-IgLON5–related disease from India. We noted not only classical phenotypes, but also unusual features such as seizures and neuroimaging abnormalities. A review of Indian literature revealed the prominence of sleep abnormalities, cognitive impairment, and movement disorders. This clinical heterogeneity suggests that a high index of suspicion is required for this disorder, considering its potentially treatable nature.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Gaig C, Graus F, Compta Y, Högl B, Bataller L, Brüggemann N, et al. Clinical manifestations of the anti-IgLON5 disease. Neurology 2017;88:1736-43.
2. Tao QQ, Wei Q, Song SJ, Yin XZ. Motor neuron disease-like phenotype associated with anti-IgLON5 disease. CNS Neurosci Ther 2018;24:1305-8.
3. Bhatia M, Singh Y. Anti IgLON5 disease - first case report from India. Sleep Medicine 2020;67:215-6.
4. Soman Pillai K, Maramattom BV, Gopalannair Santhamma S, Kishore A. Head drop and trunk flexion as an early manifestation of anti-IgLON5 disease. Mov Disord Clin Pract 2022;10:135-7.
5. Gurram S, Holla VV, Kamath SD, Prakash SS, Dubbal R, Kamble N, et al. Facio-Lingual-Palatal Myorhythmic Presentation of Anti-IgLON5 Disease. Mov Disord Clin Pract 2023;10:1427-9.
6. Bavdhankar, K, Jain N, Agrawal S, Maheshkar P, Andugulapati SS, Puntambekar S, et al. Unusual head drops, neck and truncal dystonia and sleep orthopnea with a favorable treatment response in IgLon5 antibody disease. Mov Disord Clin Pract 2024;11:575-7.
7. Kandadai RM, Yaranagula SD, Kola S, Alugolu R, Prasad V and Borgohain R. Complex movement disorder with prominent tic like movements: Expanding the clinical spectrum of IgLON5 antibody disease. Mov Disord Clin Pract 2024;11:94-6.
8. Seniaray N, Verma R, Ranjan R, Belho E, Mahajan H. Lewy body dementia associated with anti-IgLON 5 encephalitis detected on 18F fluorodeoxyglucose positron emission tomography/computed tomography and 99mTc-TRODAT single-photon emission computed tomography/computed tomography. Indian J Nucl Med 2022;37:94-6.
9. Vijayaraghavan A, Prabhu AS, KP Divya, ES Sapna, Cherian A, Narasimhaiah D, et al. Multiple system atrophy like presentation with hot-cross bun sign in anti-IgLON5 disease. Parkinsonism Relat Disord 2024;122;106073.
10. Gaig C, Compta Y, Heidbreder A, Marti MJ, Titulaer MJ, Crijnen Y, et al. Frequency and characterization of movement disorders in anti-IgLON5 disease. Neurology 2021;97:e1367-81.
11. Ryding M, Gamre M, Nissen MS, Nilsson AC, Okarmus J, Poulsen AAE, et al. Neurodegeneration induced by anti-IgLON5 antibodies studied in induced pluripotent stem cell-derived human neurons. Cells 2021;10:837.
12. Gaig C, Sabater L. Clinical presentations and antibody mechanisms in anti-IgLON5 disease. Rev Neurol 2024;180:940-9.
13. Wang Y, Wang Y, Zhao X, Zhang S, Geng Y, Zhang Z, et al. Epileptic seizures in patients with anti-IgLON5 disease. J Neuroimmunol 2022;373:577999.
14. Nissen MS, Blaabjerg M. Anti-IgLON5 disease: A case with 11-year clinical course and review of the literature. Front Neurol 2019;10;1056.
15. Gelpi E, Reinecke R, Gaig C, Iranzo A, Sabater L, Molina-Porcel L, et al. Neuropathological spectrum of anti-IgLON5 disease and stages of brainstem tau pathology: Updated neuropathological research criteria of the disease-related tauopathy. Acta Neuropathol 2024;148:53.
16. Cabezudo-García P, Mena-Vázquez N, Estivill Torrús G, Serrano-Castro P. Response to immunotherapy in anti-IgLON5 disease: A systematic review. Acta Neurol Scand 2020;141:263–70.
17. Kilani A, Srikanti R, Palaniraj S, Palaniraj A, Nalamala BR, Boppe P, et al. A rare cause of respiratory failure: Anti-immunoglobulin-like cell adhesion molecule 5 disease. Indian J Chest Dis Allied Sci 2024;66;27-30.

Supplementary Table 1: Features of anti-IgLON5 disease in the current cohort

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age (years) at presentation	49	64	62	75	60	72	52
Sex	Female	Male	Male	Male	Female	Female	Female
Time from symptom onset to diagnosis (months)	12	6	16	30	12	24	12
Comorbidities	Hypertension	Hypertension, diabetes, hypothyroidism	Hypertension	Hypertension, diabetes, coronary artery disease	Diabetes	None	Hypertension
Presentation	Epilepsy and cognitive decline	Cognitive decline and sleep disturbances	Gait abnormality, epilepsy, sleep abnormalities and bulbar dysfunction	Gait abnormality, epilepsy and sleep abnormalities	Chorea Sleep abnormalities	Sleep abnormalities and cognitive decline	Chorea
Movement disorders	Gait ataxia	Restricted vertical eye movements	Akinetic-rigid syndrome, gait ataxia	Frequent falls with restricted vertical eye movements, gait ataxia	Chorea involving face and all 4 limbs	Left eyelid closure apraxia, repetitive throat clearing, slow vertical saccades, left eye fluctuating exotropia, parkinsonism	Chorea affecting upper limbs, face and neck
Cognition	Frontotemporal syndrome, MMSE 9/30	Frontal dysexecutive syndrome with MMSE 24/30	Frontal dysexecutive syndrome with MMSE 21/30 and FAB score 6	Frontal dysexecutive syndrome	Normal	Frontal dysexecutive syndrome with ACE-III 64/100	Normal
Bulbar involvement	None	None	Bulbar palsy, stridor	Bulbar palsy	None	Breathy vocalizations likely due to bulbar involvement	Mild dysarthria
Motor involvement	Left sided hemiparesis	None	None	Wasting and fasciculations of bilateral upper limbs	None	None	None
Sleep abnormalities	Excessive sleep	Excessive sleep RBD	RBD OSA	None	Insomnia	RBD OSA Excessive day-time sleepiness	RBD OSA
Ataxia	Gait ataxia	None	Gait ataxia	Gait ataxia	None	Gait ataxia	None
Seizures	Present	None	Present	None	None	None	None
MRI	Generalized cerebral and cerebellar atrophy	Bilateral parieto-occipital atrophy	Normal	Normal	Normal	Small vessel ischemic changes	Mild generalized atrophy
PET	Bilateral temporal hypo metabolism and basal ganglia hypermetabolism	Hyper metabolism in brainstem, putamen with hypometabolism in bilateral occipital and pre-cuneus	Normal	Normal	Normal	N.A.	Hyper metabolism in bilateral basal ganglia, brainstem and cerebellum
CSF analysis (Cells/high power field, glucose and protein in mg/dL)	Cells 2 lymphocytes Protein 150 Glucose (RBS) 62 (110)	Cells 0 Protein 229 Glucose (RBS) 105 (181)	Cells 10 lymphocytes Protein 27 Glucose 62	Cells 12 lymphocytes Protein 60 Glucose 80	N.A.	Cells 0 Protein 60 Glucose (RBS) 77/134	Cells 10 lymphocytes Protein 86 Glucose 80
PSG	N.A	N.A	Reduced MSL	N.A.	N.A.	OSA, RBD	N.A
EEG	Normal	N.A	N.A.	N.A.	N.A.	N.A.	N.A

Contd...

Supplementary Table 1: Contd...

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Serum IgLON5	Positive	Positive	N.A.	Positive	Positive	Positive	Positive
CSF IgLON5	N.A.	N.A.	Positive	N.A.	N.A.	N.A.	Positive
Treatment received	MPS pulse Rituximab	MPS pulse IVIG Rituximab	MPS pulse IVIG MMF	Pulse MPS	Pulse MPS IVIG Rituximab	PLEX IVIG	MPS Pulse IVIG
Outcome	Some improvement in cognition and no further symptom-progression	Mild improvement in sleep disturbance initially, no further improvement	Death due to aspiration pneumonia and sepsis	Death due to sepsis	Mild to no improvement	Improvement in sleep and gait issues and resolution of lid closure and vocalizations	Marked improvement in chorea
Follow-up duration in months	12	6	36	6	12	12	6

MMSE: Mini-Mental Status Examination, ACE: Addenbrook Cognitive Examination, RBD: Rapid eye movement sleep (REM) -Behaviour disorder, OSA: Obstructive sleep apnea, N.A: Not available, MSL: Mean Sleep Latency, MPS: methylprednisolone, IVIG: Intravenous Immunoglobulin, MMF: Mycophenolate mofetil, PLEX: Plasmapheresis, PSG: polysomnography

Supplementary Table 2: Summary table of cases of Anti-IgLON5 disease reported from India (n=7) excluding current series

	Age at presentation in years	Sex	Duration of symptoms (months)	Presentation	MRI	PET	PSG	Antibodies in serum/ CSF	Treatment received	Outcome	Follow-up duration (in months)
Case 1[3]	58	Male	96	Sleep disturbance, gait ataxia and chorea, memory disturbances	Bilateral cortical T2 hyperintensities	N.A	OSA, PLMS, AHI-52.4	Serum	Declined immunotherapy	Some symptomatic improvement with BiPAP	N.A
Case 2[8]	76	Male	12	Memory disturbances, visual hallucinations, PSP-like syndrome, sleep disturbance, bulbar symptoms	Normal	Hyper metabolism in bilateral basal ganglia, thalami, brainstem and cerebellum with hypo metabolism in bilateral temporo-parieto-occipital cortices	N.A	Serum and CSF	IVIG	Improvement in gait and bulbar symptoms	N.A
Case 3[5]	52	Male	24	Sleep disturbances, facial-lingual-palatal myorhythmias, fasciculations	Normal	N.A	Poor sleep efficiency, undifferentiated NREM, OSA	Serum and CSF	MPS Pulse PLEX	Partial improvement in sleep and myorhythmia	1
Case 4[4]	49	Female	10	Sleep disturbances, chorea, head drops, memory disturbances, visual hallucinations	Normal	Bilateral caudate hypo metabolism	N.A	Serum and CSF	Steroids Rituximab	Partial improvement	2
Case 5[9]	55	Female	36	Imbalance and action tremors, slurred speech, Parkinsonism, sleep disturbances	Hot-cross-bun sign	N.A	REM sleep without atone	Serum and CSF	MPS pulse Rituximab	Stabilization of symptoms	4
Case 6[6]	58	Male	18	Neck and truncal dystonia, sleep disturbances, dysarthria, ALS-like features	Normal	Normal	N.A	Serum and CSF	MPS pulse IVIG Rituximab	Marked improvement	3
Case 7[7]	52	Male	5	Shoulder tics, generalised bradykinesia	Normal	N.A	N.A	Serum	MPS pulse	Marked improvement	N.A
Case 8[16]	68	Male	12	Sleep disturbances,	Mild ischemic changes and age-related atrophy	N.A	CSA and OSA, AHI 32.8, RBD, PLMI 8.3, ODI 43.5	Serum	MPS pulse, IVIG, Rituximab, mycophenolate mofetil	Worsened and needed IMV	N.A

PLMS: Periodic limb movements in sleep, AHI: Apnea-hypopnea index, BiPAP: Bilevel positive airway pressure, PSP: Progressive Supranuclear Palsy, ALS: Amyotrophic lateral sclerosis, RBD: Rapid eye movement sleep (REM) -Behaviour disorder, NREM: Non-Rapid eye movement, OSA: Obstructive sleep apnea, N.A: Not available, MSL-Mean Sleep Latency, MPS: methylprednisolone, IVIG: Intravenous Immunoglobulin, MMF: Mycophenolate mofetil, PLEX: Plasmapheresis, PSG: polysomnography, CSA: Central sleep apnea, PLMI: Periodic limb movement index, ODI: Oxygen desaturation index, IMV: Invasive mechanical ventilation

Supplementary Table 3: Summary table of characteristics of all anti-IgLON5 cases from India (n=14)

	Proportion (%) of patients (or mean)
Mean age (standard deviation) (years)	60.16 (9.16)
Duration of symptoms before presentation (months) (Median (interquartile range))	12 (12-24)
Sleep disturbances	14/15 (93.3%)
Cognitive involvement	8/15 (53.3%)
Bulbar involvement	6/15 (40%)
PSP-like syndrome	5/15 (33.3%)
ALS-like features	2/15 (13.3%)
Movement disorders	
Gait ataxia	6/15 (40%)
Chorea	4/15 (26.7%)
Dystonia	2/15 (13.3%)
Myorhythmia	1/15 (6.7%)
Tics	1/15 (6.7%)
Seizures	2/15 (13.3%)
MRI abnormal	6/15 (40%)
PET abnormal	5/9 (55.5%)
Brainstem involvement on imaging	4/15 (26.7%)
Treatments given- MPS pulse	12/15 (80%)
IVIG	8/15 (53.3%)
PLEX	2/15 (13.3%)
Rituximab	7/15 (46.7%)
Improvement in features with treatment- marked	4/15 (26.7%)
Improvement in features with treatment- partial	4/15 (26.7%)
Improvement in features with treatment- mild	4/15 (26.7%)
Deaths/IMV	3/15 (20%)

PSP: Progressive Supranuclear Palsy, ALS: Amyotrophic lateral sclerosis, MPS: methylprednisolone, IVIG: Intravenous Immunoglobulin, PLEX: Plasmapheresis, IMV: Invasive mechanical ventilation