Autoimmunity and the Airway:
A Case-Informed Scoping Review of Anti-IgLON5-Associated Vocal Fold Paralysis

Natalie Weiss, M.D., M.B.A.[1], Reginald Myles, B.S.[2], Bastien Valencia-Sanchez, M.D.[1], Ashley Pena, M.D.[3], Amy Rutt, D.O.[1]

[1]Department of Otolaryngology - Head & Neck Surgery, Mayo Clinic, Jacksonville, FL
[2]Alix School of Medicine, Mayo Clinic, Scotsdale, AZ,
[3]Department of Neurology, Mayo Clinic, Jacksonville, FL

ABSTRACT

OBJECTIVE
Anti-IgLON5 disease, a rare autoimmune neurodegenerative tauopathy first described in 2014, often involves the larynx with manifestations such as vocal fold paresis or paralysis. However, it is frequently misdiagnosed as motor neuron disease, and airway findings remain underrepresented in the literature. This scoping review synthesizes current knowledge on laryngeal involvement in Anti-IgLON5 disease and highlights implications for otolaryngologists.

DATA SOURCES
Pubmed/MEDLINE, Embase, and Scopus

REVIEW METHODS
A systematic search combined terms related to Anti-IgLON5 and laryngeal or airway manifestations. References were managed in Covidence for deduplication, screening, and extraction. Eligible studies included case reports, case series, and cohort studies describing airway involvement in English. Reports limited to sleep-disordered breathing were analyzed separately. A representative case was then added.

RESULTS
The search yielded 110 studies. Deduplication left 82, of which 44 were eligible for full-text review. A total of 25 met inclusion criteria. Commonly reported findings included sleep-disordered breathing, VF paresis, and stridor. Very few underwent laryngoscopy. Treatment was symptomatic, often including tracheostomy. Following diagnosis, treatment included IVIg, plasma exchange, steroids, or other immunotherapies. We also present the case of a 79-year-old female who developed bilateral vocal fold hypomobility requiring posterior cordotomy and, ultimately, tracheostomy. Anti-IgLON5 disease was confirmed following neuromuscular evaluation.

CONCLUSIONS
Anti-IgLON5 disease poses a diagnostic challenge for otolaryngologists, as its laryngeal manifestations can mimic more common neuromuscular disorders. Recognizing these airway signs is essential for prompt diagnosis and intervention, potentially improving outcomes in this rare and often misunderstood condition.

OBJECTIVES

BACKGROUND
- **Anti-IgLON5 disease** is a recently-described autoimmune neurodegenerative tauopathy, first reported in 2014.
- The disease is characterized by **autoantibodies against IgLON5**, leading to abnormal tau deposition in the brainstem and other neuronal regions.
- Patients may present with a broad clinical spectrum, including:
  - Parasomnias and sleep disordered breathing.
  - Bulbar symptoms such as dysphagia and dysarthria.
  - Movement abnormalities.
  - Airway manifestations such as vocal fold paresis/paralysis or stridor.

WHY DOES THIS MATTER?
- Laryngeal involvement may be the initial or only presenting symptom of Anti-IgLON5 disease (**Figure 1**).
- Findings can mimic more common disorders such as motor neuron disease, leading to diagnostic delay.
- Recognition of characteristic airway signs can trigger appropriate antibody testing, facilitating earlier diagnosis and multidisciplinary care.

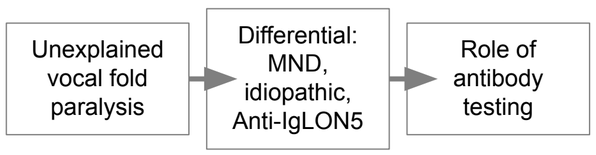

Figure 1. Diagnostic pathway flowchart

OUR AIM
- We aim to map and synthesize published evidence on laryngeal involvement in Anti-IgLON5 disease, highlighting implications for otolaryngology practice.

METHODS

FRAMEWORK & REGISTRATION
- Reported per PRISMA-ScR guidelines.
- Registered in OSF (doi: 10.17605/OSF.IO/CJEBV)

SEARCH STRATEGY
- PubMed/MEDLINE, Scopus, Embase
- Terms related to Anti-IgLON5 and larynx/airway

ELIGIBILITY
- Include: Case reports, case series, cohorts, systematic reviews reporting on Anti-IgLON5 and airway involvement
- Exclude: Basic science/animal, abstract only, reports without new patient data, non-English publication

AIRWAY FEATURES OF INTEREST
- Any studies discussing sleep-disordered breathing (stridor in sleep or sleep apnea), laryngeal dysfunction (paresis/paralysis, dysphonia, aspiration), airway interventions (tracheostomy, intubation, laryngeal surgery) were included.
- Reports limited to sleep-disordered breathing were analyzed separately.

SCREENING & EXTRACTION
- Two independent reviewers of each report; conflict resolved by consensus (**Figure 2**)
- Extracted characteristics, presentations, evaluations, interventions, and outcomes.

ANALYSIS
- Results were synthesized narratively.
- Heterogeneity of study designs precluded quantitative analysis.

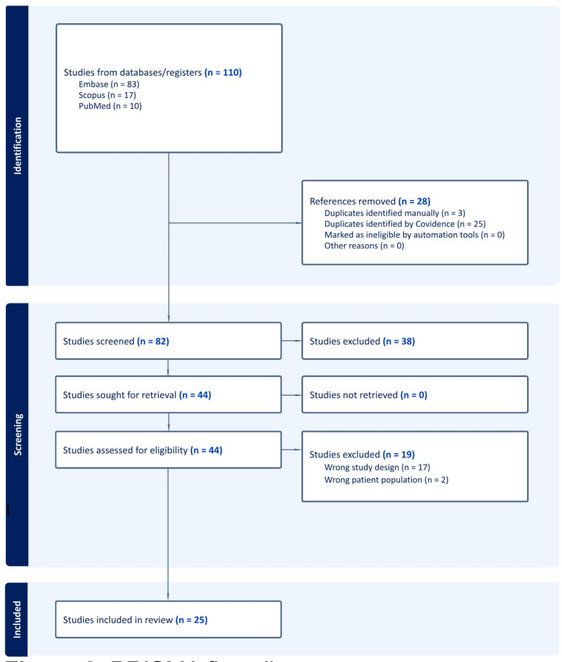

Figure 2. PRISMA flow diagram

RESULTS

STUDY CHARACTERISTICS
The search yielded 110 studies, of which 82 remained after automatic deduplication by Covidence and manual removal of remaining duplicates. From these, 44, were appropriate for full-text review. Two reviewers independently evaluated texts and conflict was resolved through consensus. Twenty-five articles remained for analysis.

Case reports were the majority (18/25) followed by cohort studies (3/25), case series (2/25), and one systematic review.

PRESENTATIONS & EVALUATIONS
Sleep-disordered breathing occurred in nearly all patients with airway involvement of Anti-IgLON5 disease. Other airway symptoms included hoarseness, dyspnea with VF paresis, choking/aspiration, or laryngospasm. Laryngoscopy was performed in a minority.

INTERVENTIONS & OUTCOMES
Treatment was largely symptomatic, including CPAP and voice therapy. Many required tracheostomy. After diagnosis with Anti-IgLON5 from the serum or CSF, treatment included IVIg, plasma exchange, steroids, cyclophosphamide, mycophenolate mofetil, azathioprine, or rituximab. Response was highly variable.

CASE REPORT
A 79-year-old female presented with shortness of breath and inspiratory stridor. She was found to have weakness in abduction of both vocal folds on laryngoscopy (**Figure 3**)

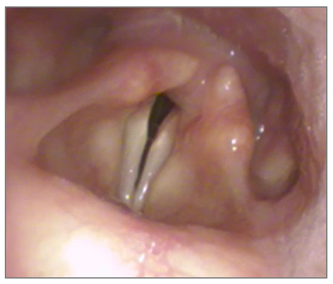

Figure 3. Poor maximal VF abduction on inhalation

She underwent left posterior cordotomy and medial arytenoidectomy. However, symptoms returned and worsened over the next 4 months. She was hospitalized and underwent right posterior cordotomy and medial arytenoidectomy, as well as tracheostomy and NG tube placement (**Figure 4**). Neuromuscular workup at that time provided a diagnosis of Anti-IgLON5 disease. She was started on IVIg a few weeks later and experienced mild improvement in symptoms. She was decannulated during her IVIg hospitalization.

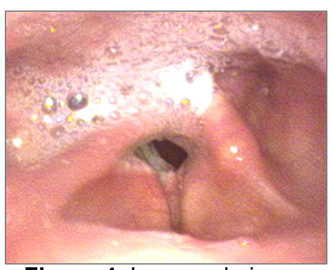

Figure 4. Improved airway patency after procedures

DISCUSSION

Most published cases of Anti-IgLON5 disease with airway involvement were single-patient reports, with sleep-disordered breathing common. Tracheostomy was frequently required. Airway problems often preceded diagnosis.

CONCLUSIONS

Otolaryngologists should maintain vigilance for Anti-IgLON5 in patients with unexplained VF immobility or stridor, as earlier recognition and multidisciplinary care may improve outcomes.

REFERENCES