Anti-IgLON5 Disease with intriguing MRI findings respond dramatically to immunotherapy

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Case report

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Abstract

Background We present the first case of Anti-IgLON5 disease with unremarkable or unspecific brain magnetic resonance imagings, and poor responsiveness to immunotherapy.

Case presentation A 37-year-old man presented with 4-day history of gait instability, dysarthria, and oculomotor abnormalities. The initial neurologic examination revealed mild unsteady gait, subtle dysarthria, and left abducent paralysis. The brain MRI imaging showed multiple, scattered diffusion restriction in the bilateral cerebral hemispheres involving left tegmentum of the midbrain, and occipital horn of right lateral ventricle, without contrast enhancement. The Anti-IgLON5 antibodies were detected in the serum (titer 1:32). Furthermore, the human leukocyte antigen (HLA) genotyping confirmed HLA-DRB1*11:01 and HLA-DRB1*15:01, HLA-DQB1*03:01 and HLA-DQB1*06:02 alleles. The symptoms of patient rapid improvement after high-dose intravenous methylprednisolone and immunoglobulins.

Conclusions In this paper, we report a new case of anti-IgLON5 disease with major symptoms of gait instability, dysarthria, and oculomotor abnormalities, with distinctive brain magnetic resonance findings, and responsive to immunotherapy.

Background

Anti-IgLON5 disease was first described as a progressive antibody-associated encephalopathy, with multiple non-specific clinical symptoms including sleep dysfunction, bulbar symptoms, progressive supranuclear palsy-like syndrome, cognitive impairment, and a variety of movement disorders. This newly discovered disease presented unremarkable or unspecific brain magnetic resonance imagings, and had poor responsiveness to immunotherapy.

Case Presentation

A 37-year-old man presented with 4-day history of gait instability, dysarthria, and oculomotor abnormalities. He did not report parasomnia (only excessive daytime sleepiness), there was no family history either. The initial neurologic examination revealed mild unsteady gait, subtle dysarthria, and left abducent paralysis. In addition, although the patient was able to walk alone, he felt unsteady with a subjective feeling of lateropulsion. The rest of his examination was normal.

During a 2-week stay in the department of neurology, magnetic resonance imaging (MRI) of the head and neck, blood, cerebrospinal fluid (CSF), electroencephalogram (EEG), and polysomnogram (PSG) were performed. There were several abnormal investigations. Firstly, the brain MRI imaging showed multiple, scattered diffusion restriction in the bilateral cerebral hemispheres involving left tegmentum of the midbrain, and occipital horn of right lateral ventricle (Fig. 1), without contrast enhancement. Secondly, initial lumbar puncture revealed positive oligoclonal bands in the CSF with normal protein, cells and glucose. Thirdly, anti-IgLON5 antibodies were detected in the serum (titer 1:32), while other autoantibodies (Hu, Yo, Ri, CV2, Ma2/Ta, amphiphysin, N-methyl-D-aspartate receptor, α-amino-3-hydroxy-5-methyl-4-

isoxazolepropionic acid receptor, contactin-associated protein-like 2, leucine-rich glioma inactivated protein 1, dipeptidyl-peptidase like protein 6, γ-aminobutyric acid b receptor, aquaporin 4, myelin basic protein, myelin oligodendrocyte glycoprotein and glial fibrillary acidic protein) remained negative in serum and CSF. Furthermore, his human leukocyte antigen (HLA) genotyping confirmed HLA-DRB1*11:01 and HLA-DRB1*15:01, HLA-DQB1*03:01 and HLA-DQB1*06:02 alleles, and did not show the same HLA association found in other reported cases[1–4]. Finally, the EGG and PSG findings were unremarkable.

The patient was initially treated with high-dose intravenous methylprednisolone and immunoglobulins, which led to a rapid improvement over a few days. When discharged, his gait instability, dysarthria, and oculomotor abnormalities completely recovered. The titer of serum anti-IgLON5 antibodies decreased to 1:10 atfer this treatment, and the initial MRI changes have lessened. The patient continued treatment with mycophenolate mofetil, and oral steroids were tapered slowly over several months.

Discussion And Conclusions

Anti-IgLON5 disease was first described in 2014 as a progressive antibody-associated encephalopathy by Sabater L et al.[4]. The main symptoms are heterogeneous, including sleep dysfunction, bulbar symptoms, progressive supranuclear palsy-like syndrome, cognitive impairment, and a variety of movement disorders[5]. These symptoms may each occur in different severity, combinations and periods, leading to various clinical subtypes. Reportedly, more than 95% cases presented unremarkable or unspecific MRI findings[5], and had poor responsiveness to immunotherapy. In contrast, our case showed distinctive brain MRI changes, particularly in left tegmentum of the midbrain, and occipital horn of right lateral ventricle, which haven't been reported before. After the treatment of corticosteroids and immunoglobulins, his symptoms improved dramatically, his anti-IgLON5 serum titer decreased from 1:32 to 1:10, and his initial brain MRI changes have lessened, all this suggests that his symptoms could be associated with the titer of anti-IgLON5 antibodies and the antibodies may play a crucial role in the pathogenesis. Additionally, the positive treatment response to immunotherapy in this patient might also be related to the young age of onset (37 years old) and the only short duration (4 days), while the youngest patient reported in the literature was 40 years old [1] and the shortest duration was 3 months[6]. In this scenario, an early diagnosis and treatment would be crucial to delay or even stop the progress of the assumed pathomechanism. A prompt intervention with immunotherapy could alter the outcome of the anti-IgLON5 disease.

Abbreviations

HLA
Human leukocyte antigen
MRI
Magnetic resonance imaging
CSF
Cerebrospinal fluid

EEG
Electroencephalogram
PSG
Polysomnogram

Declarations

Availability of Data and Materials

Not applicable

Author information

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Contributions

Yan Pi: report concept and design and drafting of the manuscript. Jingcheng Li and Kai Chang: report concept and design and editing of the manuscript for critical intellectual content. Lili Zhang: acquisition of data, interpretation of data, critical revision of final manuscript for intellectual content.

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Ethics declarations

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of the Third Military Medical University. The patient allowed authors to use those clinical data for scientific research and publication purposes, giving written informed consent.

Consent for publication

The patient allowed authors to use those clinical data for scientific research and publication purposes, giving written informed consent.

Competing Interests

The authors declare that they have no competing interests.

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Authors' contributions

Yan Pi: report concept and design and drafting of the manuscript. Jingcheng Li and Kai Chang: report concept and design and editing of the manuscript for critical intellectual content. Lili Zhang: acquisition of data, interpretation of data, critical revision of final manuscript for intellectual content.

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References

1. Chen H, Wu J, Irani SR: **Distinctive Magnetic Resonance Imaging Findings in IgLON5 Antibody Disease.** *JAMA Neurol* 2019**:**1-2.
2. Heidbreder A, Philipp K: **Anti-IgLON 5 Disease.** *Curr Treat Options Neurol* 2018, **20:**29.
3. Montagna M, Amir R, De Volder I, Lammens M, Huyskens J, Willekens B: **IgLON5-Associated Encephalitis With Atypical Brain Magnetic Resonance Imaging and Cerebrospinal Fluid Changes.** *Front Neurol* 2018, **9:**329.

4. Sabater L, Gaig C, Gelpi E, Bataller L, Lewerenz J, Torres-Vega E, Contreras A, Giometto B, Compta Y, Embid C, et al: **A novel non-rapid-eye movement and rapid-eye-movement parasomnia with sleep breathing disorder associated with antibodies to IgLON5: a case series, characterisation of the antigen, and post-mortem study.** *Lancet Neurol* 2014, **13:**575-586.
5. Gaig C, Graus F, Compta Y, Hogl B, Bataller L, Bruggemann N, Giordana C, Heidbreder A, Kotschet K, Lewerenz J, et al: **Clinical manifestations of the anti-IgLON5 disease.** *Neurology* 2017, **88:**1736-1743.
6. Moreno-Estebanez A, Garcia-Ormaechea M, Tijero B, Fernandez-Valle T, Gomez-Esteban JC, Berganzo K: **Anti-IgLON5 Disease Responsive to Immunotherapy: A Case Report with an Abnormal MRI.** *Mov Disord Clin Pract* 2018, **5:**653-656.

Figures

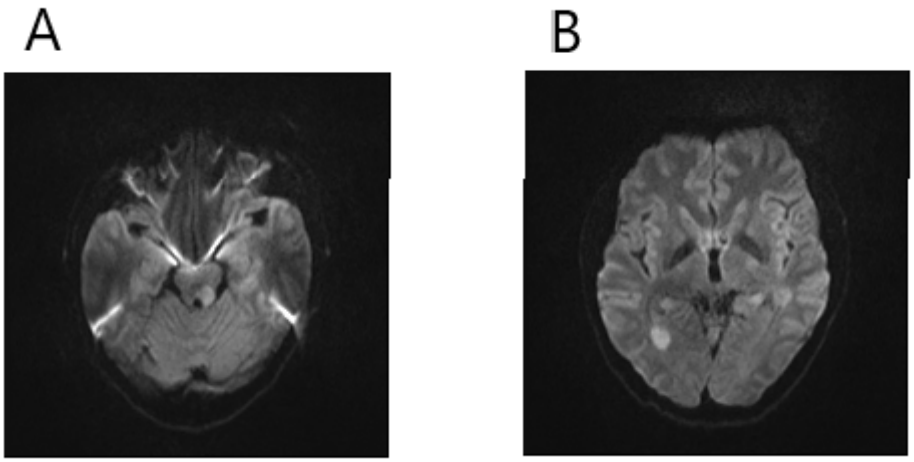

Figure 1

Brain Magnetic Resonance Imaging of the anatomy of anti-IgLON5 antibody disease. Axial diffusion trace images On the day of admission showed asymmetrical areas of reduced diffusion involving left tegmentum of the midbrain (A) and right occipital horn of the lateral ventricle (B).

Supplementary Files

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