Movement Disorders
CLINICAL PRACTICE

CASE REPORT

Chorea in IgLON5-Mediated Autoimmune Encephalitis

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IgLON5-associated autoimmunity was first described as a central nervous system disorder with prominent sleep disturbances.[1] Since the initial description, case series of this autoimmune encephalopathy have also reported various movement disorders.[2–4] Here we describe a case of IgLON5-associated autoimmune disease manifesting subacute progressive chorea, intermittent bulbar dysfunction, and sleep disorders.

Case Report

A 58-year-old right-handed Middle-Eastern man presented with an 18-month history of subacute-onset involuntary movements. He described an urge to move his legs at night with progressive worsening and the involvement of his arms, face, and neck along with other new-onset sleep-related issues reported by his wife. These included complex dream enactment, sleepwalking, vocalizations in his sleep, and episodes of severe insomnia as well as brief sleep apneic episodes. Cognitive changes, in the form of short-term memory loss and lack of attention, and anxiety were noticed. Furthermore, symptoms consistent with orthostatic hypotension, cold intolerance, constipation, and headaches were documented. He had developed acute dysarthria and dysphagia that first required the placement of a feeding tube, but spontaneously improved during the course of several weeks. He had a past medical history of type 2 diabetes with associated peripheral neuropathy, hypothyroidism, hypertension, and hyperlipidemia. Social history was unremarkable. On clinical examination, he had mild to moderate dysarthria, unremarkable oculomotor exam, moderate generalized chorea with intact reflexes, motor strength, and sensory exam (Video S1).

Peripheral blood smear, antinuclear antibodies, antiphospholipid, anticardiolipin, antimyeloperoxidase, antithyroid peroxidase, antithyroglobulin antibodies, and a serum paraneoplastic antibodies panel were within normal limits. Cerebrospinal fluid analysis was normal. Imaging studies, including a brain magnetic resonance imaging and whole-body computed tomography scan were unremarkable. The patient's symptoms and progression raised the possibility of a potential autoimmune disorder despite the absence of inflammatory markers in the cerebrospinal fluid or serum. Given the constellation of chorea, sleep-related abnormalities, dysautonomia, and fluctuating bulbar symptoms, we requested anti-IgLON5 antibodies, and the results were positive without a specified titer.[3] At 24 months after symptom onset, the patient was treated with monthly intravenous immunoglobulin 2 g/kg and high-dose oral steroids for 3 months without benefit. He was then started on monthly cyclophosphamide in conjunction with pulse steroid therapy with some subjective improvement. Olanzapine was first introduced to treat chorea, but because of hyperglycemic episodes this was switched to tetrabenazine with a slight improvement of chorea. He completed 6 months of cyclophosphamide therapy and was then lost to follow-up for 7 months. During that period, he had undergone a course of plasmapheresis followed by rituximab. At reevaluation in our institution, generalized chorea was still noted but without clear progression. However, nonmotor symptoms seemed to have worsened, including problematic insomnia, short-term memory loss, and anxiety.

Discussion

We report a case of IgLON5 antibody disease presenting with chorea, subsequently developing fluctuating bulbar dysfunction, dysautonomia, and sleep disorders. This disease is associated with antibodies targeting the extracellular domain of an immunoglobulin-like cell adhesion molecule, IgLON5. Pathologically, there has been suggestion that this is a tau-based disorder, although a more recent case report has challenged this assertion.[5,6] Clinically, it was first reported as a non–rapid eye movement and rapid eye movement parasomnia.[1] Since then, further series and case reports have demonstrated a broad spectrum of clinical manifestations, including different types of movement disorders, such as chorea, dystonia, parkinsonism, and

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progressive supranuclear palsy-like phenotype.[4,7] In a review of 70 published cases, 65% of patients developed a movement disorder,[7] which was 1 of the most common features of the disease after bulbar dysfunction (90%) and gait impairment (70%–75%). Dysautonomia and cognitive impairment were also frequent (40%–65%) in patients. Despite the absence of definitive data on treatment, immunotherapy seems to be the most promising approach, with better outcomes noted with combination therapy, second-line immunotherapy, and in those with human leukocyte antigen (HLA) haplotypes *HLA-DQB1*0501* and *HLA-DRB1*1001*.[3,8] Although there appears to be notable phenotypic heterogeneity to this disease, our patient manifested the majority of the symptoms reported in the literature at some point during his disease, highlighting the importance of continually inquiring about new symptoms. Our case demonstrates the need to consider immune-mediated disorders in patients who present to a movement disorders clinic with sleep issues, dysautonomia, and multiple neuropsychiatric and bulbar complaints. Although more studies are needed to confirm best therapeutic practice, the lack of treatment response in our case may underscore the importance of early immunotherapy in the treatment of patients with IgLON5 autoimmunity.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

S.A.: 1A, 1B, 1C, 2A

H.S.: 1A, 2B

Disclosures

Ethical Compliance Statement: We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. The authors confirm that the approval of an institutional review board was not required. Patient informed consent was obtained.

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References

1. Sabater L, Gaig C, Gelpi E, 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.
2. Simabukuro MM, Sabater L, Adoni T, et al. Sleep disorder, chorea, and dementia associated with IgLON5 antibodies. *Neurol Neuroimmunol Neuroinflamm* 2015;2:e136.
3. Honorat JA, Komorowski L, Josephs KA, et al. IgLON5 antibody: neurological accompaniments and outcomes in 20 patients. *Neurol Neuroimmunol Neuroinflamm* 2017;4:e385.
4. Gaig C, Graus F, Compta Y, et al. Clinical manifestations of the anti-IgLON5 disease. *Neurology* 2017;88:1736–1743.
5. Gelpi E, Hoftberger R, Graus F, et al. Neuropathological criteria of anti-IgLON5-related tauopathy. *Acta Neuropathol* 2016;132:531–543.
6. Erro ME, Sabater L, Martinez L, et al. Anti-IGLON5 disease: a new case without neuropathologic evidence of brainstem tauopathy. *Neurol Neuroimmunol Neuroinflamm* 2020;7.
7. Gaig C, Compta Y. Neurological profiles beyond the sleep disorder in patients with anti-IgLON5 disease. *Curr Opin Neurol* 2019;32:493–499.
8. Cabezudo-Garcia P, Mena-Vazquez N, Estivill Torrus G, Serrano-Castro P. Response to immunotherapy in anti-IgLON5 disease: a systematic review. *Acta Neurol Scand* 2020;141:263–270.

Supporting Information

Supporting information may be found in the online version of this article.

Video S1. Overview of patient's exam prior to immunotherapy demonstrating choreic movements.