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CASE REPORT

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Further insights into anti-IgLON5 disease: a case with complex clinical presentation

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Abstract

Background Anti-IgLON5 disease is an autoimmune encephalitis overlapping with neurodegenerative disorders due to pathological accumulation of hyperphosphorylated tau. It is characterized by several clinical manifestations determined by involvement of different brain areas, and mild response to first-line immunotherapies. We report a case of anti-IgLON5 disease with a multifaceted semiology and an unusually good response to glucocorticoid monotherapy.

Case presentation A 68-year-old man with type 2 diabetes was evaluated for an 8-month history of progressive gait disorder causing frequent falls. He also suffered from obstructive sleep apneas and complained of dysphonia, dysarthria, occasional dysphagia, urinary incontinence, and upper limb action tremor. Neurological examination demonstrated bilateral eyelid ptosis, limitation of ocular horizontal smooth pursuit movements, slow horizontal saccades, and lack of inhibition of the vestibulo-ocular reflex during rapid horizontal head torsions. The patient also displayed involuntary, slow, rhythmic movements of the left periorbital and perioral muscles, spreading to the ipsilateral hemipalate and hemitongue, along with bilateral negative upper limb myoclonus. There were proximal muscle wasting in the upper limbs, proximal weakness of the four limbs, and diffuse fasciculations. Ataxia of stance and gait and of the four limbs was noted. MRI of the brain and spine was unremarkable; nerve conduction studies revealed a chronic, predominantly demyelinating, sensory-motor polyneuropathy, probably due to diabetes. Routine CSF examination was unrevealing and serum GFAP level was 89.6 pg/mL; however, the autoimmunity tests revealed a high-titer positivity for anti-IgLON5 autoantibodies in both CSF and serum, leading to the diagnosis of anti-IgLON5 disease. Symptoms improved significantly after intravenous methylprednisolone.

Conclusions Hemifacial and hemiorolingual myorhythmia along with peculiar oculomotor abnormalities characterizes the multifaceted clinical picture of our case. The complex semiology of our patient may reflect multifocal targeting of the autoimmune process or sequential spreading of tau inclusions in different brain areas. Our patient's optimal response to glucocorticoid monotherapy could be underpinned by a slightly different phenotype in which autoimmunity plays a greater pathogenic role than tauopathy, with a lower burden of tau deposition. In

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such patients, neurodegeneration and tau accumulation could be merely secondary to immune-mediated neuronal dysfunction, supporting the existence of a group of glucocorticoid-responsive patients.

Keywords Anti-IgLON5 disease, Tauopathy, Oculomotor abnormalities, Hemifacial myorhythmia, Glucocorticoids, Immunotherapy

Background

Autoimmune encephalitides are a group of inflammatory brain disorders characterized by the presence of autoantibodies directed against neuronal cell-surface proteins or intracellular antigens. Their annual cumulative incidence is about 3 to 9 cases per 1,000,000 persons, but a high rate of misdiagnosis has been described, highlighting the importance of fulfilling the recently developed diagnostic criteria for autoimmune encephalitides [1–3].

Among them is anti-IgLON5 disease, whose hallmarks are the homonymous antibodies in cerebrospinal fluid (CSF) or serum [4]. Patients with anti-IgLON5 encephalitis usually have a complex neurological clinical picture which does not respond to first-line immunotherapy such as glucocorticoid monotherapy or intravenous immune globulin (IVIG), but requires treatment with second-line or even third-line combination immunotherapies, leading to only slight improvement of symptoms.

We report the case of a patient affected by anti-IgLON5 disease with a multifaceted semiology at the first evaluation, characterized by ataxia, oculomotor abnormalities, and an unusual hemifacial and hemiorolingual myorhythmia. The patient's symptoms responded promptly to glucocorticoid monotherapy.

Case presentation

A 68-year-old man was admitted to our Neurology Department, with an 8-month history of gradually progressive gait disorder, resulting in frequent backward falls (at the time of evaluation about three per week). The patient also complained of hypophonia, dysphonia, mild dysarthria, occasional dysphagia, and urinary urge incontinence. He reported action tremor of the upper limbs for one month. The patient denied experiencing dizziness, strength or sensory deficits, or other neurovegetative disturbances. Furthermore, he reported vivid and unpleasant dreams. Upon inquiry with his wife, we discovered that these dreams had been frequent over the last year, and he had been acting them out.

With regards to his previous medical history, he had type 2 diabetes, hypertension, and benign prostatic hyperplasia (BPH). He had also developed severe obstructive sleep apnea syndrome (OSAS) nearly 18 months before the onset of the gait disorder; thus, he was referred to a pneumologist who prescribed nocturnal continuous positive airway pressure (CPAP) treatment. The patient had no family history of neurological disorders.

On neurological examination, he was oriented to time and place and able to recall autobiographical memories. His speech was hypophonic, dysphonic, and slightly dysarthric, but without any aphasic features. He exhibited bilateral eyelid ptosis, bilateral limitation of ocular horizontal smooth pursuit movements, and increased latency and decreased velocity of the horizontal saccades (Video 1). Additionally, his vestibulo-ocular reflex (VOR) was not inhibited during rapid horizontal head movements, whereas he had neither diplopia nor nystagmus. Notably, he displayed involuntary, slow (~1-Hz), rhythmic, continuous movements of the left periorbital and perioral muscles, spreading to the ipsilateral hemipalate and hemitongue (Video 2). While the palatal component resembled palatal myoclonus, the whole pattern of movements of the cranial segment was consistent with hemifacial and hemiorolingual myorhythmia [5]. Furthermore, bilateral negative myoclonus of the upper limbs was observed (Video 3), with moderate bilateral proximal muscle wasting in the upper limbs, affecting the deltoid, *pectoralis major*, and *biceps brachii* muscles. Muscle strength testing revealed mild symmetrical proximal weakness of the four limbs (Medical Research Council (MRC) grade: deltoids and iliopsoas 4 bilaterally) with diffuse fasciculations in all extremities. Deep tendon reflexes (DTRs) in the upper limbs were normal, as was the right patellar reflex, while the left patellar and both ankle reflexes were absent. Cutaneous plantar responses were flexor bilaterally. Ataxia of the trunk and of the four limbs was noted (Video 4), along with bilateral upper-limb action tremor, marked unsteadiness, a wide-based gait, and a high risk of backward falls; symptoms did not worsen with eye closure. Lastly, vibration sense was moderately reduced at the ankles.

Routine blood chemistries revealed no significant abnormalities, and serum VDRL was negative. Neuropsychological testing demonstrated amnestic multidomain mild cognitive impairment (aMCImd). The patient underwent contrast-enhanced MRI of the brain and whole spine, which only displayed multiple disc protrusions and lumbar spinal stenosis at L4-L5 level. Electroencephalography (EEG) revealed a background alpha rhythm without epileptiform activity. Needle electromyography (EMG) of the four limbs and bulbar segment suggested a chronic, predominantly demyelinating, sensorimotor polyneuropathy, with greater expression in the lower extremities. Finally, he also underwent

polysomnography (PSG), which showed mildly elevated indices of apnea-hypopnea and oxygen desaturation.

Considering the rapid worsening of the symptoms (8-month history) and the multisystemic neurological involvement, we first hypothesized an autoimmune encephalitis, possibly of paraneoplastic origin, in view of the patient's age. Therefore, the patient underwent a whole-body contrast-enhanced CT scan, which only revealed a small parenchymal nodule in the lower lobe of the right lung, with apparent inflammatory features. Consequently, we initiated oral antibiotics (amoxicillin clavulanate 875/125 mg every 8 h for 10 days plus azithromycin 500 mg per day for 3 days). On repeat chest CT scan one month later, regression of the nodule was noted, leading us to conclude that it was infectious in origin.

In the subsequent days, a lumbar puncture was performed to identify autoantibodies associated with autoimmune and paraneoplastic encephalitides; cell count, glucose and protein concentrations were within the normal range. As for CSF neurodegeneration biomarkers, Aβ42 was in the lower normal range (621 pg/mL; reference values, >599 pg/mL), while the Aβ42/Aβ40 ratio was normal (0.099; reference values, >0.069), as well as P-tau181 (21.7 pg/mL; reference values, <56.5 pg/mL) and total tau (T-tau; 188 pg/mL; reference values, <404 pg/mL). The autoimmunity tests (performed with a cell-based assay, CBA) revealed a high-titer positivity for anti-IgLON5 autoantibodies in both CSF and serum, leading to a diagnosis of anti-IgLON5 disease. Finally, the serum concentration of glial fibrillary acidic protein (GFAP), quantified by single-molecule array (Simoa) technology, was 89.6 pg/mL. A summary of the patient's clinical features and CSF and instrumental findings is provided in Tables 1 and 2, respectively.

Table 1 Clinical features of the patient

Features	Specifics
Age at onset (y)	68
Sex	M
Education (y)	5
Disease duration at first evaluation (m)	8
Brainstem signs	Hypophonia
	Dysphonia
	Dysarthria
	Dysphagia
	Hemifacial and hemiorolingual myorhythmia
	Impairment of ocular horizontal smooth pursuit
	Slow horizontal saccades
	Lack of inhibition of the horizontal VOR
Cerebellar signs	Trunk and limb ataxia
	Action tremor of the upper limbs
PNS signs	Proximal upper limb muscle wasting
	Proximal symmetric muscle weakness
	Diffuse fasciculations
	Absent left patellar and bilateral Achilles reflexes
	Reduced vibration sense in the lower limbs
Other signs	OSA
	Snout reflex and brisk jaw jerk
	Bilateral negative myoclonus
	Postural tremor of the upper limbs
	Urinary urge incontinence
	MCI (formal neuropsychological testing)

m months; *M* male; *MCI* mild cognitive impairment; *OSA* obstructive sleep apnea; *PNS* peripheral nervous system; *VOR* vestibulo-ocular reflex; *y* years

Given the autoantibody finding, we started therapy with IV methylprednisolone (1000 mg daily for 5 days). At the conclusion of treatment, which had been well tolerated, we noted a significant improvement of stance, gait and limb ataxia. The patient reported only one fall in the subsequent two months: the marked decrease in frequency of falls significantly ameliorated his quality of life. Moreover, there was an increase in voice volume. Lastly, all the oculomotor abnormalities had slightly improved in both speed and amplitude. The other neurological symptoms and signs remained unchanged.

Discussion and conclusions

Anti-IgLON5 disease is characterized by a wide spectrum of clinical manifestations, the most common being sleep disorder, bulbar symptoms, gait disturbance, oculomotor abnormalities, and cognitive impairment [6]. Our patient had a multifaceted clinical picture. Indeed, hypophonia, dysphonia, dysarthria and dysphagia suggest bulbar impairment. However, other structures of the brainstem should also be considered in this case, given the presence of slow horizontal saccades, impairment of horizontal smooth pursuit, and lack of inhibition of horizontal VOR. These findings could indicate a lesion of the paramedian pontine reticular formation (PPRF) and the vestibular nuclei bilaterally. The anatomical substrate of hemifacial and hemiorolingual myorhythmia is ill-defined: it might be due to dysfunction of subcortical structures such as the Guillain-Mollaret triangle (similarly to palatal myoclonus) and/or disinhibition of other brainstem circuits [5, 7]. Ataxia that does not worsen with eye closure and is accompanied by action tremor suggests involvement of cerebellar circuits. Proximal upper-limb wasting, weakness, and diffuse fasciculations could be attributed either to peripheral neuropathy or to lower motor neuron impairment. The concurrent reduction in lower-limb vibration sense may be explained by an underlying polyneuropathy, in turn secondary to diabetes. Furthermore, urinary urgency could be attributed to dysautonomia related to IgLON5 disease rather than to BPH, considering its recent development over the last

Table 2 CSF and instrumental findings of the patient

Investigation	Specifics
Imaging	
Brain MRI with gadolinium	No abnormalities, except for point-like paramagnetic deposition in the right cerebral peduncle
Spine MRI with gadolinium	Disc protrusions between C3-C4, C6-C7, D11-D12, D12-L1, L3-L4, L5-S1 + L4-L5 spinal stenosis
Whole-body CT scan with IV contrast material	Parenchymal nodule in the lower lobe of the right lung, with possible inflammatory features
CSF	
Lymphocytes (number/μL)	0.6
Protein (mg/dL)	59.5
Glucose (mg/dL)	76
Anti-IgLON5 autoantibodies	High titer (also in serum)
Aβ40 (pg/mL)	6301
Aβ42 (pg/mL)	621 (cut-off: ≥ 599)
Aβ42/Ab40 ratio	0.099 (cut-off: ≥ 0.069)
T-tau (pg/mL)	188 (cut-off: ≤ 404)
P-tau181 (pg/mL)	21.7 (cut-off: ≤ 56.5)
Serum GFAP (pg/mL)	89.6
EEG	Background 10-Hz alpha rhythm
EMG	Marked chronic predominantly demyelinating sensory-motor polyneuropathy
Videofluoroscopy	Dysphagia for liquids, aspiration, no cough reflex
Neuropsychological testing	MCI involving working memory, constructional praxis, long-term visual-spatial memory and set-shifting abilities
Polysomnography	Performed during CPAP (12–16 cmH_2O). Mild obstructive and central episodes of desaturation and occasional mild tonic hypoxemia independent of mechanical ventilatory changes. Total AHI = 13.3/h, supine AHI = 13.3/h, ODI = 14.7/h, average SpO2 = 92.9% and lowest SpO2 = 80.0%

AHI apnea-hypopnea index; *CPAP* continuous positive airway pressure; *CSF* cerebrospinal fluid; *CT* computed tomography; *EEG* electroencephalography; *EMG* electromyography; *GFAP* glial fibrillary acidic protein; *IV* intravenous; *MCI* mild cognitive impairment; *MRI* magnetic resonance imaging; *ODI* oxygen desaturation index; *P-tau181* phosphorylated tau (at residue 181); *SpO2* oxygen saturation of peripheral blood; *T-tau* total tau

few months and its temporal association with other neurological symptoms. Finally, our patient's vivid dreams could reflect rapid eye movement (REM) sleep behavior disorder (RBD).

It is worth noting that the patient had been diagnosed with OSAS and started CPAP 18 months before the onset of the gait disorder. Indeed, approximately 68% of patients with anti-IgLON5 disease exhibit a sleep disorder with parasomnia and sleep breathing difficulty at their initial evaluation, with most eventually developing it, as observed in our patient, who also reported vivid dreams [6]. This strengthens our hypothesis that his sleep disorder with OSAs may not have been unrelated, but rather likely represented the first manifestation of anti-IgLON5 disease. Indeed, it is not uncommon for patients with this disorder to develop OSAS before other neurological symptoms manifest [5, 8].

Although many of our patient's symptoms, such as sleep disturbances, followed by gait impairment, ataxia, oculomotor disturbances, dysautonomia and MCI may be seen in patients with multiple system atrophy (MSA), progressive supranuclear palsy (PSP), and multi-infarct dementia, there are some red flags that prompted us to look for an autoimmune disorder. Considering the diagnostic criteria for autoimmune encephalitides developed by Graus and coworkers, our patient met the criteria for a possible autoimmune encephalitis, according to which further investigations should be done to reach higher levels of diagnostic accuracy [1]. Indeed, our patient had a subacute onset of working memory deficits (highlighted by neuropsychological testing), new focal CNS findings (especially brainstem and cerebellar signs), and reasonable exclusion of alternative causes. Beyond fulfilling these criteria, other important red flags for an autoimmune encephalitis were the rapid worsening of the symptoms and the multisystemic neurological involvement. Additionally, the patient's age should raise suspicion for a paraneoplastic origin of the disorder. Moreover, the absence of midbrain atrophy or pontine signal alterations did not support the diagnoses of PSP and MSA, respectively; autonomic dysfunction is not typical of PSP, and the hemifacial and hemiorolingual myorhythmia is not described for PSP nor for MSA. Finally, our patient underwent a brain MRI, which did not show signs of previous subcortical ischemic infarctions, thus ruling out the hypothesis of multi-infarct dementia. All these

considerations, along with the unremarkable instrumental findings except for antibody examinations, led us to hypothesize that the autoimmune disorder was the most probable diagnosis.

In view of the hemifacial and hemiorolingual myorhythmia, other differential diagnoses might have been taken into consideration, such as Whipple's disease. In fact, although it is not properly the typical oculomasticatory myorhythmia (OMM), a virtually pathognomonic sign of CNS Whipple's disease, orolingual myorhythmia has some features in common with OMM [9]. Moreover, Whipple's disease could be hypothesized also due to the subacute onset and other neurological signs and symptoms, such as bilateral ptosis, oculomotor dysfunction (however, the most typical sign would be supranuclear vertical gaze palsy), and cognitive impairment [9, 10]. Myorhythmia of facial and cranial muscles is also seen in the following conditions: cerebrovascular diseases (i.e. ischemic and hemorrhagic strokes of the brainstem, the Guillain-Mollaret triangle and the thalamus); autoimmune disorders such as anti-N-methyl-D-aspartate (NMDA) receptor encephalitis, encephalitis associated with celiac disease, Hashimoto's encephalopathy; iatrogenic causes (e.g., phenytoin intoxication and chronic treatment with α-interferon 2a); and von Economo's encephalitis lethargica. Moreover, hemifacial and hemiorolingual myorhythmia can be caused by every lesion in the aforementioned neural circuits, such as demyelinating plaques due to multiple sclerosis and cerebellar degeneration secondary to alcoholism [7]. Hemifacial and hemiorolingual myorhythmia also needs to be differentiated from other movement disorders, such as palatal myoclonus, facial myokymia, hemifacial spasm, tics and the so-called "rabbit syndrome", all of which may be due to several underlying causes [7]. However, the finding of anti-IgLON5 autoantibodies in both CSF and serum, along with the negativity of anti-NMDA receptor autoantibodies in both fluids, thyroid function tests within the normal range, and the absence of both iatrogenic causes and a history of alcoholism, led us to rule out these alternative hypotheses. Regarding CSF analysis, no inflammatory changes were observed, which was consistent with their relatively low prevalence (37%) reported in the literature [11]. P-tau levels were also normal; this finding was also in line with a previous investigation, despite the pathological accumulation of P-tau in this disease [11]. As regards serum GFAP concentration, higher values could have been expected, considering the slowly progressive disease onset (>4 weeks) and the generalized phenotype [11]. However, the relatively low GFAP level (89.6 pg/mL) may be in agreement with our patient's optimal response to glucocorticoid monotherapy, as further discussed below.

Furthermore, from a pathophysiological perspective, the known association between anti-IgLON5 disease and the presence of both HLA-DRB1*10:01 and HLA-DQB1*05:01 alleles highlight the importance of autoimmunity in the pathogenesis of anti-IgLON5 disease [6, 12]. However, it is well-known that its pathogenesis is not solely mediated by immune mechanisms: considering the autopsy study by Gelpi and coworkers on six patients affected by anti-IgLON5 disease, subcortical deposits of hyperphosphorylated tau are also observed, especially in the tegmental brainstem nuclei and the hypothalamus, but also in the hippocampus, reticular formation, vestibular nuclei, entorhinal cortex, cerebellar cortex, and dentate nucleus (part of the Guillain-Mollaret triangle), reflecting neurodegeneration and correlating well with the clinical manifestations of our patient [13]. Furthermore, in a more recent autopsy study, Berger-Sieczkowski and colleagues also investigated inflammatory markers in nine patients with anti-IgLON5 disease [14]. They found out a marked microglia activation in the tegmentum of the bulbar region, nucleus olivaris, and cerebellar cortex, with a specific and extensive deposition of IgG4 in the neuropil of the brainstem tegmentum, pontine base, olivary nucleus, hippocampus, and cerebellar cortex; however, there were only mild to moderate inflammatory infiltrates of T and B cells in the brainstem [14]. Accordingly, the complex semiology of our patient with symptoms appearing sequentially (chronologically: (1) OSAS; (2) RBD; (3) trunk and limb ataxia; (4) oculomotor abnormalities, bulbar symptoms such as dysphonia, hemifacial and hemiorolingual myorhythmia, urinary urge incontinence, and aMCImd) might reflect multifocal targeting of the autoimmune process or sequential spreading of tau inclusions to different brain areas, typical of neurodegenerative disorders – especially tauopathies [15]. In the literature it has not yet been defined which is the primary trigger of anti-IgLON5 disease, whether the autoimmune process or the tauopathy; consequently, some authors advocate that neuroinflammation precedes neurodegeneration, whereas others hypothesize that either the immunological response is only a secondary event or that, at least, tau deposition exacerbates the autoimmune process [4, 6, 13]. However, an experimental study has suggested that anti-IgLON5 autoantibodies determine neurodegeneration and cell death in human neurons, supporting their role as a primary trigger in the disease: indeed, in neurons derived from both human neural stem cells (hNSCs) and human-induced pluripotent stem cells (hiPSCs), the content of P-tau was higher in cultures exposed to IgG from a patient with anti-IgLON5 antibodies [16]. There exist even cases of anti-IgLON5 disease without any neuropathologic evidence of brainstem tauopathy [17]. All these findings suggest that tau pathology might be a marker of the irreversible stage

of the disease [18]. Accordingly, a higher burden of tau pathology may be one of the main reasons underlying the inadequate response of many patients with anti-IgLON5 disease to first-line immunotherapy, such as glucocorticoids, as reported in the literature. However, at variance from the common view, our patient's condition improved remarkably with glucocorticoid monotherapy, suggesting that in certain patients it might be worth initiating first-line immunotherapies with lower systemic impact [4]. Cases who promptly respond to glucocorticoids might even represent a different form of the disease in which the inflammatory-autoimmune process plays a greater role than tauopathy in disease pathogenesis, with a lower burden and progression rate of tau deposition. Therefore, in these glucocorticoid-responsive patients, neurodegeneration and tau accumulation could be merely secondary to immune-mediated neuronal dysfunction [4, 19]. Usually, patients with anti-IgLON5 encephalopathy have a poor prognosis, with a high mortality rate; in most patients, the causes of death include central hypoventilation, aspiration pneumonia due to dysphagia, and sometimes sudden death as a consequence of laryngospasm [4]. Furthermore, the work of Nissen and Blaabjerg showed that patients receiving no treatment or systemic corticosteroid monotherapy had a higher mortality than those who underwent combination therapies [20]. Nevertheless, this is not a rule, as our case demonstrates. The last follow-up of our patient was 33 days after the ending of the treatment, and he was neurologically stable, thus confirming a significant improvement of his symptoms, as previously described. Further studies, ideally randomized controlled trials (RCTs), will be required to investigate the biological underpinnings supporting the different therapeutic response in this group of patients with anti-IgLON5 disease.

Finally, our case underscores the significance of meticulously investigating a patient's sleep history during medical interviews. More in general, given the multifaceted manifestations of anti-IgLON5 disease, we suggest maintaining a low threshold of diagnostic suspicion for this disease entity in the presence of a complex pattern of neurological disturbances.

Abbreviations

aMCImd	Amnestic multi-domain mild cognitive impairment
BPH	Benign prostatic hyperplasia
CPAP	Continuous positive airway pressure
CSF	Cerebrospinal fluid
CT	Computed tomography
DTRs	Deep tendon reflexes
EEG	Electroencephalography
EMG	Needle electromyography
GFAP	Glial fibrillary acidic protein
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MSA	Multiple system atrophy
NMDA	N-methyl-D-aspartate
OSA	Obstructive sleep apnea
PPRF	Paramedian pontine reticular formation
PSG	Polysomnography
PSP	Progressive supranuclear palsy
P-tau181	Phosphorylated tau (at residue 181)
RBD	REM sleep behavior disorder
RCT	Randomized controlled trial
REM	Rapid eye movement
T-tau	Total tau
VOR	Vestibulo-ocular reflex

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-024-03837-3.

Supplementary Material 1: **Video 1.** Oculomotor disturbances, with bilateral limitation in the ocular horizontal smooth pursuit, plus increased latency and decreased speed of the horizontal saccades.

Supplementary Material 2: **Video 2.** Hemifacial myorhythmia, consisting in slow, rhythmic, continuous movements of the left periorbital and perioral muscles, spreading to the ipsilateral palate and hemitongue.

Supplementary Material 3: **Video 3.** Negative myoclonus of both upper limbs with irregular jerks.

Supplementary Material 4: **Video 4.** Ataxia of the upper limbs, shown as dysmetria in the finger-to-finger test; gait ataxia, with widening of the base and postural instability.

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Author contributions

S.P. wrote the manuscript. S.P. and F.V. performed a review of the literature. S.P. and F.V. edited the videos. A.D.G. performed measurements of neurochemical biomarkers. F.A. provided autoantibody data. F.V., A.M., S.M., L.M., C.M. and N.T. were involved in clinical decision making and patient care. F.G. supported the author and the first co-author in the pathophysiological interpretation of clinical data. All authors reviewed the manusctipt.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of IRCCS Istituto Auxologico Italiano (project DAMARE, code 2021_05_18_04). The study is in accordance with the declaration of Helsinki. The patient provided consent to publication of the case.

Consent for publication

Written informed consent was acquired from the patient described within the present study.

Consent to publish

The wife (caregiver) of the patient provided written informed consent to publish on his behalf.

Competing interests

The authors declare no competing interests.

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