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Septin-5 IgG-associated cerebellar ataxia without prominent nystagmus at presentation: a case report

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Abstract

Septin-5 IgG-associated cerebellar ataxia may be overlooked when prominent nystagmus is absent at presentation. We report a 69-year-old man with more than one month of persistent dizziness, gait and limb ataxia, and mild dysarthria, without prominent nystagmus at presentation. Magnetic resonance imaging showed no cerebellar structural lesion, signal abnormality, or atrophy. A cell-based assay detected serum Septin-5 IgG at 1:320, whereas cerebrospinal fluid Septin-5 IgG was negative. The other seven serum cerebellar antibodies and paraneoplastic antibody testing were negative. Additional testing for mGluR1 and GAD65 antibodies was negative. Methylprednisolone followed by oral prednisone and mycophenolate mofetil was associated with marked improvement within two weeks. The patient discontinued maintenance treatment after approximately one month. At one year, he remained independently ambulant without recurrent dizziness or dysarthria, although tandem gait was impaired and fine gaze-evoked nystagmus was detectable. Cerebellar imaging remained normal, and serum antibody reactivity had declined to 1:10. Prominent nystagmus should not be a prerequisite for investigating Septin-5 autoimmunity. A clinically localized subacute cerebellar syndrome warrants consideration of the disease even when cerebrospinal fluid antibody testing is negative and conventional imaging is normal.

Introduction

Autoimmune cerebellar ataxia is an important cause of acquired incoordination because neurological dysfunction may improve with immunotherapy. Septin-5 IgG, first described in 2018, identifies a rare phenotype ranging from a predominantly cerebellar syndrome to severe ataxia with additional neurological or psychiatric manifestations [1, 2]. Detailed reports have emphasized oscillopsia, nystagmus, and other conspicuous ocular motor abnormalities, often with antibodies detected in both serum and cerebrospinal fluid (CSF) [3, 4, 5]. This recognizable presentation has helped define the disease, but it can also narrow clinical suspicion.

We describe subacute cerebellar ataxia without prominent nystagmus at presentation. Serum Septin-5 IgG supported the diagnosis despite negative CSF antibody testing and normal conventional cerebellar imaging. Substantial early improvement and sustained function at one year demonstrate the clinical value of recognizing this presentation. We place the case alongside published reports to show why an inconspicuous ocular examination should not prevent antibody investigation when gait, limb, and speech findings establish cerebellar localization.

Case Report

Patient Presentation and Clinical Findings

A 69-year-old man was referred after more than one month of persistent dizziness and progressive unsteadiness. He described a heavy-headed, predominantly non-spinning sensation and a feeling of walking on cotton wool. Neck stiffness accompanied the symptoms, and pressure over the right occipital region aggravated the dizziness. Symptomatic treatment at several previous consultations had provided no

meaningful relief. His medical history included hypertension for two years, treated with nifedipine. There was no reported family history of ataxia.

He was alert and fully oriented, with preserved comprehension and no hallucinations. Recent recall and calculation were reduced; the Mini-Mental State Examination score was 26/30. Speech was mildly dysarthric. Bilateral finger–nose and heel–shin testing showed dysmetria, standing was unstable with both eyes open and closed, and tandem gait was impaired. Deep sensation, limb power, and muscle tone were preserved. The pharyngeal reflex was normal, and no other cranial nerve abnormality was recorded. Prominent nystagmus was absent at the initial examination. No autonomic dysfunction was reported. The combination of dysarthria, appendicular dysmetria, and gait incoordination established cerebellar localization.

Diagnostic Assessment

Previous computed tomography had shown minor ischemic changes and mild cerebral atrophy. Magnetic resonance angiography demonstrated mild stenosis of the right posterior cerebral artery P2 segment. Brain magnetic resonance imaging (MRI) showed no cerebellar structural lesion, abnormal T2 signal, or atrophy (Fig. 1d–f). Electromyography was unremarkable. Transcranial Doppler examination reported reduced flow velocities in the vertebral and basilar arteries, without a matching cerebellar lesion on MRI.

CSF opening pressure was 75 mm H2O. Total protein was 0.46 g/L, just above the laboratory reference range of 0.15–0.45 g/L. An eight-antibody panel for autoimmune cerebellar ataxia, using a transfected cell-based assay, detected serum Septin-5 IgG at a dilution of 1:320; testing for the same antibody in CSF was negative. The other seven serum antibodies, Homer3, ATP1A3, RGS8, GluRδ2, Sez6L2, Rab6A, and Rab6B IgG, were negative. Additional testing for mGluR1 and GAD65 antibodies was negative. Serum assay images and positive and negative controls are shown in Fig. 1a–c. Thyroid function and thyroid antibodies, antinuclear antibody testing, vasculitis screening, erythrocyte sedimentation rate, and creatine kinase were unremarkable. Additional laboratory findings are summarized in Online Resource 1.

The subacute cerebellar syndrome and antigen-specific serum reactivity supported a diagnosis of Septin-5 IgG-associated cerebellar ataxia. The mild vascular abnormalities did not provide an anatomical explanation for bilateral limb and gait incoordination. Dedicated paraneoplastic antibody testing was negative. Whole-body positron emission tomography/computed tomography (PET/CT) was not performed because of financial constraints.

Therapeutic Intervention

Therapeutic Intervention
Methylprednisolone was started at an initial dose of 250 mg and subsequently reduced, followed by oral prednisone. Mycophenolate mofetil was added for maintenance immunosuppression. The planned outpatient regimen included prednisone 20 mg/day for at least three months. The treatment sequence and reported clinical landmarks are presented in Table 1 and Fig. 1g.

Table 1
Clinical course of the present patient

Time point	Clinical findings	Antibody and imaging findings	Treatment
Presentation	Persistent dizziness; dysarthria; bilateral limb and gait ataxia; no prominent nystagmus	Serum Septin-5 IgG 1:320; seven other serum cerebellar antibodies negative; mGluR1 and GAD65 antibodies negative; CSF Septin-5 IgG negative; paraneoplastic antibody testing negative; CSF protein 0.46 g/L; cerebellar MRI normal	Methylprednisolone initially 250 mg, then reduction and oral prednisone; MMF added
Two weeks	Dizziness markedly improved; dysarthria resolved; finger–nose accurate; tandem walking possible	No repeat antibody result reported at this landmark	Oral prednisone 20 mg/day planned for ≥ 3 months; MMF maintenance
About one month of oral maintenance	Patient felt substantially better	No assessment documented at the time of stopping treatment	Patient stopped prednisone and MMF on his own
One year	Independent walking; no recurrent dizziness or dysarthria; impaired tandem gait; fine gaze-evoked horizontal nystagmus; no downbeat nystagmus	Serum Septin-5 IgG 1:10; no cerebellar MRI signal abnormality or atrophy	Clinical stability after self-discontinuation; residual examination findings persisted

Time points are reported relative to presentation or the start of oral maintenance, as specified. CSF cerebrospinal fluid; IgG immunoglobulin G; MMF mycophenolate mofetil; MRI magnetic resonance imaging. The 1:10 follow-up result denotes residual reactivity.

Results

Early Clinical Response

Within two weeks, dizziness had substantially improved and dysarthria had resolved. Finger–nose testing became accurate, and tandem walking was possible. A weakly positive Romberg sign persisted with the eyes closed. The improvement involved both the patient's presenting symptoms and directly observed cerebellar signs.

One Year Follow-up

After approximately one month of oral maintenance therapy, the patient stopped prednisone and mycophenolate mofetil on his own because he felt substantially better. At one year, he remained clinically stable, reported no recurrent dizziness, had no dysarthria, and walked independently. Tandem gait remained impaired. Rightward gaze elicited fine left-beating horizontal nystagmus; downbeat nystagmus was absent. Repeat MRI again showed no cerebellar signal abnormality or atrophy. Serum Septin-5 IgG reactivity had

declined from 1:320 to 1:10. Follow-up documented sustained functional improvement with residual tandem gait and ocular motor signs.

Discussion

Cerebellar Ataxia Without Prominent Initial Nystagmus

The distinguishing feature of this case is a definite cerebellar syndrome without prominent nystagmus at presentation. Dysarthria and bilateral appendicular and gait ataxia established localization, while CSF antibody negativity and normal MRI added further diagnostic challenges. Dizziness and imbalance in this setting can be attributed to peripheral vestibular disease or incidental vascular findings, obscuring an acquired cerebellar disorder. Fine gaze-evoked nystagmus was documented at one year, emphasizing that the diagnostic challenge concerned the initial presentation. A complete cerebellar examination should therefore guide antibody investigation even when ocular motor findings are inconspicuous.

In the expanded series, seven of eight patients had prominent eye movement disorders [2]. This category encompasses oscillopsia, abnormal pursuit, square-wave jerks, and nystagmus, which describe different ocular symptoms and signs. The present case draws attention to a cerebellar presentation with inconspicuous initial nystagmus. Gait and limb ataxia together with dysarthria established cerebellar localization and guided antibody investigation. The fine gaze-evoked nystagmus recorded at one year adds a longitudinal ocular motor finding to this presentation.

Clinical Spectrum in Published Reports

The discovery series, its later clinical extension, and detailed individual reports provide the main clinical descriptions of Septin-5 autoimmunity [1, 2, 3, 4, 5]. Table 2 compares the available individual case descriptions, while Table 3 presents source-specific clinical, imaging, and outcome frequencies. In the largest series, all eight patients with Septin-5 IgG had cerebellar ataxia, seven had prominent eye movement disorders, and two had coexisting Septin-7 IgG [2]. One of the latter developed apathy, emotional blunting, and poor insight. The original four clinically characterized patients also illustrate vestibular onset, oscillopsia, tremulousness, and subsequent encephalopathy [1]. Thus, the disorder is cerebellar-predominant but not uniformly limited to motor coordination.

Table 2
Individual clinical descriptions of Septin-5 IgG associated cerebellar ataxia

Report and patient	Cerebellar and other features	Ocular findings	Serum / CSF Septin-5 IgG	Cerebellar imaging	Treatment and outcome
Honorat 2018, P2 [1] F, 60	Vestibular onset with vertigo and vomiting → gait ataxia	Nystagmus NR	Positive / positive	Normal	Spontaneous improvement; independent; mRS 0 at 77 months
Honorat 2018, P3 [1] M, 62	Ataxia; truncal/limb myoclonus → encephalopathy	Prominent eye movement disorder	Positive / positive	NR	Treatment and outcome NR; follow-up 1 month
Honorat 2018, P4 [1] F, 59	Rapid spinocerebellar syndrome; tremulousness	Nystagmus NR	Positive / positive	NR	Oral corticosteroid and PLEX; initial improvement; death at 6 months
Honorat 2018, P5 [1] M, 47	Headache → subacute ataxia	Prominent oscillopsia	Positive / unavailable	Vermian atrophy	IVMP then IVIG; independent with residual ataxia; mRS 1 at 54 months
San Martin 2021 [3] M, 58	Gait ataxia; no dysarthria or appendicular dysmetria	Oscillopsia; downbeat and gaze-evoked nystagmus; ptosis	Positive / positive	Unremarkable	Corticosteroids, IVIG, CYC, RTX; minimal improvement
Wischmann 2023 [4] F, 54	Gait, limb, truncal ataxia; dysarthria; depression/behavioral change	Upbeat nystagmus; saccadic pursuit; oscillopsia	1:10,000 / 1:320	Normal brain/spinal MRI	Corticosteroids, PLEX, RTX, then bortezomib-containing treatment; moderate sustained improvement

Sources: Honorat et al. [1], Herrero San Martin et al. [3], Wischmann et al. [4], and Nijim et al. [5]. H18 patient labels preserve the discovery report numbering. Individual reports and the expanded series are summarized separately because cases may overlap. NR denotes unreported or unavailable information. The 2022 series is summarized using its original denominators in Table 3. Oscillopsia denotes a visual symptom; nystagmus denotes an ocular motor sign. CYC cyclophosphamide; F female; IVIG intravenous immunoglobulin; IVMP intravenous methylprednisolone; M male; MMSE Mini-Mental State Examination; mRS modified Rankin Scale; PLEX plasma exchange; RTX rituximab.

Report and patient	Cerebellar and other features	Ocular findings	Serum / CSF Septin-5 IgG	Cerebellar imaging	Treatment and outcome
Nijim 2024 [5] M, 53	Post-COVID-19 ataxia; dysarthria; diplopia; facial weakness	Horizontal nystagmus; square-wave jerks; exotropia	Positive / positive	No explanatory cerebellar lesion; nonspecific extracerebellar foci	IVMP, IVIG, PLEX, RTX, CYC, later MMF; partial improvement; wheelchair at 31 months
Present case M, 69	Dizziness; gait and limb ataxia; dysarthria; MMSE 26/30	No prominent initial nystagmus; fine horizontal nystagmus at one year	1:320 / negative	No cerebellar lesion, abnormal T2 signal, or atrophy; unchanged at one year	Corticosteroids and MMF; marked improvement by 2 weeks; independent at one year

Sources: Honorat et al. [1], Herrero San Martin et al. [3], Wischmann et al. [4], and Nijim et al. [5]. H18 patient labels preserve the discovery report numbering. Individual reports and the expanded series are summarized separately because cases may overlap. NR denotes unreported or unavailable information. The 2022 series is summarized using its original denominators in Table 3. Oscillopsia denotes a visual symptom; nystagmus denotes an ocular motor sign. CYC cyclophosphamide; F female; IVIG intravenous immunoglobulin; IVMP intravenous methylprednisolone; M male; MMSE Mini-Mental State Examination; mRS modified Rankin Scale; PLEX plasma exchange; RTX rituximab.

Table 3
Reported clinical characteristics and outcomes with original denominators

Source and population	Reported finding	n/N (%)
Hinson 2022 [2]	Cerebellar ataxia	8/8 (100.0)
Hinson 2022 [2]	Prominent eye movement disorder	7/8 (87.5)
Hinson 2022 [2]	Coexisting Septin-7 IgG	2/8 (25.0)
Hinson 2022 [2]	Additional psychiatric phenotype	1/8 (12.5)
Honorat 2018 [1]	Vestibular onset with vertigo/nausea/vomiting	1/4 (25.0)
Honorat 2018 [1]	Oscillopsia at onset	2/4 (50.0)
Honorat 2018 [1]	Accompanying tremulousness	2/4 (50.0)
Honorat 2018 [1]	Later encephalopathy	1/4 (25.0)
Hinson 2022 [2]	Normal MRI among cases with imaging information	4/7 (57.1)
Hinson 2022 [2]	Focal cerebellar atrophy on MRI	2/7 (28.6)
Hinson 2022 [2]	Focal cerebellar FDG hypermetabolism on PET	1/7 (14.3)
Hinson 2022 [2]	Improvement during immunotherapy among reported outcomes	4/6 (66.7)
Hinson 2022 [2]	Spontaneous improvement among reported outcomes	1/6 (16.7)
Hinson 2022 [2]	Death among reported outcomes	1/6 (16.7)

Honorat 2018 describes four clinically characterized patients from six antibody-positive individuals [1]. Hinson 2022 contains eight Septin-5 cases; imaging information was available in seven and outcomes in six [2]. Reports from overlapping clinical experience are presented separately. Imaging categories describe the seven reported imaging observations. Outcome percentages use all six available outcomes. Exact 95% confidence intervals appear in Online Resource 1. The published aggregate eye movement category is broader than nystagmus, and paired specimen availability is recorded in Table 2.

The literature also contains clinically useful contrasts. The 2021 patient had marked ocular symptoms and gait ataxia without dysarthria or appendicular dysmetria [3]. The 2023 patient had severe gait, limb, and truncal ataxia with upbeat nystagmus and psychiatric symptoms [4]. The 2024 patient developed a disabling syndrome after COVID-19 and remained substantially impaired despite extended treatment [5]. Together, these reports define a spectrum of appendicular, ocular, and neuropsychiatric involvement. The discovery and expanded series arose from the same diagnostic program, and potential overlap with later reports prevents their simple addition into an independent pooled case count.

Negative CSF Antibody Testing and Serum Reactivity

The serum-positive, CSF-negative result adds a paired-specimen finding to the clinical spectrum described in earlier detailed cases, in which paired positivity was commonly reported [1, 3, 4, 5]. Our patient underwent testing in both compartments: serum Septin-5 IgG was detected at 1:320, while the CSF result was negative. Table 2 records specimen availability separately, including the unavailable CSF result in one original case [1].

A negative CSF antibody assay can therefore accompany a compatible cerebellar syndrome with serum Septin-5 IgG. Paired serum and CSF investigation characterizes the antibody distribution in the individual patient and supports the interpretation of antigen-specific reactivity alongside the clinical findings. In this patient, the observed serum reactivity, bilateral cerebellar signs, and subsequent clinical course formed a concordant diagnostic pattern. The negative CSF finding describes antibody detection in that specimen under the assay conditions.

Serum reactivity is interpreted in the context of the clinical syndrome and the assay used. The original studies combined tissue-based screening with antigen-specific confirmation to characterize septin autoimmunity [1, 2]. Laboratory platform, specimen timing, and dilution thresholds provide the context for comparing serum and CSF results. In this case, a transfected cell-based assay identified serum Septin-5 IgG. The decline in serum reactivity from 1:320 to 1:10 accompanied clinical improvement over one year, providing longitudinal concordance. Clinical recovery coexisted with residual serum reactivity at follow-up.

Cerebellar Dysfunction with Normal Structural Imaging

Normal cerebellar MRI at presentation and one year is an integral feature of the case. It documents persistent absence of a visible cerebellar lesion despite an initially convincing cerebellar examination. In the expanded Septin-5 series, four of seven patients with imaging information had normal MRI, two had focal cerebellar atrophy, and one had a focal FDG-PET abnormality [2]. Figure 2 displays these observations alongside the clinical phenotype. The denominator is patients with imaging information, rather than seven uniformly examined MRI scans.

The clinical and imaging pattern is consistent with reversible cerebellar network dysfunction. Septin-5 participates in synaptic vesicle regulation, and experimental work with IgG from septin-autoimmune patients demonstrated neuronal surface binding and suppression of network spiking and bursting [2]. These findings provide biological plausibility for dysfunction without macroscopic atrophy, as observed on this patient's structural imaging. In a broader autoimmune ataxia cohort, reported abnormality detection was higher for brain FDG-PET than structural MRI (85.5% versus 39.1%) [6]. This broader evidence supports considering brain metabolic imaging in patients whose clinical syndrome remains unexplained by structural MRI.

Differential Diagnosis in a Patient with Normal Cerebellar MRI

The diagnostic strategy should integrate time course, localization, associated signs, and neural antibody findings [7]. A vascular explanation was unconvincing because the syndrome developed over more than one month, involved bilateral appendicular coordination and gait, and lacked a corresponding cerebellar lesion. Mild posterior cerebral artery stenosis and reduced Doppler velocities did not account for that distribution. Peripheral vestibular disease likewise did not explain dysarthria and bilateral limb dysmetria.

Preserved deep sensation and unremarkable electrophysiology argued against a sensory neuropathic explanation. No ophthalmoplegia was recorded to support a Miller Fisher presentation within the Guillain–Barré spectrum. Subacute onset, substantial improvement, and subsequent stability favored an acquired immune disorder over a continuously progressive degenerative or hereditary ataxia. Multiple system atrophy

of cerebellar type commonly involves autonomic dysfunction and evolving motor features [8]. This patient had no reported autonomic dysfunction, retained normal limb power and tone, and showed sustained functional improvement. These clinical features, considered together with the time course and MRI findings, favored an acquired immune-mediated cerebellar disorder.

Dedicated paraneoplastic antibody testing was negative. Whole-body PET/CT was not completed because of financial constraints, limiting the assessment for an occult malignancy in this older patient [9]. This is the principal limitation of the malignancy evaluation. The patient had no gluten-related symptoms or coeliac disease, and gluten ataxia was not favored clinically [10]. Other neural antibody-associated ataxias can produce a similar subacute syndrome. Anti-mGluR1 disease often includes additional cognitive, behavioral, or neurological manifestations, while Homer-3 autoimmunity can resemble multiple system atrophy clinically and radiologically [11, 12]. GAD65-associated ataxia offers another immune-mediated differential, including cases with broader neurological autoimmunity [13]. Testing for mGluR1 and GAD65 antibodies was negative, as were the seven other serum cerebellar antibodies, including Homer3. Serum Septin-5 IgG was the positive cerebellar antibody identified in this patient. Table 4 summarizes the discriminating findings and their application to this patient.

Table 4
Differential diagnosis and interpretation in the present case

Diagnostic alternative	Distinguishing clinical features	Findings and interpretation in this patient
Posterior circulation ischemia	Abrupt onset with focal deficits and a corresponding cerebellar or brainstem lesion.	Symptoms evolved over more than one month. Bilateral limb dysmetria and dysarthria had no corresponding MRI lesion; mild right P2 stenosis did not explain the syndrome.
Peripheral vestibular disorder	Vertigo and imbalance predominate, without appendicular dysmetria or cerebellar dysarthria.	Bilateral finger–nose and heel–shin abnormalities together with dysarthria established a central cerebellar syndrome, making an isolated peripheral vestibular cause unlikely.
Sensory ataxia	Impaired proprioception, with greater unsteadiness when visual compensation is removed.	Deep sensation was normal, and standing was unstable with both eyes open and closed. Appendicular dysmetria and dysarthria favored cerebellar ataxia.
Guillain–Barré/Miller Fisher spectrum	Peripheral weakness or areflexia; Miller Fisher syndrome characteristically includes ophthalmoplegia, ataxia, and areflexia.	Limb power was preserved, electromyography showed no evident peripheral nerve abnormality, and no ophthalmoplegia was recorded. These findings did not support this diagnosis.
Hereditary cerebellar ataxia	A progressive course, compatible family history, and associated neurological features may provide clinical clues.	There was no family history of ataxia. The subacute onset and improvement during immunotherapy favored an acquired immune-mediated disorder.
MSA-C [8]	Progressive cerebellar ataxia with autonomic dysfunction and evolving motor features; pontocerebellar atrophy may develop.	There was no autonomic dysfunction; limb power and tone were normal, and MRI showed no cerebellar atrophy. The subacute, treatment-responsive course favored immune-mediated ataxia.
Other antibody-associated cerebellar ataxias [11–13]	mGluR1, Homer-3, and GAD65 autoimmunity can produce a similar subacute cerebellar syndrome.	mGluR1 and GAD65 antibody testing was negative. Serum Homer3, ATP1A3, RGS8, GluRδ2, Sez6L2, Rab6A, and Rab6B IgG were also negative; serum Septin-5 IgG was positive at 1:320.
Paraneoplastic cerebellar degeneration [9]	Subacute cerebellar dysfunction associated with malignancy; paraneoplastic antibodies assist the clinical evaluation.	Paraneoplastic antibody testing was negative. Whole-body PET/CT was not completed because of financial constraints, limiting the assessment for an occult tumor.
Gluten ataxia [10]	Cerebellar ataxia associated with gluten sensitivity or coeliac disease.	The patient had no gluten-related symptoms or coeliac disease, and gluten ataxia was not favored clinically.

The table presents the clinical distinctions and findings recorded in this patient. MSA-C multiple system atrophy with cerebellar features; PCA posterior cerebral artery; PET/CT positron emission tomography/computed tomography.

Treatment Response and Longitudinal Assessment

The patient's early improvement was substantial: dizziness receded, dysarthria resolved, limb coordination improved, and tandem walking became possible during the corticosteroid-based regimen. Independent walking and absence of recurrent presenting symptoms were sustained at one year. This clinical course supports treating a concordant acquired cerebellar syndrome before visible cerebellar injury becomes a requirement for action.

Published outcomes span spontaneous improvement, improvement during immunotherapy, persistent severe disability, and death [1, 2, 3, 4, 5]. In the expanded series, four of six patients with outcome data improved with immunotherapy, one improved spontaneously, and one died [2]. These source-specific outcomes are summarized in Table 3. The bortezomib-containing regimen in the refractory 2023 case and prolonged treatment escalation in the 2024 case illustrate the range of immunotherapies used in the reported clinical courses [4, 5]. Our patient improved during combined corticosteroid and mycophenolate treatment and remained independently ambulant at the one-year follow-up. Maintenance therapy had been self-discontinued after approximately one month. Residual tandem gait impairment and fine gaze-evoked nystagmus were still present. Serial examination, walking function, and residual cerebellar signs should guide follow-up; antibody titers provide complementary information.

Clinical Importance within Autoimmune Ataxia

The clinical importance of Septin-5 ataxia lies in the possibility of recognizing and treating a disabling acquired syndrome that may be missed by familiar diagnostic expectations. Its numerical contribution to all antibody-associated cerebellar ataxias remains undefined. In one prospective cohort, 23 of 55 patients with subacute ataxia met criteria for autoimmune ataxia; expanded antibody testing included Septin-5, and no positive case was reported [14]. Among the 22 patients with neural IgG, the observation is 0/22 (exact 95% confidence interval 0–15.4%); the whole autoimmune cohort gives 0/23 (0–14.8%). Figure 2 displays the antibody-positive subgroup alongside the other neural IgG categories in that cohort.

Recent diagnostic laboratory data reported nine Septin-5-positive specimens and rounded positivity of approximately 0.01% [15]. This estimate describes specimens submitted for diverse neurological indications. The prospective autoimmune ataxia cohort and the diagnostic laboratory study therefore provide complementary clinical and laboratory descriptions. Antigen definition also matters: Septin-7-only reactivity and antibodies directed against unresolved or multimeric septin complexes have been described in distinct neurological presentations [16, 17]. The literature comparison retains these antigenic distinctions when describing Septin-5-associated cerebellar disease.

Septin-5 IgG-associated cerebellar ataxia should remain in the differential diagnosis of subacute gait and limb ataxia when prominent nystagmus is absent at presentation. In this patient, serum antibody reactivity and improvement during immunotherapy accompanied negative CSF Septin-5 IgG, negative paraneoplastic antibody testing, and persistently normal cerebellar MRI. Clinical localization should guide investigation and prevent potentially treatable cases from being overlooked.

Declarations

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Author contributions. Jingyu Shi: Conceptualization, methodology, investigation, and writing - original draft. Bingjie Chen: methodology, investigation, and writing - original draft.Yuanhua Wu: Methodology, investigation, data curation. Jing Cai: Validation and writing - review and editing. Yongxue Hu: Conceptualization, supervision, and writing - review and editing. Jingyu Shi and Bingjie Chen contributed equally to this work and share first authorship.

Ethics approval and consent to participate

Not applicable for this single de-identified case report.

Consent for publication

Written informed consent for publication of the clinical details and accompanying images was obtained from the patient.

Data availability. The clinical findings supporting this report are presented in the article and Online Resource 1. The source counts and exact confidence intervals underlying the descriptive literature summaries are provided in Online Resource 1. Individual clinical records are not publicly available because they contain potentially identifiable health information.

Use of artificial intelligence. OpenAI Codex (OpenAI) assisted with English-language editing. The authors are responsible for the final review, accuracy, and approval of all content.

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Figures

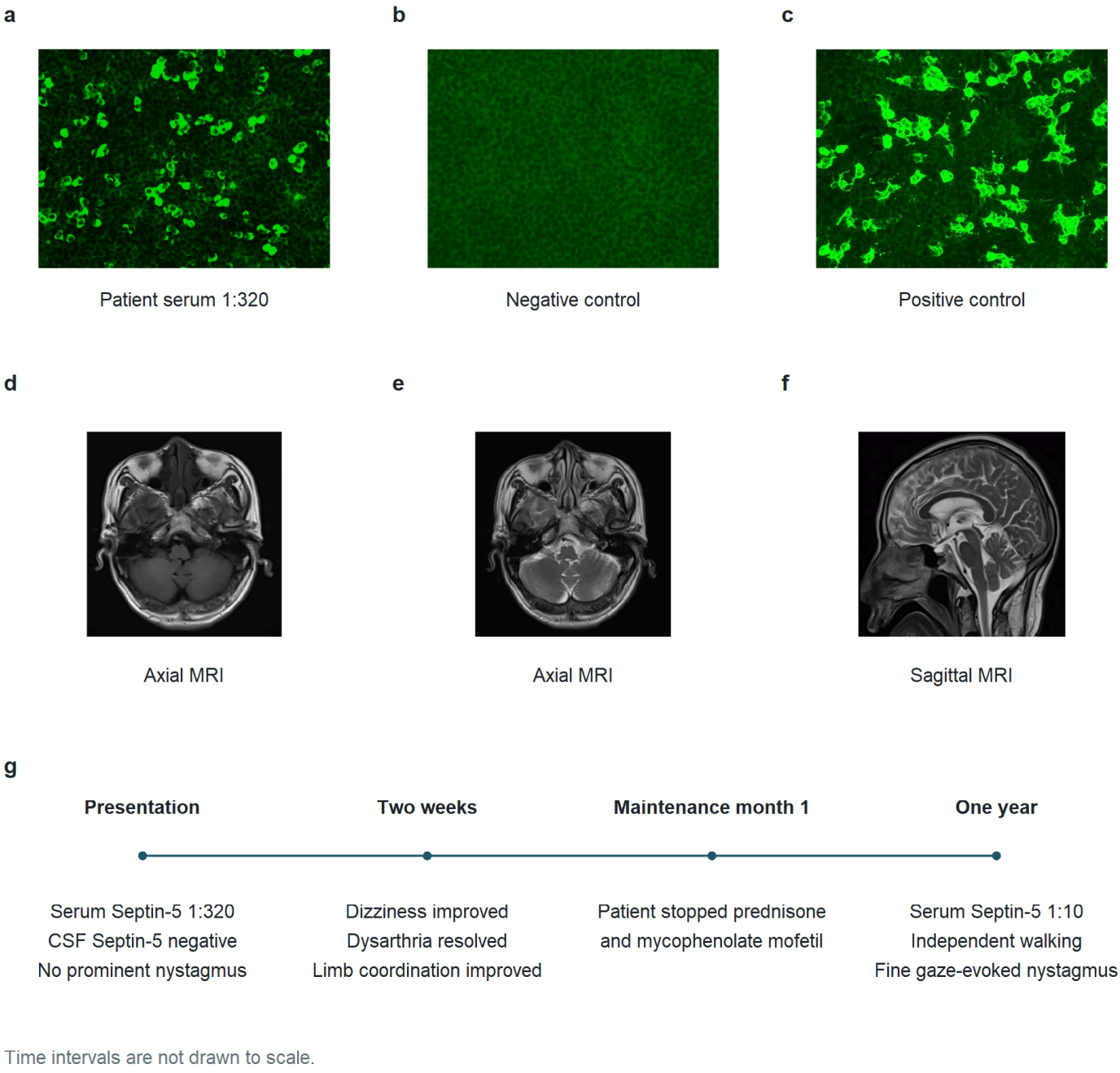


Figure 1

a–c Serum cell-based assay showing patient Septin-5 IgG reactivity at a reported dilution of 1:320 (a), a negative control (b), and a positive control (c). The other seven serum cerebellar antibodies and paraneoplastic antibody testing were negative. Additional testing for mGluR1 and GAD65 antibodies was negative; CSF Septin-5 IgG was negative. d–f Axial and sagittal MRI panels show no visible cerebellar structural abnormality. g Clinical course and antibody results at the reported landmarks; intervals are not drawn to scale

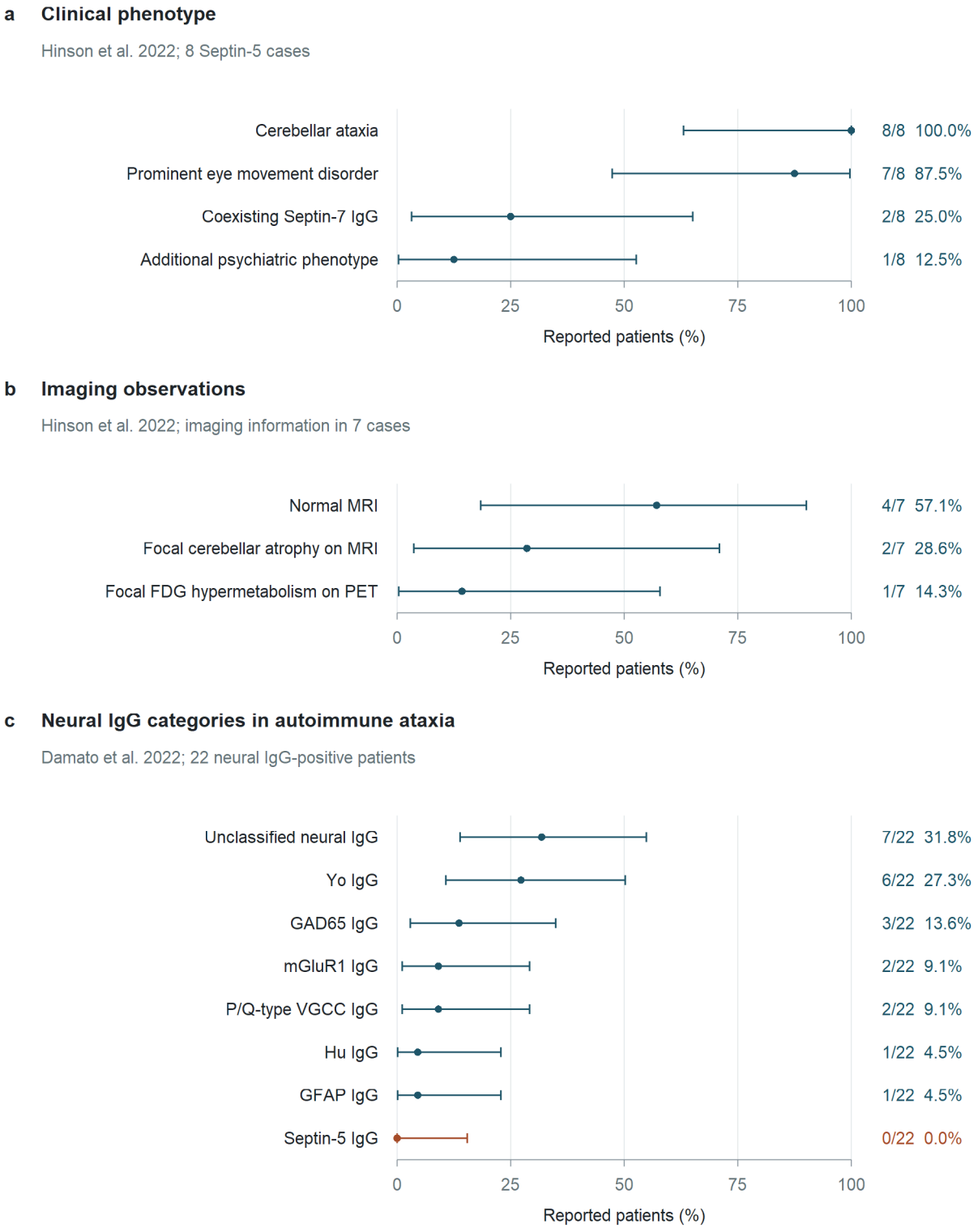


Figure 2

a Clinical phenotype in eight Septin-5 cases [2], using the source's broad eye movement disorder category. b Imaging observations in seven cases with available imaging information [2]. c Neural IgG categories in the 22 antibody-positive patients within a 23-patient autoimmune ataxia cohort [14]. Septin-5 testing was included. Points show proportions; whiskers show two-sided exact 95% binomial confidence intervals. The

0/22 Septin-5 observation has an upper limit of 15.4%. Each panel retains its source population and denominator

Supplementary Files

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