Supplementary Table. Patients with high-titer GAD65 antibodies but a more likely diagnosis for their neurological presentation

Patient	Brief clinical description of neurological presentation	Concern raised for core or secondary manifestation of GAD65 neurological autoimmunity?	More likely alternative diagnosis	Sustained response to immunotherapy reported?	Systemic autoimmunity reported?[1]	Serum anti-GAD65 titer (nmol/L)	CSF anti-GAD65 titer (nmol/L)
Non-neuroinflammatory diagnoses							
1	Child with epilepsy and febrile seizures dating back to infancy; left mesial temporal sclerosis on MRI	Yes (Epilepsy)	Febrile seizures resulting in mesial temporal sclerosis	No trial	Yes, T1DM, thyroid disease, adrenal insufficiency	2245	8.34
2	Middle-aged adult with chronic pain and fatigue; normal tone and paraspinal tenderness on examination	Yes (SPSD)	Fibromyalgia	No trial	Yes, thyroid disease	111	0.33
3	Middle-aged adult with bilateral hand tingling and gait difficulties; gait ataxia on examination	Yes (Cerebellar Ataxia)	Subacute combined degeneration due to B12 deficiency	No trial	Yes, thyroid disease, pernicious anemia	57.8	-
4	Middle-aged adult with acute-onset vertigo and imbalance, followed by vague sense of dizziness without objective neurological findings; peripheral vestibular dysfunction on initial vestibular testing	Yes (Cerebellar Ataxia/Brainstem Dysfunction)	Vestibular neuritis followed by PPPD	No trial	No	2136	-
5	Middle-aged adult with rapidly progressive behavioral change/cognitive decline and motor neuron disease; father had amyotrophic lateral sclerosis	Yes (Cognitive Impairment)	Frontotemporal dementia with amyotrophic lateral sclerosis	No trial	No	3077	20.9
6	Older adult with insidious short-term memory loss and temporal lobe-onset seizures; equivocal right hippocampal T2-hyperintensity/atrophy on MRI; decreased uptake in posterior cingulate on PET scan	Yes (LE/Cognitive Impairment)	Alzheimer's disease	No, trialed corticosteroids	Yes, thyroid disease, adrenal insufficiency	33.1	-
7	Older adult with more rapidly progressive ataxia after milder gait difficulties for several years and dysautonomia; cruciform	Yes (Cerebellar Ataxia)	Multiple system atrophy-cerebellar type	No trial	Yes, T1DM, thyroid disease	614	0.75

	pontine T2-hyperintensity on MRI						
8	Middle-aged adult with abnormal movements of face/shoulders elicited by swallowing; reported abdominal stiffness and pain in lower extremities	Yes (SPSD)	Functional neurological disorder, diabetic peripheral neuropathy	No trial	Yes, T1DM	136	-
9	Young adult with headache, neck and back pain dating back to childhood/adolescence; some reported low back stiffness/spasms; multiple tender points on examination	Yes (SPSD)	Fibromyalgia	No, trialed IVIG and PLEX	No	36.8	-
10	Middle-aged adult with low back pain/tightness, calf fasciculations and eyelid twitching; clinical diagnosis of anxiety	Yes (SPSD)	Myofascial low back pain, Anxiety	No trial	No	869	-
11	Middle-aged adult with insidious executive dysfunction; epileptiform discharges on EEG, frontoparietal hypometabolism on PET scan; CSF biomarker profile consistent with Alzheimer's disease	Yes (Epilepsy/Cognitive Impairment)	Alzheimer's disease	No trial	Yes, pernicious anemia	334	1.86
12	Middle-aged adult with insidious spastic paraparesis without sensory or bowel/bladder involvement; reported low back pain/spasms and left leg stiffness	Yes (SPSD/Myelopathy)	Primary lateral sclerosis	No trial	Yes, thyroid disease	248	0.31
13	Adolescent with rapidly progressive spastic dysarthria/dysphagia after respiratory infection; pathogenic mutation in ATP1A3 gene	Yes (Brainstem Dysfunction)	ATP1A3 gene-related neurological disease	Yes, improved with rituximab after failing corticosteroids, IVIG and PLEX[2]	No	2680	-
14	Young adult with orthostatic lightheadedness, fatigue, abdominal bloating	No	Postural orthostatic tachycardia syndrome	No trial	No	214	-
15	Young adult with insidious limb weakness, ptosis and dysphagia; muscle biopsy found evidence of a chronic and severe myopathy	No	Inherited myopathy	No, trialed IVIG, steroids and abatacept	Yes, T1DM, pernicious anemia	61.4	-

16	Young adult with two generalized tonic-clonic seizures in the setting of hyperglycemia	Yes (Epilepsy)	Provoked seizures due to hyperglycemia	No trial	Yes, T1DM	24	-
17	Older adult with dysphagia, dysarthria, and hand weakness; upper and lower motor neuron signs on examination; evidence of lower motor neuron involvement on EMG	No	Amyotrophic lateral sclerosis	No trial	No	68.3	-
18	Older adult with insidious amnestic syndrome; hippocampal atrophy on MRI	Yes (Cognitive Impairment)	Alzheimer's disease	No trial	Yes, T1DM	192	-
19	Middle-aged adult with insidious sensory symptoms in legs; length-dependent, axonal, predominantly sensory neuropathy on NCS/EMG; mother has idiopathic peripheral neuropathy	No	Inherited neuropathy	No trial	Yes, thyroid disease	137	-
20	Child with five generalized tonic-clonic seizures in the setting of hypocalcemia	Yes (Epilepsy)	Provoked seizures due to hypocalcemia	No trial	Yes, autoimmune polyglandular syndrome type 1 (hypothyroidism, hypoparathyroidism, adrenal insufficiency)	28.2	-
21	Middle-aged adult with insidious amnestic syndrome; parietal lobe hypometabolism on PET scan	Yes (Cognitive Impairment)	Alzheimer's disease	No, trialed corticosteroids	Yes, thyroid disease, pernicious anemia	168	0.37
22	Middle-aged adult with insidious sensory loss with insensitivity to pain, length-dependent sensorimotor peripheral neuropathy with mixed axonal and demyelinating features on NCS/EMG	No	Inherited neuropathy	No trial	No	388	-
23	Middle-aged adult with gait difficulty followed by urinary urgency, dysarthria, antecollis and myoclonus; parkinsonism on examination; T2-hyperintensity of posterolateral putamen on MRI	No	Multiple system atrophy-parkinsonian type	No trial	No	43.2	-
24	Older adult with insidious amnestic syndrome;	Yes (Cognitive Impairment)	Alzheimer's disease	No, trialed IVIG	Yes, T1DM	95.5	-

	frontotemporal more than parietal hypometabolism on PET scan						
25	Middle-aged adult with insidiously progressive gait difficulties; findings of length-dependent peripheral neuropathy without cerebellar signs on examination; outside NCS/EMG documenting peripheral neuropathy	Yes (Cerebellar Ataxia)	Diabetic peripheral neuropathy	No trial	Yes, T1DM, thyroid disease	24.1	-
26	Middle-aged adult with episodic gait unsteadiness correlating to timing of carbamazepine dose; negative genetic testing for episodic ataxia; history of epilepsy secondary to traumatic brain injury	Yes (Cerebellar Ataxia)	Side effect of carbamazepine; recommended switching to levetiracetam but no follow-up available	No, trialed corticosteroids	No	198	-
27	Older adult with insidious mild amnestic syndrome and subjective feeling of weakness; partial improvement after treatment of B12 deficiency	Yes (Cognitive Impairment)	Alzheimer's disease, B12 deficiency	No trial	Pernicious anemia, vitiligo	51.7	0.19
28	Older adult with insidious leg weakness/spasms; upper motor neuron signs in legs on examination; electrophysiologic evidence of motor neuron disease in cervical, thoracic and lumbar segments on NCS/EMG	Yes (SPSD/Myelopathy)	Amyotrophic lateral sclerosis	No trial	Yes, T1DM	38.7	-
29	Young adult with insidious difficulty walking and low back/leg stiffness/spasms; evidence of myotonia on EMG; pathogenic mutation in CLCN1 gene	Yes (SPSD)	Becker's myotonia	Yes, improved with corticosteroids[3]	Yes, thyroid disease	33	1.1
30	Middle-aged adult with ataxic dysarthria, left-sided ataxia/dystonia and stiffness of left leg; ATP1A3 mutation of uncertain clinical significance; brother with atypical parkinsonism	Yes (Cerebellar Ataxia/SPSD)	ATP1A3-associated neurological disease	No, trialed IVIG and corticosteroids	Yes, T1DM	889	3.72
31	Older adult with insidious cognitive decline with rapid worsening after heart surgery;	Yes (Cognitive Impairment)	Dementia with Lewy bodies	No, trialed corticosteroids	No	123	0.82

	fluctuations in attention; history of dream enactment behavior in sleep; parkinsonism on examination						
32	Young adult with limping related to leg pain; equivocally increased tone in legs but overall "quite normal" neurological examination	Yes (SPSD/Myelopathy)	Myofascial pain syndrome	No trial	Yes, T1DM, pernicious anemia	23.6	-
33	Adolescent with new-onset psychosis, delusions, disorganized thoughts, and insomnia with impaired memory/concentration, followed by catatonia; mild dysmorphism; chromosome 22q11.1 microdeletion identified	Yes (Cognitive Impairment)	Primary psychotic disorder (reported higher risk with chromosome 22q11.1 microdeletion)	No, trialed steroids and IVIG	No	28.1	-
34	Adolescent with episodic vertigo and gait unsteadiness with headache 50% of the time; triggers reported include certain foods, bright lights, loud sounds, and foul odors	Yes (Cerebellar Ataxia)	Vestibular migraine	No trial	Yes, T1DM	53.4	-
35	Child with episodes of mouth-opening, head tilt and breath-holding with preserved awareness in patient with developmental delay and hand-wringing; no abnormality on EEG during episodes	Yes (Epilepsy)	Primary complex motor stereotypy	No trial	No	1514	-
36	Older adult with insidious difficulty walking long distances; mild parkinsonism on examination; decreased striatal dopamine transporter density on DaTscan	No	Idiopathic Parkinson's disease	No trial	Yes, thyroid disease	33.1	-
37	Young adult with Trisomy 21, visual and auditory hallucinations	No	Primary psychotic disorder	No, trialed corticosteroids, IVIG and rituximab	Yes, thyroid disease, celiac disease	35.4	-
38	Middle-aged adult with mild cognitive complaints (less efficient at work, some forgetfulness); essentially normal neuropsychometric	Yes (Cognitive Impairment)	Depression/ Anxiety	No, only non-sustained subjective benefit with corticosteroids and IVIG	Yes, thyroid disease	364	-

	testing aside from concern for clinical depression/anxiety						
39	Older adult with chronic right-sided facial pain, exacerbated by changes in barometric pressure and radiating right occipital pain; right occipital notch tenderness on examination	No	Chronic migraine, occipital neuralgia	No trial	No	459	-
40	Older adult with insidious sensory loss in feet and imbalance; mild findings of sensory neuropathy in feet on examination stable over years; length-dependent small-fiber neuropathy on TST	No	Idiopathic length-dependent small fiber neuropathy	No trial	No	258	-
41	Older adult with insidious cognitive decline, bilateral posterior temporal and parietal hypometabolism on PET scan	Yes (Cognitive Impairment)	Alzheimer's disease	No trial	No	161	-
42	Middle-aged adult with insidious leg weakness and gait difficulties; spastic quadriparesis with impaired vibration/ proprioception in legs on examination	Yes (Cerebellar Ataxia/Myelopathy)	Subacute combined degeneration due to B12 deficiency	No trial	Yes, pernicious anemia	470	-
43	Middle-aged adult with chronic hypersensitivity to touch in feet and intermittent painful color change in toes and fingers; high arches, hammertoes and allodynia in feet on examination	No	Inherited neuropathy, Raynaud's phenomenon	No trial	No	237	-
44	Middle-aged adult with episodic paralysis lasting hours but preserved consciousness and ability to swallow; episodes provoked by anxious situations; normal ictal serum potassium; no findings of periodic paralysis on NCS/EMG	No	Functional neurological disorder	No trial	No	461	-
45	Middle-aged adult with longstanding depression with psychotic features; presented to hospital with impaired attention/concentration/anxiety in context of multiple psychosocial stressors; resolved	Yes (Cognitive Impairment)	Exacerbation of known psychiatric disease	No trial	Yes, thyroid disease, pernicious anemia	45.3	-

	in hospital with nutrition and hydration						
46	Middle-aged adult with chronic leg muscle cramps; normal neurological examination aside from witnessed cramp in foot; cramps resolved with gabapentin	No	Muscle cramps	No trial	Yes, pernicious anemia	219	-
47	Young adult with chronic fatigue, poor sleep and orthostatic lightheadedness after numerous stressful life events; clinical concern for depression; normal neurological examination	No	Orthostatic intolerance, Somatic symptoms of depression	No trial	No	29.2	0.14
48	Young adult with chronic sensory symptoms in feet and hands; glove-and-stocking distribution sensory loss on examination; evidence of chronic length-dependent axonal peripheral neuropathy on EMG	No	Idiopathic length-dependent large fiber neuropathy	No trial	No	30.7	-
49	Young adult with chronic diffuse upper body pain and reported stiffness; variably stiff posturing but no objective stiffness, spasms or paraspinal hypertrophy on examination; diffuse tenderness	Yes (SPSD)	Fibromyalgia	No, trialed IVIG with only non-sustained response	Yes, T1DM	39.6	-
50	Middle-aged adult with headache, poor concentration, dizziness and difficulty sleeping after head injury	Yes (Cognitive Impairment)	Post-concussive syndrome	No trial	Yes, T1DM	434	-
51	Older adult with memory complaints and feeling of exhaustion in context of B12 deficiency, anemia, hypothyroidism and worsening depression; partial improvement with B12 supplementation	Yes (Cognitive Impairment)	B12 Deficiency, Depression	No trial	Yes, thyroid disease, pernicious anemia	348	-
52	Middle-aged adult with chronic intermittent paresthesias of the hands and feet that improve with movement, feeling of hand “swelling”, sense of imbalance, and heat intolerance; only equivocal sensory loss in hands	No	Chronic idiopathic anhidrosis	No trial	No	1377	-

	and feet on examination; diffuse anhidrosis sparing hands on TST; normal NCS/EMG						
53	Young adult with tremulousness, spasms and internal feeling of vibration after starting ziprasidone for bipolar disorder; normal neurological examination	Yes (SPSD)	Side effect of ziprasidone, recommended discontinuation	No trial	Yes, T1DM	149	0.32
54	Young adult with intermittent stuttering of speech, feeling of head heaviness and cognitive difficulties; variable stuttering but otherwise normal neurological examination	Yes (Cognitive Impairment)	Functional neurological disorder	No trial	Yes, thyroid disease	31.5	-
55	Middle-aged adult with insidious numbness and tingling in hands and feet, stable for last year; findings of both mild length-dependent sensory loss and right-sided spasticity/hyperreflexia on examination; mild axonal sensorimotor peripheral neuropathy and C5/C6 radiculopathies on NCS/EMG; severe cervical spinal and foraminal stenosis due to degenerative spondylosis on MRI	Yes (Myelopathy)	Compressive myelopathy/ radiculopathy, Diabetic peripheral neuropathy	No trial	No (has type 2 diabetes mellitus)	69.3	-
56	Middle-aged adult with chronic feeling of low energy, body aches, stiffness, “brain fog”, and postural lightheadedness/ dizziness dating back to childhood; episodic kicking/flailing of legs elicited by medication injection	Yes (SPSD)	Postural orthostatic tachycardia syndrome, Functional neurological disorder	No, trialed IVIG and then SCIG with only non-sustained response	No	216	-
57	Middle-aged adult with remote upper extremity paresthesias and more recently weakness; mild neck flexor and proximal upper extremity weakness/ hyporeflexia and lower extremity hyperreflexia on examination; motor neuron	Yes (Myelopathy)	Subacute combined degeneration, followed by bibrachial amyotrophic diplegia (limited follow-up)	No trial	Yes, thyroid disease, pernicious anemia, vitiligo	322	1.14

	process affecting cervical segments on NCS/EMG; cervical cord atrophy and equivocal posterior column T2-hyperintensity on MRI; previously treated B12 deficiency						
58	Young adult with dysarthria, dysphagia, hand weakness and right-sided stiffness developing over one year; flaccid dysarthria, right arm weakness and spasticity in all limbs on examination; evidence of diffuse motor neuron process on NCS/EMG	No	Amyotrophic lateral sclerosis	No, trialed IVIG	No	45.8	-
59	Middle-aged adult with limb weakness, slurred speech, dysphagia and involuntary laughing/crying developed over ten years (more rapidly over three years); spastic dysarthria, mild proximal right arm and lower extremity weakness with brisk reflexes and scattered fasciculations on examination; evidence of diffuse motor neuron process on NCS/ EMG	No	Amyotrophic lateral sclerosis	No, trialed steroids and IVIG	Yes, thyroid disease	284	0.49
Neuroinflammatory diagnoses							
60	Middle-aged adult with insidious gait difficulties, leg weakness and numbness, right arm tremor; previous episodes of double vision and history of right eye blurring; distractible tremor, “astasia abasia” and give-way weakness on examination; lesions typical of demyelination on MRI	Yes (Cerebellar Ataxia)	Multiple sclerosis with functional overlay	No trial	No	82.8	-
61	Young adult with progressive gait imbalance, blurred vision, intermittent diplopia; optic disc pallor, cerebellar signs and left leg weakness on examination;	Yes (Cerebellar Ataxia)	Multiple sclerosis	Yes, stabilized/mildly improved with rituximab	No	72.5	-

	extensive lesions typical of demyelination on MRI						
62	Middle-aged adult with episode of limb dysesthesias and abdominal tightness, and right followed by left eye vision loss; right optic nerve swelling and left optic nerve pallor on examination; several lesions concerning for demyelination on MRI	Yes (Myelopathy)	Multiple sclerosis	Yes, improved with corticosteroids	Yes, thyroid disease	23.9	-
63	Older adult with persistent mild bilateral leg numbness/heaviness for two years; previous episodes of vision loss, numbness and facial weakness; lesions in cervical cord concerning for demyelination on MRI	Yes (Myelopathy)	Multiple sclerosis	No trial	Yes, thyroid disease, pernicious anemia	25.1	-
64	Middle-aged adult with fluctuating ptosis and diplopia, followed by jaw weakness with chewing; left ptosis, ophthalmoparesis, facial weakness, subtle flaccid dysarthria and mild deltoid weakness on examination; abnormal jitter on NCS/EMG; positive acetylcholine receptor antibodies; no thymoma diagnosed	Yes (Brainstem Dysfunction)	Myasthenia gravis	No, trialed IVIG with only non-sustained response and limited follow-up thereafter	No	419	-
65	Older adult with neck weakness, followed by dysarthria and dysphagia; bilateral ptosis with sustained upgaze, bifacial weakness and neck extensor weakness on examination; abnormal jitter on NCS/EMG; positive acetylcholine receptor antibodies; no thymoma diagnosed	Yes (Brainstem Dysfunction)	Myasthenia gravis	Yes, improved with IVIG and mycophenolate	Yes, thyroid disease	434	-
66	Middle-aged adult with new-onset difficulty chewing and dysphagia, followed by fluctuating ptosis and transient diplopia; positive acetylcholine	Yes (Brainstem Dysfunction)	Myasthenia gravis	Yes, improved with IVIG	Yes, thyroid disease	251	-

	receptor antibodies; thymoma diagnosed						
67	Older adult with subacute proximal muscle weakness and slurred speech; evidence of myopathy on NCS/EMG; inflammatory myopathy on muscle biopsy; thymoma diagnosed	No	Paraneoplastic myositis	Yes, improved with corticosteroids	No	42.7	-
68	Middle-aged adult with difficulty walking; lower extremity weakness, upper motor neuron signs, gait and limb ataxia on examination; clinical history of relapses; lesions typical of demyelination on MRI	Yes (Cerebellar Ataxia/Myelopathy)	Multiple sclerosis	No trial	Yes, T1DM	136	-
69	Older adult with new-onset dysphagia followed by respiratory failure; evidence of neuromuscular junction defect on outside NCS/EMG; positive acetylcholine receptor antibodies; no thymoma diagnosed	Yes (Brainstem Dysfunction)	Myasthenia gravis	Yes, improved with IVIG and PLEX	No	260	-
70	Young adult with transverse myelitis and recurrent optic neuritis; MOG-IgG positive by live cell-based assay	Yes (Myelopathy)	MOG-IgG-associated disease	Yes, improved with corticosteroids	Yes, thyroid disease, pernicious anemia	2068	16.1
71	Middle-aged adult with cognitive impairment and seizures following allogenic stem cell transplant, nodular dural enhancement with multifocal lesions on MRI	Yes (Epilepsy/Cognitive Impairment)	Central nervous system graft-versus-host disease with documented ocular and gastrointestinal involvement	Yes, improved with corticosteroids	Yes, thyroid disease, adrenal insufficiency	3108	154

[1]Systemic autoimmunity refers to presence of T1DM, thyroid disease, pernicious anemia, adrenal insufficiency, vitiligo or celiac disease.

[2]Improvement in temporal relationship to rituximab administration may have been natural history of disease, as ATP1A3-associated neurological disease may present with subacute episodes of neurological decline following infection with spontaneous recovery.

[3]Improvement in temporal relationship to steroids may have been related to baclofen and carbamazepine, which were started at the same time.

Age stratification is as follows: child, less than 12 years of age; adolescent, 13-18 years of age; young adult, 19-45 years of age; middle-aged adult, 46-65 years of age; older adult, greater than 65 years of age.

ATP1A3 = ATPase Na+/K+ transporting subunit alpha 3; CLCN1 = chloride voltage-gated channel ; CSF = cerebrospinal fluid; DaTscan = dopamine transporter (DAT) single photon emission computerized tomography; EEG = electroencephalography; NCS/EMG = nerve conduction studies/electromyography; GAD65 = glutamic acid decarboxylase-65;

IVIG = intravenous immunoglobulin; LE = limbic encephalitis; MOG = myelin oligodendrocyte glycoprotein; MRI = magnetic resonance imaging; PET = positron emission tomography; PLEX = plasma exchange; PPPD = persistent postural-perceptual dizziness; SCIG = subcutaneous immunoglobulin; SPSD = stiff-person spectrum disorders; T1DM = type 1 diabetes mellitus; TST = thermoregulatory sweat test