**Table e-1:** Clinical, laboratory, and radiographic summary of each patient case

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient #/sex/age of onset** | **Presentation summary/****phenotype** | **Visual symptoms** | **Co-existing autoantibodies** | **Co-existing autoimmune disease** | **CSF Profile** | **Imaging or other pertinent ancillary testing** | **Immunotherapy tried** | **Time of follow up** |
| 1/F/37 | Prominent visual symptoms 10 years before evolution to classic SPS including diaphragmatic and laryngeal involvement with later progression to cognitive symptoms and epilepsy | Yes | None | Autoimmune thyroiditis, Systemic sarcoidosis | Normal | Body PET-CT demonstrated hyper-metabolic inferior cervical, thoracic and abdominal pelvic lymphadenopathy, subsequently diagnosed with non-caseating granulomatous disease on biopsy | Yes | 17 years |
| 2/F/41 | Visual symptoms of visual snow, palinopsia, photophobia, intermittent diplopia, visual hallucinations several years prior to lower extremity stiffness and spasms | Yes | GAD65 antibody 0.25 nmol/L (ref ≤ 0.02 nmol/L) at MCL | Autoimmune thyroiditis, vitiligo | Normal except for matched OCBs | Brain MRI with whole brain atrophy for age, subsequently developed worsening lower extremity stiffness | Yes | 2 years |
| 3/F/54 | SPS with features of atypical parkinsonism | No | GAD65 antibody 0.46 nmol/L (ref ≤ 0.02 nmol/L) at MCL | None | Elevated IgG index and 19 unique OCBs | Brain PET-CT with hypometabolism involving the temporal and parietal regions | Yes | 3 years |
| 4/M/71 | SPS variant with cerebellar ataxia, diplopia | Yes; diplopia | GAD65 >250 IU/mL (Ref 0.0 -5.0 IU/mL) at ARUP | Autoimmune diabetes (LADA); Hashimoto’s thyroid disease; vitiligo | N/A | Brain MRI with mild superior cerebellar atrophy | None (patient declined) | 1.5 years |
| 5/M/33 | Autoimmune epilepsy with status epilepticus on presentation | No | None | None | 8 WBCs, normal protein | Brain MRI with contrast enhancement in the medial temporal lobes | Yes | 6 months, deceased (overdose) |
| 6/F/75 | Initially stiff limb syndrome with progression to SPS with atypical parkinsonism, cognitive symptoms (MoCA 20/30) | No | GAD65 18.1 nmol/L (ref ≤ 0.02 nmol/L) and -N-type Calcium channel ab 0.05 nmol/L (ref ≤ 0.03 nmol/L) at MCL | autoimmune diabetes (LADA), vitiligo, and pernicious anemia | N/A | Normal brain MRI and negative DaTscan | Yes | 4 years |
| 7/F/40 | Visual decline followed by slowly progressive memory decline (MoCA 16/30); history of papillary thyroid cancer (s/p radioablation and thyroidectomy) | Yes; visual fields showed significant constriction of her visual fields bilaterally and slow VEPs | None | None | N/A | Brain MRI with one T2/FLAIR hyperintense subcortical lesion, otherwise normal | No (patient declined) | 1.5 years |
| 8/F/39 | SPS | Yes, oscillopsia | GAD65 79.9 IU/mL (ref 0.0-5.0 IU/mL) at ARUP | Autoimmune diabetes (LADA), autoimmune thyroiditis | Normal | Brain MRI with few scattered nonspecific T2/FLAIR hyperintense lesions in deep, subcortical white matter bilaterally, as well as in pons. | Yes | 2 years  |
| 9/M/55 | SPS with parkinsonism and abrupt onset of dysautonomia, significant new onset anxiety and hyperstartle | Yes; photophobia (resolved with PLEX) | GAD65 0.03 nmol/L (ref ≤ 0.02 nmol/L) at MCL | Autoimmune thyroiditis | normal WBC, elevated protein 125 mg/dl, 0 OCBs | Normal brain MRI, positive DaTscan | Yes | 9 months |
| 10/F/17 | Autoimmune epilepsy with status epilepticus on presentation, course complicated by significant psychiatric symptoms and suicide attempt | No | GAD65 0.17 nmol/L (ref ≤ 0.02 nmol/L) and P/Q type calcium channel antibody at 0.06 nmol/L (ref ≤ 0.02 nmol/L) at MCL | None | WBC 11 with 96% lymphs, normal protein, 0 OCBs | Normal brain MRI; EEG with extreme delta brush | Yes | 1 year |
| 11/F/45 | Classic SPS with difficulty walking, muscle spasms, anxiety and hyperstartle reflex | Yes; intermittent diplopia, palinopsia, photophobia, constricted visual fields and poor night vision. Automated visual fields with profound constriction and ERG abnormal | GAD65 0.12 nmol/L(ref ≤ 0.02 nmol/L) and P/Q-type calcium channel antibody 0.04 nmol/L (ref ≤ 0.02 nmol/L) at MCL | Granulomatosis with polyangiitis of the lung (biopsy confirmed) diagnosed one year prior to SPS symptoms | Normal, GlyR ab neg in CSF  | Normal brain MRI | Yes | 1.5 years |
| 12/M/46 | Long-standing history of idiopathic PD diagnosed at age 39 with development of new temporal lobe epilepsy, personality changes and spells of full body spasms | No | None | vitiligo | N/A | Brain MRI with T2 hyperintense focus in the posterior right temporal lobe; positive DaTscan; EMG with continuous muscle activity consistent with SPS | Yes | 4 years |
| 13/F/62 | Autoimmune encephalitis with subacute cognitive decline, hallucinations, tremor, gait dysfunction and profound hyperstartle reflex | Yes; visual hallucinations of faces and people as well as visual disturbance with wavy lines and spots in her vision (not formed objects) | GAD65 0.24 nmol/L (ref ≤ 0.02 nmol/L) at MCL | Sjogren’s syndrome with sicca symptoms and antibody positive | Normal WBCs and elevated protein at 90 mg/dL | Normal brain MRI | Yes | 8 months |
| 14/M/57 | Classic SPS with the addition of diffuse fasciculations | No | None | None | N/A | Normal brain and spinal MRIs | Yes | 4 months |
| 15/M/44 | SPS with additional symptoms of fasciculations, myalgias and arthralgias | No | None | Vitiligo, ulcerative colitis, autoimmune diabetes (LADA), psoriasis, and celiac disease | N/A | Normal brain and spinal MRIs | No (mild symptoms) | 3 months |
| 16/F/61 | Choreiform movements of face, jaw and chin bilaterally progressing to left arm with increasing severity; dysphagia | Yes; blurry vision and black spots in vision | Positive striational antibody at a titer of 1:960 at MCL | Autoimmune thyroiditis (positive TPO and ANA at 1:2560 anti-centromere pattern); pernicious anemia (elevated gastric parietal antibody); primary biliary sclerosis (elevated mitochondrial antibody) | Normal, negative OCBs, GlyR ab negative in CSF | Brain MRI with mild scattered subcortical and periventricular white matter hyperintensities and stable diffusion weighted abnormality in the left basal ganglia/caudate. | Yes | 4 years |
| 17/M/71 | Subacute progressive ataxia, dysarthria, ophthalmoplegia, rigidity over 5 weeks. Failed treatment with IVIg and PLEX; transitioned to hospice. Passed away 2 months after onset. | No | None | None | Elevated WBC at 12 (77% lymphs) and protein of 110 mg/dL | Normal brain MRI | Yes | 2 months |

Abbreviations: ANA, Antinuclear antigen; ARUP, Associated Regional and University Pathologist Inc. Laboratories; CSF, cerebrospinal fluid; DM, diabetes mellitus; ERG, electroretinogram; GAD, glutamate decarboxylase; GlyR ab, glycine receptor antibody; IVIg, intravenous immunoglobulin-G; MCL, LADA, latent autoimmune diabetes in adults; Mayo Clinic Laboratories; MoCA, Montreal cognitive assessment; MRI, magnetic resonance imaging; OCB, oligoclonal bands, PD, Parkinson’s disease; PET-CT, positron emission tomography-computed tomography; PLEX, plasma exchange; SPS, stiff person syndrome; TPO, thyroperoxidase; WBC, white blood cell count; VEPs, visual evoked potentials

**Table e-2:** Treatment response for each patient treated with immunotherapy

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| --- | --- | --- | --- | --- | --- | --- |
| **Patient #** | **Steroids** | **PLEX** | **IVIg** | **Rituximab** | **Other immunotherapy** | **Symptomatic therapy of benefit** |
| 1 | Initiated 5 years after visual symptom onset with no benefit and tried again 15 years later and no benefit; significant side-effects (adrenal suppression) | N/A | Initiated 5 years after visual symptom onset with no benefit. Tried again 15 years later for SPS symptoms with no benefit after 1.5 years | Initiated 15 years after SPS symptom onset with no effect; developed *C. difficile* so discontinued  | Cyclophosphamide: initiated after failure of rituximab, tolerated 1st monthly infusion | High dose baclofen and diazepam with relief in diaphragmatic spasms |
| 2 | 6 week trial of IVMP 1 year after visual symptom onset; subtle if any benefit and had irritability | N/A | N/A | N/A | N/A | CBD oil |
| 3 | N/A  | 3 years after symptom onset, initially with good response; effect gradually lost on repeated cycles | Initiated 2 years after symptom onset, no significant side effects but only noted very mild benefit with mobility | 3 years after symptoms onset. No benefit. | N/A | Diazepam, Carbidopa-levodopa, Gabapentin |
| 5 | Responded to high dose, but return of seizures when tapered to 40 mg prednisone, initiated at onset during hospitalization | N/A | N/A | N/A | N/A | N/A |
| 6 | N/A | N/A | Initiated 4 years after onset of stiff limb symptoms with benefit but, developed side-effects  | N/A | N/A | Gabapentin, Diazepam |
| 8 | N/A | N/A | Beneficial with spasms initiated 3 years after symptom onset, discontinued due to loss of insurance | N/A | Mycophenolate mofetil initiated 2 years after symptom onset; progressed on this therapy | N/A |
| 9 | N/A | Initial improvement with gait, muscle spasms and dysautonomia and resolution of photophobia initiated 6 months after symptom onset | Started after positive response to PLEX 6 months after symptom onset, improvement with every two week dosing with muscle spasms, stiffness and dysautonomia, but developed DVT | Initiated 7 months after symptom onset, followed 8 months with some improvement, but ongoing disability. | N/A | Diazepam, carbidopa-levodopa |
| 10 | Unclear benefit during acute hospitalization | N/A | Initial improvement on presentation with seizure control and cognition during acute hospitalization | Initial improvement with one dose of rituximab during acute hospitalization with resolution of seizures for 5 months. Relapse with recurrent seizures and psychiatric symptoms at 6 months after initial presentation, now maintained on chronic therapy and stable one year with controlled seizures on 3 AEDS. | N/A | Lacosamide, zonisamide, clobazam |
| 11 | N/A | Initiated 4 years after symptom onset with short term benefit, continued on monthly PLEX with bridge to rituximab. | Did not tolerate  | Initiated for duel therapy of granulomatosis with polyangiitis and SPS 4 years after SPS presentation, tolerated and followed for 6 months with clinical improvement. | N/A | Diazepam |
| 12 | N/A | Initiated 5 years after onset of epilepsy, initial improvement seizure frequency and anxiety | Did not tolerate | Initiated 2 months after PLEX and tolerated and followed for 4 months with unclear benefit | N/A | Diazepam, baclofen, carbidopa-levodopa |
| 13 | N/A | N/A | Initiated during acute hospitalization at presentation with initial improvement in cognition and hallucinations with objective improvement on MoCA but not back to baseline | Started 5 months after symptom onset and slow gradual improvement over 9 months of treatment and MoCA normalized (27/30) | N/A | N/A |
| 14 | Initiated 7 years after symptom onset with 50-60% improvement with high dose oral prednisone but with significant side effects | N/A | Initiated 7 years after symptoms onset, followed for 2 months with no benefit and discontinued due to side effects | N/A | N/A | Diazepam |
| 16 | Initiated 4 years after symptom onset with mild benefit | Initiated 7 years after symptom onset; no benefit  | Initiated 4.5 years after symptom onset; no benefit | N/A | Mycophenolate mofetil tried 4 years after symptom onset for over 1 year with no benefit | Benztropine with initial benefit but stopped due to allergic reaction. Low dose clonazepam and baclofen mildly beneficial. |
| 17  | Initial benefit with 3 days IVMP initiated during acute presentation then worsening when tapered below 40 mg prednisone | No benefit | No benefit | N/A | N/A | N/A |

Abbreviations: CBD, cannabidiol; DVT, deep venous thrombosis; IVIg, intravenous immunoglobulin; IVMP, intravenous methylprednisolone; mg, milligrams; MoCA, Montreal Cognitive Assessment; PLEX, plasma exchange; SPS, stiff-person syndrome