Latent Autoimmune Diabetes in Stiff-Person Syndrome

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GAD antibody (GADA) positivity is a hallmark of autoimmune diabetes and the rare autoimmune neurological disorder Stiff-Person Syndrome (SPS). Concomitant SPS and classical type 1 diabetes (T1D) have been described in case reports (1–3). A recent series of SPS reported the prevalence of T1D at 43% (4). However, the presence of alternative forms of autoimmune diabetes, such as latent autoimmune diabetes in adults (LADA) in SPS, is not well described. We report on two cases of SPS and LADA.

A 72-year-old woman presented unable to walk after a 6-month history of progressive right leg stiffness, light touch–induced foot spasms, and pain. Examination revealed her right foot was plantarflexed and inverted with no active or passive movement in the right ankle or knee due to increased tone. Diabetes was diagnosed 18 months prior and treated with an oral sulfonylurea.

Blood investigations were normal except for a mildly elevated creatine kinase. Cerebral and spinal MRI was unremarkable and cerebrospinal fluid (CSF) examination was normal (oligoclonal bands absent). Recordings of the cutaneomuscular reflexes with surface electrodes identified changes consistent with SPS. Serum GADA was positive and there was no positivity for other islet autoantibody specificities. A glucagon stimulation test demonstrated relative insulin deficiency and genetic risk for T1D (Table 1).

Table 1—Summary of LADA and SPS cases

	Case 1	Case 2
Age at diabetes diagnosis (years)	70	40
Age at SPS diagnosis (years)	72	78
Age at insulin requirement (years)	NA	42
HbA_{1c} at LADA diagnosis, % (mmol/mol)	7.8 (62)	6.8 (51)
GADA (units/mL) (ref. <5.0 units)	71	>2,000
Basal C-peptide (nmol/L)	0.34	<0.03
Glucagon-stimulated C-peptide (nmol/L)	0.62	<0.03
Class II HLA	DQ2,8	DQ2,8

The patient had no response to intravenous immunoglobulin (IVIG), so after a positive trial of intrathecal baclofen, a baclofen pump was implanted allowing independent ambulation.

A 78-year-old woman was investigated for worsening episodic brief truncal and lower-limb muscle spasms (stimulated by movement) present for 25 years. She developed progressive rigidity in truncal and lower-limb musculature and a phobia of walking in public. She had been extensively investigated previously, including an unremarkable MRI of brain and spinal cord. A previous diagnosis of a functional neurological disorder occurred years earlier. Cranial nerve and upper-limb neurological examinations were normal. Lower limbs were markedly rigid, knee and ankle jerks were pathologically brisk, and she had extensor plantar responses.

She was diagnosed with diabetes at age 40 after a symptomatic presentation. Her diabetes was initially stabilized with oral hypoglycemic medication but progressed to requiring insulin within 2 years of diagnosis. Her diabetes is managed with basal-bolus insulin.

Serum and CSF GADA were >2,000 units/mL. Other CSF investigations were unremarkable. A glucagon stimulation test demonstrated absolute insulin deficiency and genetic risk for T1D (Table 1).

The diagnosis of SPS was based on the classic clinical findings, positive GADA, and suggestive ancillary investigations. Induction and maintenance of IVIG treatment were ineffective, and subsequently plasma exchange resulted in functionally independent mobility.

In both cases, diabetes preceded the diagnosis of SPS, insulin was not required initially, and the individuals were assumed to have type 2 diabetes. Subsequent testing identified insulin deficiency and DQ2,8

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phenotypes consistent with autoimmune diabetes. SPS and T1D share HLA genetic risk, with a majority of SPS patients possessing the DQ2 phenotype (5). These cases highlight the different forms of autoimmune diabetes in SPS and are consistent with the notion that LADA is an autoimmune disease.

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