

Brief communications

Antidopaminergic antibodies in a patient with a complex autoimmune disorder and rapidly progressing Parkinson's disease

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CASE REPORT

A female patient was well until the age of 34 years, when she began to experience subfebrile temperatures and symmetric polyarthritis requiring treatment with nonsteroidal antirheumatic drugs (Table I, 1978). Three years later, she had autoimmune-mediated pancytopenia, Raynaud's phenomenon, dry mouth, aphthous ulcers, and photosensitivity. Diagnosis of systemic lupus erythematosus (SLE) was established, and good recovery was achieved with prednisone therapy and plaquenil. Four years later, she was hospitalized because of autoimmune thyroiditis, which resolved after treatment with prednisone and azathioprine. Eleven years after onset, central nervous system (CNS) involvement with depression, concentration difficulties, and memory disturbances was noted; and 2 years later, the patient had rapidly progressing Parkinson's disease (PD) with bradykinesia, rigidity, and tremor. Because of the CNS symptoms the patient was readmitted (Table I, 1992). No antineuronal antibodies were detected in cerebrospinal fluid (CSF).¹ However, antibodies against dopaminergic cells (anti-DA), demonstrated by immunohistochemical methods,² could be detected in serum (Table I). Neuropsychologic testing confirmed the existence of severe deficits. Magnetic resonance imaging of the brain was normal, but a positron emission tomographic scan documented functional abnormalities as expected in PD. A substitution therapy with levodopa (300 mg/day, combined with a decarboxylase inhibitor) resulted in a marked improvement of the extrapyramidal symptoms.

Two years later she was reevaluated (Table I, 1994). Meanwhile, levodopa had been increased to 750 mg per day. No signs of active SLE were noted, but the patient

Abbreviations used

anti-DA:	Anti-dopaminergic antibodies
CSF:	Cerebrospinal fluid
CNS:	Central nervous system
PD:	Parkinson's disease
SLE:	Systemic lupus erythematosus

complained about unresolved neuropsychologic problems and tremor. The findings in CSF were unremarkable, with the exception of the IgG index (measured as the ratio of IgG to albumin in CSF to serum), which was 0.79 (normal, below 0.6), indicating intrathecal IgG production. Four months later, the patient noted a rapidly spreading vitiligo in her face and over the extremities. At that time levodopa had been increased to 1200 mg/day, and bromocriptine (20 mg-three times daily) and selegiline (5 mg/day) had been added for treatment of PD.

To determine whether anti-DA might be an as yet unrecognized phenomenon of SLE, 10 serum and two CSF samples from patients with clinically and serologically active disease (five with cerebral involvement) were tested for the presence of anti-DA (Table II). Although high background stain was noted in all of the samples, none of the serum or CSF samples contained detectable amounts of anti-DA.

DISCUSSION

Our patient has a complex autoimmune disorder involving connective tissue, the thyroid, the skin, and the CNS. Chronic polyarthritis, depression, neuropsychologic deficits, and symptoms of PD characterize the clinical picture. Antibodies typical for connective tissue diseases (rheumatoid factor, antinuclear antibodies, anti-centromer antibodies) were found together with antibodies specific for dopamine-producing cells (anti-DA).

In reviewing this patient's history, the key question is whether the multi-organ involvement has a common underlying cause or whether the connec-

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J ALLERGY CLIN IMMUNOL 1995;96:688-90.

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0091-6749/95 \$5.00 + 0 1/54/65638

TABLE I. Laboratory findings in our patient

	1978	1981	1985	1987	1988	1989	1991	1992	1993	1994
ANA	40	320	80		—	—	40	40	40	40
anti-dsDNA/-Sm	—	—	—		—	—	—	—	—	—
RF (WR)	+	56		+	64	64		256	56	58
anti-cm								80		
anti-neuronal AB in CSF								—		
anti-DA in serum*								+	+	+
anti-DA in CSF								—	—	—
ESR (mm/hr)	20	32	95	28		16	10	12		14

Laboratory results are stated as positive (+), negative (—), or quantified in titers.

ANA, Anti-nuclear antibodies (homogenous staining pattern); RF, rheumatoid factor; WR, Waaler-Rose; anti-dsDNA/-Sm, SLE-specific antibodies; anti-cm, anti-centromer antibodies; ESR, erythrocyte sedimentation rate.

*Anti-DA in serum of the patient were demonstrated immunohistochemically with substantia nigra of the rat as substrate.²

tive tissue disorder and the PD constitute two different entities. Depression and cognitive impairment are frequent manifestations of neuropsychiatric SLE, and neuronal antibodies in CSF were found in 90% of patients with cerebral lupus.¹ Reports indicate that extrapyramidal symptoms, such as chorea and hemiballismus, may complicate SLE; but PD has not yet been described as being associated with SLE. Whether immune mechanisms play a role in the pathogenesis of PD is a matter of debate.²⁻⁴ In our patient, who is apparently prone to demonstrate autoimmune phenomena, a pathogenic role of the immune system in the decrease of the striatal dopaminergic activity, as shown by positron emission tomography would seem likely. It is conceivable that autoimmune mechanisms initiate destruction of dopaminergic cells, but also that toxic or degenerative events lead to exposure of cryptic antigens, which subsequently elicit a humoral immune response and thereby promote the loss of dopaminergic neurons.

In this patient, the CSF protein level was normal, indicating an intact blood-brain barrier, but the IgG index in CSF was slightly elevated, suggesting intrathecal production of immunoglobulins.⁵ With the assay we used, however, no anti-DA could be demonstrated in CSF. It is possible that anti-DA, although present in significant amounts, were below the detection limit of our assay. Second, because substantial loss of dopaminergic neurons precedes the clinical appearance of extrapyramidal symptoms, the findings could reflect a late stage of the immunoinflammatory disease, with the serum antibodies being merely reminiscent of the acute process. Third, anti-DA in sera of patients with SLE could be an as yet unrecognized feature without any pathogenic importance. To address this last possibility, 10 serum

TABLE II. Characteristics and findings of 10 patients with SLE

	All F
Sex	
Mean age (yr)	39.2
Range (yr)	26-63
Cerebral involvement	5
ANA titer range*	160 to >2560
anti-dsDNA†	+ in 8 sera
anti-DA serum	—
anti-DA CSF (n = 2‡)	—

ANA, Antinuclear antibodies; anti-dsDNA, antibodies to double-stranded DNA.

*Antinuclear antibodies were measured with human laryngeal tumor cells as substrate; the staining pattern was homogenous for all 10 patients.

†Measured by enzyme immunoassay.

‡One patient (40 years old) had acute cerebral lupus requiring high-dose prednisone therapy, and one patient (63 years old) was hospitalized because of a severe flare-up of SLE.

and two CSF samples from patients with clinically and serologically active SLE (five with cerebral involvement) were analyzed for the presence of anti-DA. However, no antibodies with specificity to dopaminergic cells could be detected in any of the samples. Thus the finding of anti-DA is an individual characteristic of our patient and not a general epiphenomenon of SLE. It seems conceivable therefore that these specific antibodies, which may be cytotoxic,⁴ played a role in the development of PD at the very young age of our patient.

In summary, this is the first report on an association of SLE and PD. The presence of anti-DA in this patient and the absence of anti-DA in a control population consisting of patients with active SLE support the hypothesis that autoimmune pathogenic mechanisms may promote the development of PD in individual cases.

We thank Harry Bluestein, MD, University of California, San Diego, for measuring antineuronal antibodies in CSF and serum samples and for valuable advice. We also thank Klaus L. Leenders, MD, and Angelo Antonini, MD, of Paul Scherrer Institute, Villigen, Switzerland, for performing PET scans and for helpful discussions.

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***Allium cepa* seeds: A new occupational allergen**

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We present a case of occupational asthma caused by IgE-mediated sensitization to red onion (*Allium cepa*, Brunswick variety) seeds in a seed-packing factory worker. To our knowledge, there are no earlier reports of occupational allergy caused by Liliaceae plant seeds.

CASE REPORT

A 27-year-old female smoker without an atopic background was referred to us because of episodes of rhinoconjunctivitis, which had begun 1 year before evaluation. In the last few months before consultation, she had also complained of asthma attacks. The patient believed that her symptoms were caused by contact with red onion seeds. She had been working for 3 years in a room without an air extraction system in which a machine

Abbreviations used

SDS-PAGE: Sodium dodecylsulfate-polyacrylamide gel electrophoresis
SPT: Skin prick test

packed the seeds into bags; she had to put these bags in boxes. The patient had mild symptoms on contact with onion seeds other than red onion seeds. Handling other seeds, including those of the Liliaceae family (asparagus, leek) did not elicit any symptoms. She touched and ate raw and cooked onions without experiencing symptoms.

Results of physical examination, blood cell count, basic biochemistry, and chest and sinus roentgenograms were normal. Total IgE was 136 kU/L. Specific IgE to onion (CAP System; Pharmacia, Uppsala, Sweden) was negative. Basal spirometry revealed no abnormalities.

Extracts

Three 10% wt/vol extracts were prepared. For extract 1, 30 gm of crude red onion seeds in 30 ml of phosphate-buffered saline (PBS) were shaken for 24 hours at room temperature. The extract was then centrifuged for 15 minutes at 1500 g, and the supernatant was dialyzed against PBS and saline solution and finally filtered through a 0.22 µm filter. Extract 2 was made with

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Supported in part by a grant of Fondo de Investigaciones Sanitarias (90/0107-3).

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J ALLERGY CLIN IMMUNOL 1995;96:690-3.

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