Possible gluten sensitivity in multiple system atrophy

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Celiac disease (CD) is an intestinal syndrome characterized by immunologic intolerance to dietary gluten leading to mucosal atrophy and malabsorption. Neurologic complications occur in 8 to 10% of patients with the disease.[1] Neurologic impairment can be the only manifestation of gluten sensitivity. Gluten sensitivity is indicated by increased levels of circulating antibodies to gliadin.[2] Most patients with gluten sensitivity carry a particular HLA variant, DQ2, or in a few cases HLA DQ8.[3] A high frequency of gluten sensitivity in the absence of signs and symptoms of classic CD has been found in patients with certain neurologic syndromes of unknown etiology, including cerebellar ataxia.[4]

Multiple system atrophy (MSA) is a sporadic, adult-onset neurodegenerative disease of unknown etiology. We studied the occurrence of gluten sensitivity in a population of MSA patients versus patients affected by idiopathic PD.

Patients and methods. We studied 16 patients with MSA (8 men, 8 women) with a mean age of 62.5 years (SD 8 years); mean disease duration was 5.4 years (SD 2.3 years) and 16 patients with PD (10 men, 6 women) with a mean age of 61.9 years (SD 7.2 years); mean disease duration was 5.8 years (SD 4 years) consecutively seen in our movement disorder clinic. A diagnosis of probable MSA was made according to Quinn's criteria. Twelve of 16 patients with MSA had predominant parkinsonism (MSA-P), while four of them had predominant cerebellar features (MSA-C). PD patients fulfilled UK PD Society Brain Bank diagnostic criteria.

Gastrointestinal complaints except constipation were investigated in all patients. Indicators of malabsorption, including hemoglobin, folate, iron, and calcium, were screened in both groups. IgG and IgA antigliadin antibodies (AGA) were detected by ELISA (Alfa-Gliatest, Eurospital, Trieste, Italy) in duplicate 5-μL serum samples. Antiendomysium antibodies (EMA IgA) were measured by indirect immunofluorescence.

Subjects with positive AGA or EMA test results underwent HLA typing and were offered endoscopic biopsy of the duodenal mucosa to evaluate for the presence of gluten-sensitive enteropathy. Histologic diagnosis criteria were villous atrophy, elongated crypts, and increase of intraepithelial lymphocytes in the lamina propria.[2] All subjects gave informed consent.

Results. No difference was observed in age and disease duration between groups, but disease severity was higher in MSA-P (median Hoehn & Yahr stage 4) than in PD patients (median Hoehn & Yahr stage 3; table).

Three of 16 patients with MSA (18.7%) had raised IgA AGAs (>3 U/mL; normal values <1 U/mL). HLA typing of IgA AGA–positive patients revealed in all cases the presence of an HLA-DQ2 phenotype; HLA typing was performed in 10 of 29 of the AGA-negative patients, none of whom had the DQ2 or DQ8 variant. Two patients with raised AGAs underwent endoscopic biopsy that showed nonspecific duodenitis with increased intraepithelial lymphocytes but no villous atrophy in either patient. There was no difference in neurologic findings between the IgA AGA–positive patients and the other IgA AGA–negative, MSA-C, and MSA-P patients. Mild cortical and subcortical atrophy on MRI was present in two IgA AGA–positive patients (Patients 17 and 32). In Patient 20, who refused duodenal biopsy, brain MRI showed moderate cerebellar atrophy and small hyperintense lesions on T2 in the frontal white matter, and a nerve conduction study revealed mild axonal sensorimotor neuropathy. No PD patient was AGA or EMA positive.

We found no difference in gastrointestinal complaints between antigliadin-positive and -negative patients. None of the patients enrolled in the study reported diarrhea, weight loss, or flatulence, which are typical features of classic CD.

Discussion. The prevalence of gluten sensitivity in Italy ranges from 1 in 184 to 1 in 305 based on population studies.[5,6] Three of our 16 patients with MSA had positive IgA AGA vs none of 16 PD patients. This frequency (18.7%) is higher than that observed in large population studies and is similar to that we found in patients with idiopathic ataxia,[7] suggesting a possiblerole for gluten sensitivity in the pathogenesis of some cases of MSA. Alternatively, gluten sensitivity might be responsible for some cases phenotypically resembling MSA. To determine the prevalence of gluten sensitivity in MSA, our findings need to be confirmed in a larger cohort of patients with a healthy control comparison group.

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Table *Demographic and clinical features of patients with PD and MSA*

Patient no./sex/ age, y	Diagnosis	Disease duration, y	Hoehn & Yahr stage	Signs of possible malabsorption	AGA/EMA
1/F/55	PD	4	2	No	N
2/M/70	PD	1	1.5	No	N
3/M/54	PD	3	1.5	No	N
4/M/53	PD	8	2.5	No	N
5/F/72	PD	10	3	Hypocalcemia	N
6/M/64	PD	1	1.5	No	N
7/F/65	PD	10	3	No	N
8/M/58	PD	1	1.5	No	N
9/F/61	PD	7	3	No	N
10/F/45	PD	8	3	No	N
11/M/63	PD	5	3	No	N
12/M/65	PD	8	3	No	N
13/M/65	PD	15	3	Iron deficiency	N
14/F/67	PD	1	2	No	N
15/M/64	PD	7	3	No	N
16/F/70	PD	5	2.5	Folate deficiency	N
17/M/69	MSA-P	4	5	Mild hypocalcemia	IgA AGA +
18/F/53	MSA-C	10	—	Iron deficiency, hypocalcemia	N
19/M/73	MSA-C	4	—	No	N
20/M/71	MSA-C	5	—	No	IgA AGA +
21/M/67	MSA-P	5	4	No	N
22/F/60	MSA-P	6	5	No	N
23/F/48	MSA-C	7	—	No	N
24/F/65	MSA-P	7	5	No	N
25/F/68	MSA-P	6	3	No	N
26/M/65	MSA-P	5	4	No	N
27/F/54	MSA-P	3	4	No	N
28/M/75	MSA-P	6	2.5	No	N
29/M/52	MSA-P	2	2.5	Iron deficiency	N
30/F/59	MSA-P	10	4	No	N
31/F/64	MSA-P	5	4	No	N
32/M/57	MSA-P	2	2	Hypocholesterolemia	IgAAGA+

AGA = antigliadin antibodies; EMA = antiendomysium antibodies; MSA = multiple system atrophy; N = normal; MSA-P = MSA with predominant parkinsonism; MSA-C = MSA with predominant cerebellar features.

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