Anti-gastric parietal cell antibodies for autoimmune gastritis screening in juvenile autoimmune thyroid disease.

Valeria Calcaterra[1], Chiara Montalbano[1], Federica Vinci[1],Emanuela Miceli[2], Corrado Regalbuto[1], Riccardo Albertini[3], Daniela Larizza[1].

[1]Pediatric Endocrinology Unit, Fondazione IRCCS Policlinico San Matteo e Università degli Stdudi di Pavia, Pavia, Italy
[2]First Department of Internal Medicine, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, University of Pavia, Pavia, Italy
[3]Laboratory of Clinical Chemistry, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy.

Background

Autoimmune thyroid disease (ATD) is the most common etiology of acquired thyroid dysfunction in pediatricsATD is multifactorial, in that a genetic predisposition combines with environmental risk factors to promote disease onset. ATD may occur alone or may coexist with other organ-specific autoimmune diseases, such as celiac disease, type 1 diabetes and, more rarely, autoimmune gastritis (AIG). AIG is a chronic inflammatory disease characterized by the destruction of parietal cells of the corpus and fundus of the stomach, finally presenting with atrophy of the mucosa. Recent reports have described this condition in pediatric patients, especially in association with other autoimmune diseases. Diagnosis of pediatric AIG is important due to poor outcomes and risk of malignancy, moreover, this condition is often underestimated in the clinico-diagnostic work-up, leading to delayed time to diagnosis.

The association between ATD and AIG is very poorly characterized in the pediatric age. Here, we review the prevalence of anti-gastric parietal cell antibodies (PCA) in young patients with ATD. We also evaluated the development of AIG during follow-up, in order to define the usefulness of these markers for AIG screening in patients with chronic autoimmune disease.

Patients and methods

We analyzed 220 children and adolescents (184 F/36 M; 11.28 ± 6.37 yrs) with ATD (186 with autoimmune thyroiditis, AT and 34 with Graves' disease, GD) in follow-up (average 7.07 ± 5.41 yrs) at the Endocrinological Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Table 1.

The diagnosis of ATD was based on the finding of one or more positive thyroid autoantibodies and a thyroid ultrasound characterized by a lack of homogeneity, with a hypogenic or mixed echopattern.

At the initial ATD diagnosis and annually thereafter, blood counts and PCA levels were measured. In patients positive for PCA, plasma gastrin, cromogranin A, vitamin B_{12}, iron and ferritin levels were measured; patients were also tested for H. Pylory stool antigens. The PCA-positive patients older than 18 years were invited to undergo a gastroscopic exam.

The AIG diagnosis was based on the histological examination of multiple specimens obtained during the gastroscopic procedure. Biopsies were read by an experienced pathologist blinded to any of the patients' endoscopic or clinical information. The degree of gastritis was assessed according to the Updated Sydney System.

	Autoimmune thyroiditis	Graves' disease
Patient (number)	186	34
Gender (F/M)		
-number	153/33	31/3
-percentage	82.3/17.7	91.2/8.8
Age at diagnosis (years)	12.5 ± 3.8	12.7 ± 1.7
Follow up (years)	7.5 ± 5.3	8.7 ± 7.2
Therapy (yes/no)	98/88	34/34
Other autoimmune diseases		
-celiac disease	25/186	1/34
-vitiligo	11/186	0
-alopecia	7/186	0
-psoriasis	1/186	1/34
-multiple sclerosis	0	1/34

Results

At diagnosis, only one patient was positive for PCA. During monitoring (average 2.7 ± 2.8 yrs), PCA positivity was detected in 10 (4.5%) subjects (5F/5M; mean age 12.6±3.4 yrs). The mean age at PCA positivity in AT patients was 15.2 ± 4.4 years and in GD subjects 17.2 ± 5.8 years (p=0.6). The prevalence of PCA positivity was not significantly different in GD (2/34; 5.8%) versus AT patients (8/186; 4.3%), p=0.9. PCA positivity was detected after 2.7 ± 2.7 years of follow-up in AT and 4.4 ± 4.0 years in GD patients (p=0.4).

There was a higher prevelance of autoantibody positivity in female patients, both in the AT and GD groups (p=0.02 and p=0.03, respectively). No correlation between therapy and autoantibody positivity was noted.

At positive PCA detection, five out of 10 PCA-positive patients had iron deficiency (50%), four had vitamin B_{12} deficiency (40%), two had anemia (20%), three had hypergastrinemia (30%) and two had elevated chromogranin values (20%). The clinical and biochemical data of the PCA-positive subjects are reported in Table 2. During follow-up, none of the PCA positive subjects became negative. We proposed gastroscopic evaluation in the five ATD patients (all without gastrointestinal symptoms). All of the subjects agreed to undergo the exam.

As reported in Table 2, the gastroscopic examination with histological evaluation of the bioptic tissue confirmed the presence of AIG in all patients. In patient n. 1, foveolar hyperplasia was detected; in patients 4 and 5 lymphocytic infiltration, moderate atrophy of body gastric mucosa and pseudo-pyloric metaplasia were observed; in patient n. 6 lymphocytic infiltration and foveolar hyperplasia were noted and in patient n. 8 foveolar hyperplasia, lymphocytic infiltration, linear and micronodular ECL-cell hyperplasia were observed.

In the two patients positive for H. pylori stool antigen, infection was confirmed at biopsy and eradication was successfully performed.

Table 2. Clinical and biochemical features of the PCA positive patients during follow-up.

Patients	Diagnosis	Sex	Age at ATD diagnosis	Age at PCA positivity	Anemia	Iron deficiency	Vitamin B12 deficiency	Hyper-gastrinemia	Hyper-chromogranin	H. Pylori infection	AIG diagnosis	Age at AIG diagnosis
1	AT	F	16.7	17.5	yes	yes	no	no	no	no	yes	18
2	AT	M	9.8	10.4	no	yes	no	no	no	no	ND	-
3	AT	M	5.9	8.4	no	no	no	yes	no	no	ND	-
4	AT	F	8.9	15.3	no	yes	yes	yes	yes	no	yes	21
5	AT	F	15.1	22	yes	yes	no	yes	yes	yes	yes	23
6	AT	M	13.7	13.7	no	no	yes	no	no	yes	yes	19
7	AT	F	14.3	18.3	no	no	no	no	no	no	ND	-
8	AT	M	15.9	16.6	no	no	yes	no	no	no	yes	26
9	GD	M	11.5	13.1	no	yes	yes	yes	no	no	ND	-
10	GD	F	14.0	21.3	no	no	no	no	no	no	ND	-

AT autoimmune thyroidits; AIG autoimmune gastritis; GD Graves disease; PCA anti-gastric parietal cell antibodies; ND not detected; F female; M male

Conclusions

In conclusion, the association between ATD and AIG should also be considered in young patients. PCAs play an important part in the progression of corpus atrophy and are a useful marker to detect subjects at risk for this condition. Due to the longer life expectancy of the pediatric population and considering the relatively high risk of malignant transformation, early surveillance monitoring is mandatory for children and adolescents with ATD.