CLINICAL RESEARCH STUDY

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Occurrence and Risk Factors for Autoimmune Thyroid Disease in Patients with Atrophic Body Gastritis

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ABSTRACT

PURPOSE: To investigate the occurrence of and risk factors for autoimmune thyroid disease in atrophic body gastritis patients.

METHODS: Cross-sectional study on 401 consecutive outpatients with atrophic body gastritis. Diagnostic work-up of thyroid disease was completed in 319 atrophic body gastritis patients (225 women, median age 55.5 years [range 17-95 years]). Data on anagraphics, lifestyle, family history, and biochemical and histological items were obtained at baseline, and associations between atrophic body gastritis and autoimmune and nonautoimmune thyroid diseases were explored through descriptive statistics and logistic regression analyses.

RESULTS: Of the 319 atrophic body gastritis patients, 169 (53%) had an associated thyroid disorder, and 89 (52.7%) of these were unaware of it. The thyroid disease was autoimmune in 128 patients (75.7%) and nonautoimmune in 41 patients. Logistic regression showed that risk factors for having autoimmune thyroid disease in atrophic body gastritis patients were female sex (odds ratio [OR] 5.6, 95% confidence interval [CI], 2.6-12.1), presence of parietal cell antibodies (OR 2.5, 95% CI, 1.1-5.5), and presence of metaplastic atrophy (OR 2.2, 95% CI, 1.0-5.0).

CONCLUSIONS: Autoimmune thyroid disease and atrophic body gastritis occur in a closely linked fashion, suggesting that atrophic body gastritis patients should be investigated for an occult autoimmune thyroid disease, in particular women and those with positive parietal cell antibodies.

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KEYWORDS: Atrophic body gastritis; Autoimmune thyroid disease; Intrinsic factor antibodies; Parietal cell antibodies; Pernicious anemia

Atrophic body gastritis is a chronic, often symptomless disorder affecting the corporal mucosa. It is characterized by disappearance of the oxyntic glands, leading to loss of production of chlorhydric acid and intrinsic factor.[1] Hypochlorhydria causes loss of feedback on gastrin production, thus, hypergastrinemia together with low pepsinogen I levels is a well-established biochemical marker for atrophic body gastritis.[2,3] Atrophic body gastritis is epidemiologically and biologically linked to the development of the intestinal-type gastric adenocarcinoma and gastric carcinoid type I,[4-6] and frequently presents clinically with pernicious anemia.

Atrophic body gastritis, in particular when associated with pernicious anemia, is often considered an autoimmune disorder, supported by the frequent presence of parietal cell and intrinsic factor autoantibodies as well as by its association with other autoimmune diseases.[7] Recent data give evidence that *Helicobacter pylori* infection, which is able to induce atrophy of the gastric mucosa,[8,9] may be the trigger of gastric autoimmunity,[10,11] but, as recently reported, a clear distinction between autoimmune atrophic gastritis and *H. pylori*-induced atrophic gastritis is difficult.[12,13]

The association of atrophic body gastritis with thyroid disorders has been described since the early 1960s,[14-16] long before routine gastroscopy and a histological consensus classification of gastritis were introduced.[17] The term "thy-

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rogastric syndrome" has been used to define the presence of thyroid autoantibodies or autoimmune thyroid disease in patients with pernicious anemia,[15,18-20] which, in turn, was considered synonymous with atrophic body gastritis.[21] However, many of these older studies assessed the association between gastritis and thyroiditis only on the basis of gastric or thyroid autoantibodies, without a complete diagnostic work-up of the stomach or the thyroid.[14,15,18,19] To our knowledge, recent studies assessing the frequency of autoimmune thyroid disease in patients with atrophic body gastritis are lacking, and the entity of the association between these 2 disorders is not known. Thus, the aim of the present study was to investigate the occurrence of and risk factors for autoimmune thyroid disease in atrophic body gastritis patients.

CLINICAL SIGNIFICANCE

- More than half of patients with atrophic body gastritis were found to have thyroid disease.
- Half of the thyroid disease cases were previously undiagnosed, and most (76% of cases) were autoimmune.
- Autoimmune thyroid disease was associated with female sex and parietal cell antibodies, but not with pernicious anemia.
- Patients with atrophic body gastritis should be assessed for occult autoimmune thyroid disease.

MATERIALS AND METHODS

Patients

As the result of a screening program for atrophic body gastritis, we consecutively diagnosed this condition in 401 outpatients (269 women; median age 55 years [range 20-95 years]) who presented to our gastroenterology department for long-standing dyspepsia (n = 86) or were referred from the hematological department for anemia (n = 302) or from the endocrinology department for autoimmune thyroid disease (n = 13).[22,23] At the time of diagnosis, a structured questionnaire comprising anagraphical, lifestyle, and family history items was filled in for each patient.

The diagnosis of atrophic body gastritis was based on histologic confirmation of gastric body mucosal atrophy, fasting hypergastrinemia, and low pepsinogen I levels.[22,23] All patients underwent gastroscopy with antral (n = 3) and corporal (n = 3) biopsies stained with hematoxylin and eosin for conventional histological evaluation and with Giemsa stain for *H. pylori* determination.[22,23] The degree of gastritis was assessed according to the updated Sydney System.[24] Atrophy of the body and antral mucosa was defined as focal or complete replacement of oxyntic or pyloric glands by metaplastic pyloric or intestinal glands, respectively.[22,23] All patients underwent serological studies: fasting gastrin levels by a specific radioimmunoassay (normal value <40 pg/mL);[22,23] pepsinogen I levels by a commercial radioimmunoassay kit (Pepsik, Sorin, Saluggia, Italy) (normal value >20 ng/mL);[23] parietal cell antibodies by a commercial kit (Autostat, Cogent Diagnostic Ltd, Edinburgh, UK);[22,23] intrinsic factor antibodies by an indirect enzyme-linked immunosorbent assay (ELISA);[25] and *H. pylori* immunoglobulin G antibodies by a commercial ELISA kit (Bio–Rad, Milan, Italy).[9,22]

The diagnosis of pernicious anemia was defined as a hemoglobin concentration <14 g/dL for men and <12 g/dL for women, mean corpuscular volume ≥100 fL, low levels of vitamin B_{12} (normal values 190-950 pg/mL), response to vitamin B_{12} therapy, and histological confirmation of gastric body mucosa atrophy.[26]

None of the patients included in the study was on treatment with proton pump inhibitors or H_2 receptor antagonists. All patients gave written informed consent to the study, which was approved by the local Ethics Committee.

Evaluation of Thyroid Status

A careful clinical history for thyroid disease was collected in all atrophic body gastritis patients. Those with a positive clinical history were referred for endocrinological evaluation at a single center in order to confirm the diagnosis of thyroid disease; those with a negative clinical history were invited to undergo a biochemical/immunological (serum iodothyronines, basal thyrotropin, and serum antiperoxidase antibodies) and ultrasonographic evaluation of the thyroid status (Figure).

Thyroid hormones and autoantibodies were determined by commercial kits: free triiodothyronine and free thyroxine levels by radioimmunoassay (Ares-Serono, Milan, Italy); basal thyrotropin levels by immunoradiometric assay (Radim Techland, Liege, Belgium); and antiperoxidase antibodies by a radioligand assay (Radim Techland). By ultrasonography, thyroid gland size, echogenicity of the parenchyma, and nodular lesions were evaluated.

Patients in whom the biochemical/immunological or ultrasonographic evaluation gave abnormal results were referred for endocrinological evaluation at the same single center, in order to define the diagnosis of autoimmune or nonautoimmune thyroid disease. The diagnosis of autoimmune thyroiditis was based on the presence of antiperoxidase antibodies (antibody titers stably >200 U/mL in at least 2 separate measurements) and characteristic ultrasound features (ie, nonhomogeneous pattern with diffuse reduction of echogenicity), according to Rago et al,[27] in the presence, but even in the absence of mild or overt hypothyroidism.[28] Also, patients with the presence of only antiperoxidase antibodies but normal morphofunctional thyroid parameters were classified as having autoimmune thyroid disease.[27] Thyroid atrophy was diagnosed in the presence of reduced thyroid volume and ultrasound-detected diffuse fibrosis of the gland. Graves' disease was diagnosed in patients with