Autoimmune Gastritis. A Clinicopathologic Study of 25 Cases

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Summary

The histopathological diagnosis of autoimmune gastritis (AG) in its early stages can be a diagnostic challenge. Even some advanced cases with complete atrophy of the corpus mucosa may be difficult to recognize. To establish the diagnosis of autoimmune gastritis, several histological features should be assessed and combined with immunostains for enterochromaffin cell-like (ECL) cells and G-cells. The main histological criteria include a mononuclear infiltrate within the lamina propria, foci of destruction of oxyntic glands, intestinal metaplasia (IM), pyloric metaplasia, and parietal cell pseudohypertrophy. These criteria were evaluated in our series of 25 patients with achlorhydria and/or megaloblastic anemia. Some of our patients presented with nonspecific gastrointestinal symptoms. The age ranged between 46 and 79 years; one male patient was only 31 years old. Histologically, the corpus mucosa displayed in all cases chronic inflammation with focal complete IM and advanced pyloric metaplasia. In 4 patients, oxyntic glands were destructed in some sites. There was a pancreatic metaplasia of acinar type in 2 patients and a minimal focal pseudohypertrophy of parietal cells in the 31-year-old man. A tubular adenoma with a low-grade dysplasia was found in one female patient. Immunohistochemically, chromogranin-A highlighted linear or nodular hyperplasia of ECL cells in 19 patients, and adenomatoid ECL hyperplasia in one case (80%). In the remaining cases hyperplasia of ECL cells could not be recognized from their normal count. In 13 cases (52%) a few ECL cells were seen also in IM. Regarding associated pathology, in one woman with nodular ECL cell hyperplasia, a gastric carcinoid was removed endoscopically. The reaction with gastrin antibody revealed in 11 cases (44%) a small number of G cells in IM in the corpus mucosa. In 18 patients, antral mucosa was examined as well. In 8 patients, the mucosa was normal; in 10 cases, a mild chronic inactive gastritis was diagnosed, and in 15 patients G-cell hyperplasia was found. In accordance with other studies, we show that the diagnosis of AG may be established microscopically in endoscopic specimens of the gastric body mucosa when histologic features and immunohistochemical detection of ECL and G cell hyperplasia are combined.
Key words: autoimmune gastritis – histology – immunohistochemistry - ECL cell hyperplasia – G cells

Souhrn
Autoimunní gastritis. Klinickopatologická studie 25 případů

Bioptické hodnocení autoimunní gastritidy (AG) je v časné fázi onemocnění a často i u pokročilého zánětu s kompletní atrofií korporální sliznice žaludku obtížné. Ke stanovení diagnózy AG se v posledních letech doporučuje posuzování několika histologických nálezů, doplněné imunohistochemickým průkazem buněk podobných enterochromafinním (ECL) buňkám a G buněk. Histologické nálezy zahrnují mononukleární infiltraci lamina propria, ložiskovou destrukci oxyntických žlazek, intestinální metaplazii (IM), pylorickou metaplazii a pseudohypertrofii parietálních buněk. Tato kritéria autoři použili při bioptickém vyšetřování korporální sliznice žaludku u 25 nemocných s achlorhydrií a/nebo megaloblastickou anémií; u části nemocných byly uvedeny nepříznačné gastrointestinální potíže. U 24 nemocných se věk pohyboval mezi 46–79 lety, jeden muž byl 31letý. Histologický nález v korporální sliznici žaludku odpovídal u všech nemocných chronické gastritidě s ložiskovou kompletní IM a s pokročilou pylorickou metaplazií, u 4 nemocných byla nalezena fokální destrukce oxyntických žlázek, u dalších dvou pankreatická metaplazie acinárního typu a u 31letého muže minimální ložisková pseudohypertrofie parietálních buněk. U jedné ženy byl diagnostikován tubulární adenom s dysplazií nízkého stupně. Imunohistochemické vyšetření s chromograninem-A prokázalo u 20 nemocných (80%) lineární nebo nodulární a jednou adenomatoidní hyperplazii ECL buněk, u ostatních nebylo možno rozlišit prostou hyperplazii od normálního počtu ECL buněk. U jedné ženy s nodulární hyperplazií ECL buněk byl při endoskopickém vyšetření odstraněn karcinoid. V reakci s protilátkou proti gastrinu se v 11 případech (44 %) v IM korporální sliznice vyskytovaly ojedinělé G buňky. U 18 nemocných byla sou-

časně vyšetřena sliznice antra žaludku. U 8 z nich měla sliznice normální nález, 10krát byla přítomna mírná chronická neaktivní gastritida a u 15 nemocných hyperplazie G buněk. Naše nálezy, podobně jako výsledky předchozích studií, prokázaly, že histologické vyšetření, doplněné imunohistochemickým průkazem ECL a G buněk umožňuje stanovit diagnózu AG v endoskopických biopsiích korporální sliznice žaludku.

Klíčová slova: autoimunní gastritis – histologie - imunohistochemické vyšetření – hyperplazie ECL buněk – G buňky

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Autoimmune gastritis (AG), or type A atrophic gastritis, is a chronic inflammatory process that typically involves the corpus mucosa in a diffuse manner (4, 8, 18). A high proportion of patients have circulating autoantibodies against the microsomes of parietal cells and intrinsic factor autoantibodies, which are detected in 55–60% cases. Thus a proportion of patients with AG will develop pernicious anemia due to vitamin B 12 deficiency (4). There is also a common association with other organ-specific autoimmune diseases, and patients frequently have shared autoantibodies against the various tissues (14). AG is a dynamic disease in which involvement of the mucosa increases in severity with age. In fully established AG, the body mucosa is inflamed and shows extensive atrophy with replacement of the oxyntic glands by intestinal and pyloric metaplastic epithelium, and enterochromaffin-like (ECL) cell hyperplasia. The antral mucosa tends to be spared, although there may be associated mild chronic gastritis. There is an absolute increase in the number of antral gastrin+ cells (G cells) in response to the hypochlorhydria, and this is accompanied by raised serum levels of gastrin. The hypergastrinemia has a trophic effect on the ECL cells in the glands of the body mucosa, leading to ECL cell hyperplasia (4, 9, 13, 18). Patients with AG may present with achlorhydria, hypergastrinemia, anti-parietal cell and/or anti-intrinsic factor antibodies, and pernicious anemia. In some cases, however, the manifestation of AG is nonspecific with gastrointestinal symptoms such as dyspepsia, nausea, vomiting, gastrointestinal reflux disease (13, 18) or unexplained microcytic anemia (18). A histologic diagnosis under these clinical manifestations of AG is difficult. Therefore, in our study of 25 cases of AG, we employed the recommended histological criteria and immunostains for chromogranin (to evaluate for ECL cells presence and hyperplasia) and gastrin (to exclude antral and antral-oxyntic transitional gastric mucosa) (4, 8, 13, 18), to establish the diagnosis of AG in endoscopic specimens of gastric body mucosa.

Material and Methods

The group of 25 patients included 14 men and 11 women. The age of 24 of them ranged between 46 and 79 years (mean age: men 68, women 65 years). One patient was only 31 years old. In 16 patients achlorhydria and/or megaloblastic anemia and atrophic gastritis were diagnosed clinically. Nine patients suffered merely from nonspecific gastrointestinal symptoms. Anti-parietal cell antibodies, anti-intrinsic factor antibodies, and serum gastrin level were not examined in any patient. The endoscopic examination with a biopsy was repeated once or twice in 4 men and 4 women in an interval of 1 month – 5 years. No patient had any other autoimmune disease. Proton pump inhibitors (PPI) were not applied in any patients. On endoscopy, one or two samples of the gastric body mucosa were obtained from each patient. In 18 patients, 1–2 samples of the antral mucosa were obtained as well (without an information of precise localization).

The specimens for microscopic examination were fixed in 10% neutral formol, embedded in paraffin using standard procedures and stained with hematoxylin-eosin, Periodic acid Schiff/-Alcian blue at pH 2.5, and with silver impregnation technique according to Warthin-Starry.

For immunohistochemistry, the following primary antibodies were employed: chromogranin-A (DAK-A3 pepsin 1:400 DAKO Glostrup), gastrin (Gastrin pepsin polyclonal, 1:500 DAKO Glostrup), MUC2 (Cep58, MW 1:400, Novocastra, Newcastle), MUC5AC (CLH2, MW 1:400, Novocastra, Newcastle), MUC6 (CLH5, MW 1:400, Novocastra, Newcastle). Sections 4 μ thick were cut from the specimen and placed on slide coated with 3-aminopropyltriethoxy-silane (Sigma). The sections were then deparaffinized and predigested by pepsin. The primary antibodies were visualized using the supersensitive streptavidin-biotin peroxidase complex (BioGenex, San Ramon, CA, USA). The color was