The diagnosis of gastritis

Michael Vieth

Helmut Neumann

Christina Falkeis

Abstract

After Babylonian confusion over the histological classification of gastritis, the Sydney system brought standardization and reproducibility to the diagnostic field of gastric biopsies. Even some shortcomings do not reduce the importance of the Sydney system for classification of gastritis. Essentially gastritis is a purely histological diagnosis. Herein we describe further diagnostic criteria for the diagnosis of gastritis and show the time-dependent changes in frequencies of various types of gastritis over more than 25 years at the Institute of Pathology in Bayreuth. Pathologists should be encouraged to address the etiology of inflammatory infiltrates to enhance the clinical value of a histological diagnosis on gastric biopsies.

Keywords classification; etiology; gastritis; histology; Sydney system

Introduction

Gastritis is a histological diagnosis. Prerequisites are at least two antral biopsies, each taken at 3 cm proximal the pyloric sphincter from the lesser and greater curvature and two biopsies from the corpus (body) close to the middle of the greater curvature. Gastritis itself is a diagnosis that was used quite frequently in the 19th century but later it evolved into a clinical diagnosis to describe upper abdominal complaints with widespread introduction of endoscopes, biopsy techniques and the re-discovery of *Helicobacter pylori* in 1983. The first description of gastric Helicobacter dates back to Italy in 1892 by Bizzozero. In fact, in 1958 the Greek physician John Lykoudis introduced antibiotic treatment for peptic ulcer disease and to "treat the infectious etiology of gastritis".[1] The diagnosis of gastritis has thereby evolved into confirming a possible etiology for the observed inflammation to inform further therapy.

The updated Sydney system is the classical classification system for grading and diagnosing gastritis. It was first introduced in 1990[2,3] and revised in 1994.[4] Before 1990, diagnosis of gastritis was non-standardized, non-validated and often not clinically relevant. The main problem was that diagnoses could not be compared worldwide. In addition to the histological component of the Sydney system, an endoscopic component was introduced but this was quickly abandoned with the realization that endoscopic criteria were poorly reducible and seldom correlated with the histologically based etiology of the gastritis.[5]

Michael Vieth *MD Director, Institute of Pathology, Bayreuth Clinic, Bayreuth, Germany. Conflicts of interest: none declared.*

Helmut Neumann *MD Consultant, Internal Medicine I, Erlangen University, Erlangen, Germany. Conflicts of interest: none declared.*

Christina Falkeis *MD Consultant, Institute of Pathology, Klinikum Bayreuth, Bayreuth, Germany. Conflicts of interest: none declared.*

The Sydney system brought convincing diagnostic tools and descriptions in the form of a visual semi-quantitative scale for pathologic evaluation. These allowed the pathologist standardization and validation of the diagnosis of gastritis.[6]

Before the Sydney system was introduced, for example, the German ABC-scheme of gastritis gave at least the etiological base for gastritis, such that A for stood for autoimmune gastritis, B for bacterial (later: Helicobacter) gastritis and C for chemical reactive gastritis.

It turned out that the ABC-scheme was the perfect addendum to the Sydney system with its easily reproducible grading scale that provided the etiology for the gastritis as an integral part of the diagnosis to such that the clinicians could easily plan further therapeutic steps.

On the other hand, the Sydney system also has a few shortcomings. The Sydney system was designed for antral and corpus biopsies only. There is no grading proposal for cardiac mucosa, although whether such an additional scheme would add any relevant information is debatable.[7] Other shortcomings are related to the grading itself: e.g. grading atrophy in the antrum is extremely difficult and in the corpus there has been debate concerning whether loss of glands close to lymphatic aggregates should be regarded and graded as atrophy or simply inflammation pushing glands aside.[8] Shortcomings of the etiology mainly revolve around the distinction between normal mucosa and chemical/reactive gastritis and the status after successful eradication of Helicobacter (so called ex-Helicobacter gastritis or post-Helicobacter gastritis). Validated criteria for these distinctions are not readily available. It is extremely difficult for pathologists to differentiate between gastritis with focal atrophy due to present or former Helicobacter infection and subsequent scar-forming e.g. after mucosal breaks and cases with true autoimmune gastritis with loss of parietal and chief cells leading to atrophy and a status of so called pre-atrophic autoimmune gastritis. This situation is further complicated by the notion that some patients, for unclear reasons, present with autoimmune gastritis with remnant islands of preserved oxyntic mucosa in the corpus. Further shortcomings also remain in the risk evaluation for gastric carcinoma. However, with the help of the Sydney system the so called corpus dominant Helicobacter gastritis showing more inflammation in the corpus or so called pangastritis with equal distribution of inflammation in antrum and corpus has been associated with a higher risk (up to 34 fold) for development of gastric carcinoma compared to the classical antrum predominant Helicobacter gastritis.[9] On the other hand, it is known that finding intestinal metaplasia and/or atrophy close to the angularis zone at the lesser curvature of the gastric body is a risk factor for gastric carcinoma but this zone is not one of the biopsy sites of the Sydney system.[4] This observation has led to several more intensified biopsy protocols and scoring systems such as OLGIM and OLGA. These scoring systems are somewhat helpful in identifying patients at higher risk for gastric carcinoma but these are most applicable to patients with Helicobacter gastritis and lead to unrealistically high cancer risk scores in patients with chemical/reactive gastritis and intestinal metaplasia.[10]

Endoscopic diagnosis of gastritis

Endoscopy is essential in the diagnostic evaluation of gastritis. However, only histopathological analysis of biopsy specimens

can offer reliable diagnosis of gastritis and preneoplastic gastric conditions. Very recently, the *European Society of Gastrointestinal Endoscopy*, the *European Helicobacter Study Group*, the *European Society of Pathology*, and the *Sociedade Portuguesa de Endoscopia Digestiva* have combined efforts to develop evidence-based guidelines for the management of patients with precancerous conditions of the stomach. These guidelines state that standard white-light endoscopy cannot accurately differentiate between and diagnose preneoplastic gastric conditions. Various gastric endoscopic appearances have been proposed to be reliable for in vivo diagnosis of gastritis. These include antral nodularity for *Helicobacter pylori* gastritis or absence of gastric rugal folds and presence of visible vessels in the gastric mucosa for severe atrophic gastritis. Nevertheless, while the former has a predictive value of >90%, it is only present in a minority of patients. The latter suffers from a low sensitivity of 48% and 14%, in the gastric corpus and antrum, respectively.[11] Within recent years, advanced endoscopic imaging techniques have been implemented into daily routine clinical practice. These include dye-based and dye-free chromoendoscopy techniques, optical magnification endoscopy, and optical biopsy techniques, including confocal laser endomicroscopy and endocytoscopy. Various studies have already suggested that dye-based chromoendoscopy, particularly when used with optical magnification, can detect intestinal metaplasia. The most commonly used dye-agents include methylene-blue, indigo-carmine, or acetic acid, which are mostly applied via standard spraying catheters. Recent data have also indicated that dye-free chromoendoscopy, using either optical chromoendoscopy (i.e. Narrow Band Imaging; NBI) or virtual chromoendoscopy (i.e. FICE, i-scan) have a good sensitivity and specificity for diagnosis of gastric lesions. Similar results have also been shown for optical biopsy techniques, allowing high-power magnification of the tissue thereby allowing analysis of cellular and subcellular features of the gastric epithelium. In this context, it has also been shown that optical biopsy techniques have the potential to diagnose *H. pylori* and associated type-B gastritis.[12]

Despite the ongoing development of advanced endoscopic imaging techniques, the conventional, physical biopsy is not to be replaced. The most widely accepted classification and grading system of gastritis is reflected in the updated Sydney system. The system recommends two biopsies from the antrum (3 cm from the pylorus, greater and lesser curvatures), one from the *incisura angularis*, and two additional biopsies from the corpus (one from lesser curvature, 4 cm proximal to the incisura, and from the middle of the greater curvature). Although the additional value of biopsies from the incisura remains controversial, biopsy sampling and clear labeling in separate vials is of pivotal importance as atrophic gastritis and intestinal metaplasia are regularly inhomogeneously distributed throughout the stomach.[4]

How to diagnose histologically

Since using the Sydney system remains controversial for routine evaluation, the following discussion is more practical. Cancer risk assessment systems like OLGA or OLGIM will not be further discussed.

Gastric mucosa without pathological changes usually shows few lymphocytes and plasma cells esp. in the antrum and no atrophy nor intestinal metaplasia. Sparse lymphatic aggregates can be seen in some cases, especially in corpus mucosa.

Chemical/reactive gastritis

In chemical/reactive gastritis, which by definition is limited to the antral mucosa, lymphocytes and plasma cells within the lamina propria are slightly increased leading to the Sydney grading: "slightly chronic, not active gastritis". There is a possibility of overdiagnosing normal gastric mucosa as chemical reactive gastritis. In order to avoid this, further criteria should be fulfilled, namely increasing number lamina propria ascending smooth muscle fibers, apical fibrosis, capillary ectasia and foveolar hyperplasia of the surface epithelium[4,12] (Figure 1).

It should be noted, however that after successful Helicobacter eradication, both antrum and corpus show slightly to moderately increased numbers of lamina propria lymphocytes and plasma cells but no active inflammatory changes and frequently basal remnants of lymphoid follicles and aggregates and often a slight tendency towards regenerative changes. In some individuals, these changes may persist after eradication therapy, whilst in others can evolve over time (especially in the antrum) into a histological picture similar to that of chemical reactive gastritis. A minority seems to normalize over time.[13] So called serum scars tend to normalize within 3 months. In some individuals IgG antibodies can persist for years.[14]

Ex-*Helicobacter* gastritis (prior or post-*Helicobacter* gastritis)

The diagnosis of so called ex-Helicobacter gastritis can easily be made if previous reports indicate a prior active *Helicobacter* gastritis and previous eradication therapy or antibiotic treatment for other reasons. From these cases it is possible to extrapolate to identify cases with ex-Helicobacter gastritis even without the knowledge of prior eradication therapy or prior proven active Helicobacter gastritis. Such cases display lymphoid aggregates and follicles in combination with a slight or moderate chronic gastritis of antral and corpus mucosa.[13]

Helicobacter gastritis

Active Helicobacter infection or Helicobacter gastritis should be diagnosed whenever active inflammatory infiltrates can be seen. In *H. pylori* gastritis these infiltrates should be diffuse rather than focal, in contrast to cases with *Helicobacter heilmannii* infection, in which inflammatory infiltrates are more focal. A band-like inflammatory infiltration of the upper half of the mucosa is typical. Chronicity of the inflammation is manifest by infiltration of lymphocytes and plasma cells. According to the Sydney system, activity is diagnosed from the number of neutrophilic granulocytes. Sparse neutrophilic granulocytes within the lamina propria are graded as slight activity, infiltration into the surface epithelium is graded as moderate activity and presence of foveolar abscesses is graded as marked activity. Chronicity depends of the number of lymphocytes and plasma cells. Sparse lymphocytes and plasma cells can be seen in normal gastric mucosa, can make it difficult to differentiate normal versus slight chronic gastritis. In our practice, we regard all infiltrates above sparse as slight chronic infiltration (space in between the inflammatory cells about five