The Detection of Premalignant Gastric Lesions by Conventional and Magnifying Endoscopy

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Introduction: Early diagnosis of gastric neoplasia involves both the detection and surveillance of patients with premalignant gastric lesions. Magnifying endoscopy allows the analysis of the fine mucosal structure and microvascular architecture.
Material and methods: The aim of our study is to identify specific patterns associated with premalignant gastric lesions by magnifying endoscopy in conjunction with chromoscopy. We performed conventional upper endoscopies and we selected a number of patients for chromodiagnostic and magnification. We classified the endoscopic patterns in normal and abnormal (modified) patterns. Target biopsies were obtained from magnified areas and we analyzed the correspondence with the histological findings.
Results: We identified specific pit patterns for normal gastric mucosa and for inflamed mucosa. A tubular pattern was associated with the detection of intestinal metaplasia. An irregular pattern and abnormal microvessels were endoscopic findings associated with the detection of high-grade dysplasia. An irregular form of collecting venules was detected in areas with atrophic gastritis.
Conclusions: An initial selection of patients based on conventional endoscopic findings is mandatory. Gastric mucosal changes identified by magnifying endoscopy raise the number of detected premalignant lesions by targeted biopsies. Our work emphasizes the current challenges related to the use of these endoscopic methods.

Keywords: magnifying endoscopy, chromoendoscopy, conventional endoscopy, patterns, premalignant

Introduction

Gastric carcinoma represents the second most common cause of cancer deaths. Advanced cancer is the final step in a process of morphological transformation of gastric mucosa, from chronic gastritis and gastric atrophy to intestinal metaplasia, dysplasia and invasive neoplasia. Considerable efforts have been made for the development of tools that are to be used for the recognition of premalignant gastric lesions. Conventional endoscopy remains an important tool for the diagnosis of premalignant changes of gastric mucosa, based on multiple biopsies. The use of novel endoscopic imaging technologies, such as magnifying endoscopy, permits an analysis of the mucosal architecture and increases the chance of detecting premalignant lesions by targeted biopsies. We performed magnification endoscopy in conjunction with chromoscopy in order to identify atrophic gastritis, intestinal metaplasia, dysplasia and to establish the practical usefulness of these methods. The goal of our investigation was to detect specific patterns corresponding to premalignant gastric lesions on histopathologic evaluation.

Material and methods

We present the preliminary results of a three years duration study that started in September 2010. In this stage of the study we intend to present different patterns obtained by magnifying chromoendoscopy in patients examined between September 2010 and February 2011 as well as the current challenges in performing the endoscopic procedures and in interpretation of images. Informed consent was obtained from all patients before the endoscopic examinations. All magnification endoscopy procedures were performed using an Olympus Gif-Q 160Z high-magnification endoscope, which provides up to 115 times magnification. The patients were under sedation with Propofol. As a first step, we performed conventional upper endoscopies. We identified patients with atrophic gastritis, gastric polyps or other gastric lesions: erosions, ulcers, nodular appearance of the mucosa, erythema. Patients with advanced gastric cancer were excluded from the study. Patients with suspected gastric diseases were examined using the magnifying endoscopy, in order to improve the detection of premalignant lesions. For better identification of the lesions, we used magnification in conjunction with chromoscopy (methylene blue or acetic acid). We took endoscopic photographs with relevant conventional and magnified views and we obtained targeted biopsies from these areas. We studied the correlation between mucosal patterns and the histological conditions. We classified the magnifying endoscopic pattern as follows: normal patterns and abnormal (modified) patterns. Magnified images were evaluated by three endoscopists. Previous published reports on normal magnified mucosa and modified mucosa with corresponding patterns were used for proper evaluation. One pathologist with experience in gastrointestinal tract histopathology examined all biopsied specimens in the Department of Pathology. A chi-squared test was adopted for comparisons between endoscopic patterns and histological findings and a p-value of less than 0.05 was considered statistically significant.

Results

Twenty-eight patients were enrolled in our study. All the patients went through conventional endoscopy followed

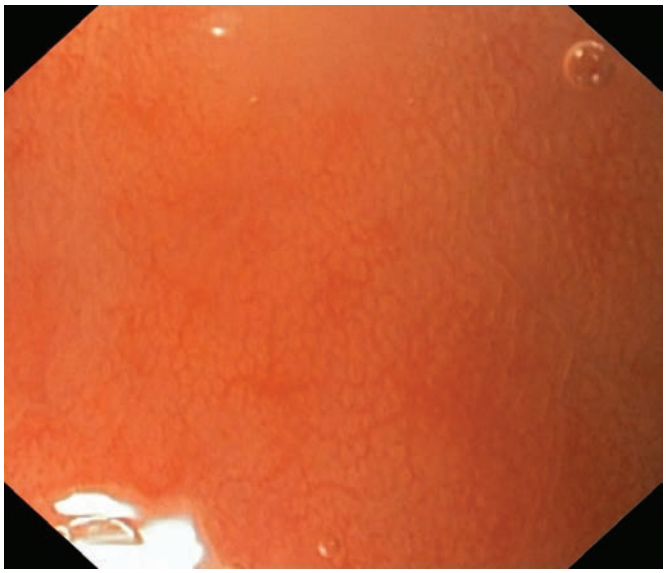

Fig. 1. Magnified endoscopic view of normal gastric body: honeycomb-like appearance of subepithelial capillary network (SECN) and the collecting venules (CVs)

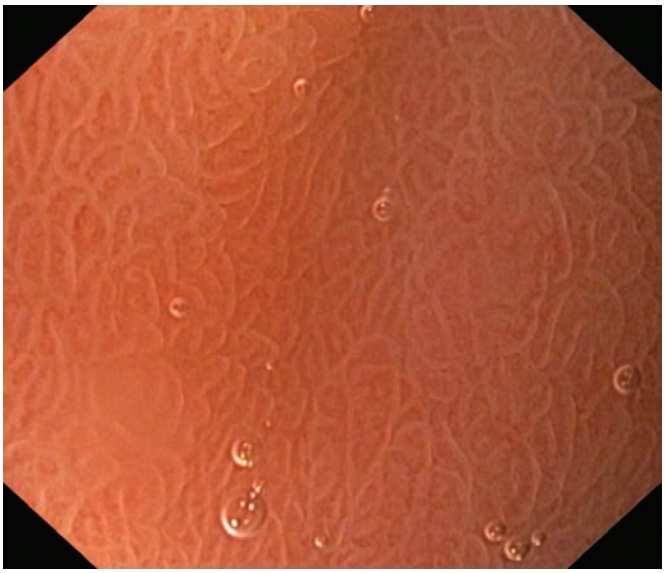

Fig. 2. Magnified endoscopic view of normal antral mucosa: regular coil-shaped SECN pattern

by magnifying endoscopy examinations. In the stomach, we analyzed two different anatomical findings by magnifying endoscopy: the mucosal structure and the microvascular architecture. We detected specific magnified views in the gastric body and antral area. In the normal gastric body we noticed a specific honeycomb-like appearance of subepithelial capillary network (SECN) and the collecting venules (CVs) (Fig. 1). Microvascular architecture of the antral mucosa showed a specific coil-shaped SECN, without the detection of CVs (Fig. 2).

Chronic gastritis and atrophic gastritis

We obtained a magnified appearance of large white pits and surrounding erythema that were associated to Helicobacter pylori (Hp) induced gastritis; collecting venules and regular SECN were not visible (Fig. 3). We detected 18 areas with an irregular form of collecting venules (Fig. 4). All these areas were atrophic gastritis on histologic evaluation ($p = 0.0614$). Magnifying endoscopic observation was helpful for the identification of the patients with extended atrophy. These patients were selected for dye application and targeted inspection, followed by biopsies from suspicious areas. In some situations the differentiation between modified mucosa due to inflammation or malignant transformation is difficult. The presence of irregular vessels and the variation in the caliber of vessels are specific vascular patterns in early gastric cancer. We performed conventional endoscopies and we selected the patients with superficial elevated lesions or flat lesions for magnification. We detected the loss of regular SECN pattern on magnification without the presence of irregular microvessels in 17

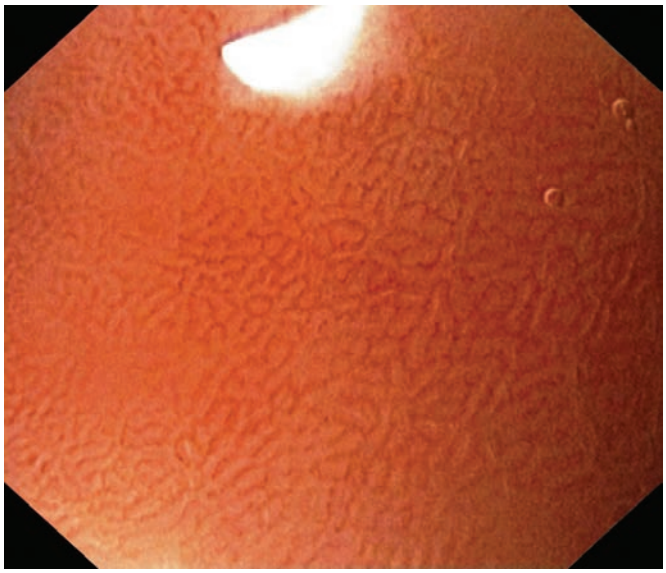

Fig. 3. Magnified endoscopic view of Hp-associated gastritis mucosa: white pits surrounded by erythema

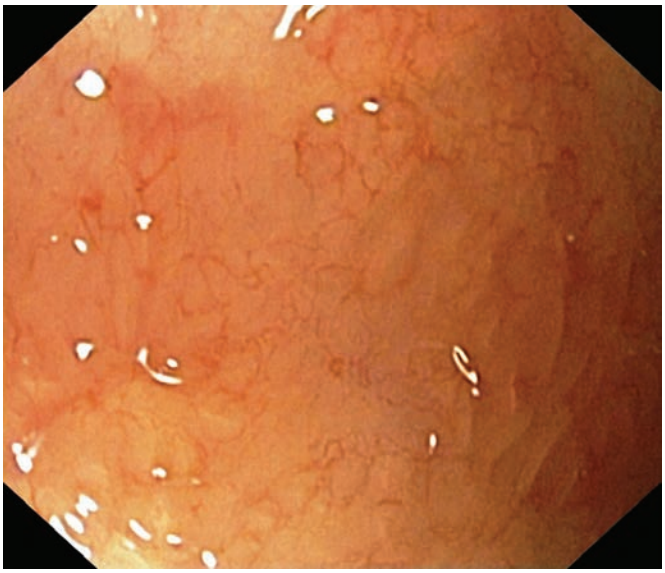

Fig. 4. Magnified endoscopic view of atrophic gastritis: irregular form of CVs

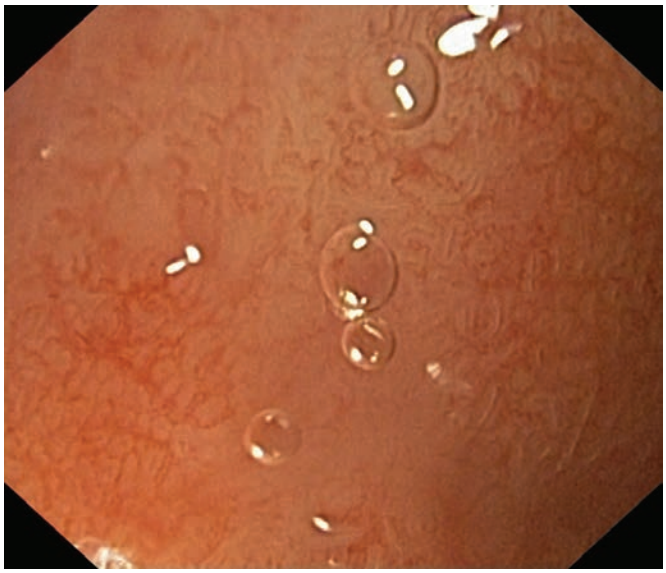

Fig. 5. Endoscopic high magnification image of antral mucosa: areas with the disappearance of the regular SECN pattern

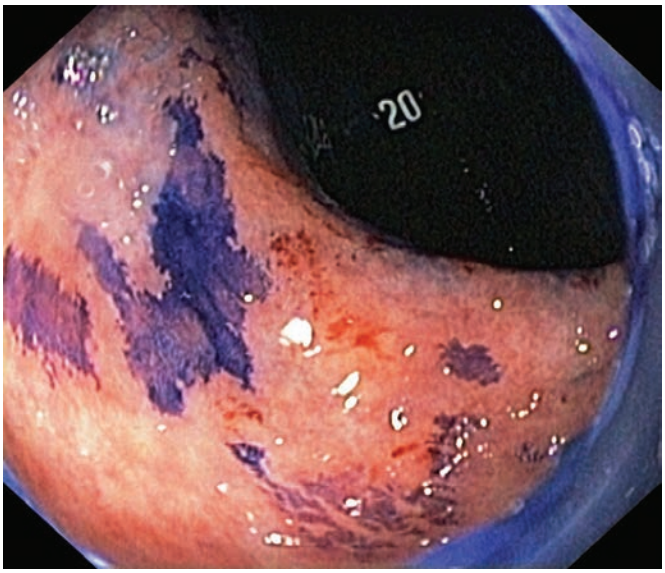

Fig. 6. The detection of stained areas after methylene blue application

areas (Fig. 5). The histopathological evaluation demonstrated chronic gastritis with intestinal metaplasia in 14 of these modified areas (p = 0.0004).

Gastric intestinal metaplasia and low-grade dysplasia (LGD)

We applied a mucolytic agent (10% N-acetylcisteine) on the mucosa followed by a solution of methylene blue 0.5% that was sprayed over the mucosa. Three minutes later we washed the mucosa with water and we removed the methylene blue in excess. Methylene blue is a vital stain that is taken by absorbent tissue such as the small intestinal epithelium. We used it for the better detection of intestinal metaplasia in gastric mucosa (Fig. 6). Twenty-one areas of mucosa with blue homogeneous staining were obtained and specific pit patterns were identified by magnification: tubular pits, blue small pits (Fig. 7). Targeted biopsies were taken from these areas and the diagnosis of intestinal metaplasia was confirmed in 20 cases (p = 0.0013). We detected 9 areas showing a heterogeneous staining mucosa and the loss of clear pattern (Fig. 8). It was difficult to achieve a good interobserver agreement when different patterns were not clearly detected. Targeted biopsies are mandatory to clarify the diagnosis, because the detection of irregular patterns raises a high suspicion for dysplasia. In these cases, 5 areas with intestinal metaplasia (p = 0.637) and 3 areas with LGD were identified by histopathologic evaluation.

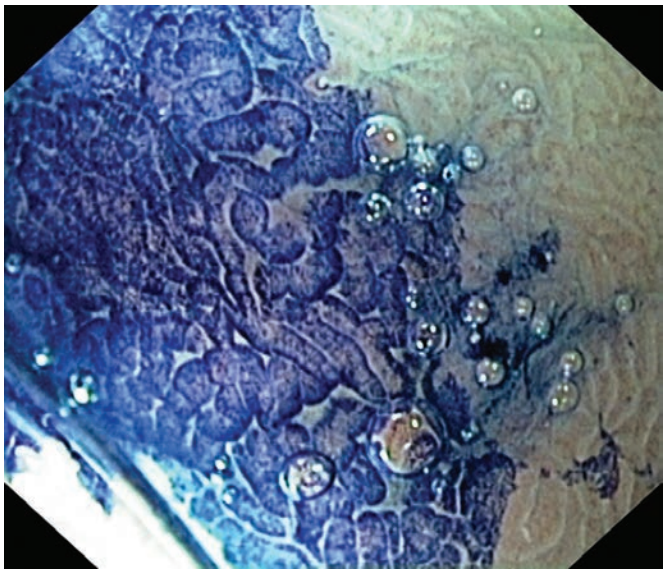

Fig. 7. Stained areas showing tubular pit pattern on magnification

High-grade dysplasia (HGD)

A patient with modified antral mucosa was examined by conventional endoscopy that showed small reddened lesions and erosions. We performed magnifying endoscopy using 10 ml of 1.5% acetic acid. This contrast stain highlights the surface of the mucosa, allowing the identification of subtle mucosal patterns. Under magnification, we identified 4 areas presenting an irregular pattern that replaced the normal coil-shaped pattern. We also detected abnormal microvessels and variation of vessel caliber (Fig. 9). Biopsy specimens were taken in each area with a different endoscopic pattern. The histopathologic examination showed HGD in all of these areas (p = 0.0286).

Discussions

The diagnosis of premalignant lesions and the performance of surveillance depend on random biopsy technique. Because these lesions are multifocal and may be present in normal appearing mucosa, the diagnosis can be missed on conventional examination. Magnification chromoendoscopy has been proposed as a useful tool for the detection of gastric premalignant lesions [1] and early neoplasia [2] but the selection of patients based on endoscopic findings at previously conventional examination could enhance the diagnostic accuracy. The first in vivo description of charac-

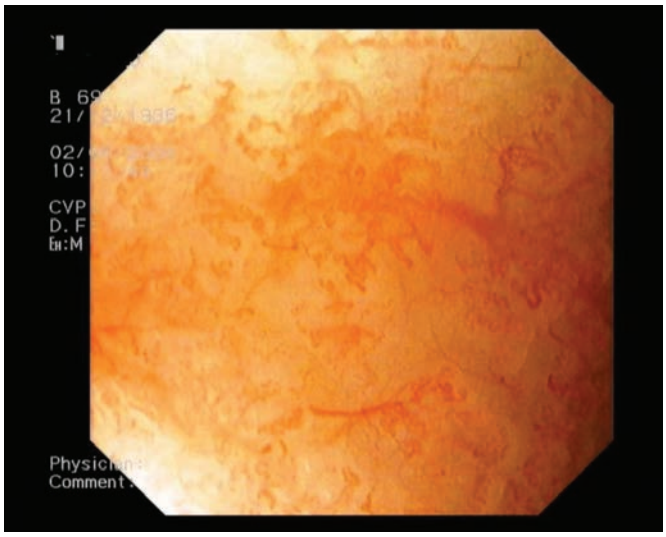

Fig. 9. Endoscopic high magnification image of antral mucosa after acetic acid application showing abnormal microvessels: irregular length, caliber and distribution

teristic patterns of the gastric mucosa belongs to Yagi [3] and Yao [4]. We observed these specific patterns of gastric mucosa free from pathologic changes in order to differentiate them from the mucosal changes due to inflammation, atrophy or neoplasia. We tried to identify the endoscopic patterns associated with premalignant lesions on histologic evaluation. The areas showing an irregular form of CVs were associated with atrophic gastritis. The blue stained areas exhibiting tubular pattern are strong predictors for the detection of intestinal metaplasia. The irregular pattern and abnormal microvessels are characteristic findings for HGD. Mucosal patterns corresponding to intestinal metaplasia and dysplasia were previously defined by Dinis-Ribeiro et al. [5]. It is important to determine whether premalignant lesions are localized or diffusely distributed into the gastric mucosa. From this point of view, the substantial contribution of magnifying chromoendoscopy was emphasized by our work. After dye application and magnification, we identified areas with atrophic gastritis and intestinal metaplasia, impossible to detect on conventional endoscopy. Some authors reported major challenges that may hinder the routine use of magnification chromoendoscopy: the lack of endoscopists specifically trained in these techniques, the lack of standardization of this method and the absence of a unified classification of the mucosal patterns [6,7]. We are also facing similar problems in our clinical practice, the interpretation of different endoscopic images being quite challenging in some situations. Controlled studies on a larger number of patients are needed before the widespread use of magnification endoscopy and chromoscopy in daily practice. In Romania this endoscopic technique is available only in four gastroenterology departments, our work being mainly focused on the clinical application of the method in order to achieve standardized terminologies and criteria.

Conclusions

Magnifying endoscopy in association with chromoscopy provides a promising alternative for the detection of premalignant gastric lesions and for a better surveillance of the patients. The selection of the patients based on previous conventional endoscopic examination is mandatory in order to increase the diagnostic accuracy.

Acknowledgement

This paper is partly supported by the Sectorial Operational Programme Human Resources Development (SOP HRD), financed from the European Social Fund and by the Romanian Government under the contract number POSDRU 60782.

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