The Usefulness of Magnifying Chromoendoscopy with Methylene Blue in the Detection of Specialized Intestinal Metaplasia and Dysplasia in Barrett's Esophagus — a Preliminary Report

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Background: Barrett's esophagus appears in relation with gastroesophageal reflux disease, which damages the normal squamous mucosa; the injury heals through a metaplastic process in which columnar cells replace squamous ones. The specialized intestinal metaplasia has a malignant potential, but the diagnosis is often difficult in conventional endoscopy.
Aim: Our purpose was to evaluate the results of magnifying chromoendoscopy using methylene blue in the diagnosis of specialized intestinal metaplasia and dysplasia in Barrett's esophagus.
Methods: Nine patients with proven or suspected Barrett's esophagus in conventional endoscopy underwent magnified chromoendoscopy with methylene blue for confirming and/or monitoring the intestinal metaplasia or for detecting dysplasia. Biopsies were taken from sites coloured with methylene blue and from regions with particular patterns according to Endo's classification.
Results: Specialized intestinal metaplasia was reported in 16 out of 29 biopsies; one biopsy proved low grade dysplasia and two samples showed indefinite for dysplasia. The sensitivity and specificity of methylene blue staining in detection of specialized intestinal metaplasia were 87% and 66% respectively (p=0.005). Taking into consideration Endo's classification, tubular and villous patterns had a significant correlation with SIM detection (p=0.0004) with a sensitivity and a specificity of 66% and 100%.
Conclusions: Magnifying chromoendoscopy with methylene blue allows targeted biopsies for SIM and dysplasia detection; it also allows the selection of the site of the biopsy according to pitpattern.

Keywords: magnifying chromoendoscopy, specialized intestinal metaplasia, methylene blue, pitpattern

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Introduction

Barrett's esophagus is a condition in which the normal non-keratinized squamous epithelium lining in the distal oesophagus is replaced by columnar epithelium: gastric (or fundic), transitional (or cardial) and intestinal (or specialized) metaplasia. Barrett's esophagus (BE) is a pre-malignant condition because specialized intestinal metaplasia (SIM) is associated with an increased risk of esophageal adenocarcinoma [1,2]. The diagnosis of BE relies initially on the endoscopic recognition of the columnar lined distal esophagus and is confirmed by histological examination. Video endoscopy is the first examination used to visually detect esophageal mucosal pathology and it allows the endoscopist to identify abnormal tissue, but this endoscopic method has some limitations: long procedure because of increased number of biopsies, risk of missing zones of dysplasia or even microinvasive adenocarcinoma [3]. Magnified chromoendoscopy is a special technique in which staining agents are applied to the esophageal mucosa to improve visualization of the Barrett mucosa. The stains enable the endoscopists to see surface patterns so that abnormalities such as dysplasia or even early neoplasia, lesions that are difficult to detect with white light endoscopy, can be detected more easily with diagnostic and therapeutic implications for clinical care [4,5].

Material and methods

This is a prospective, single center study, conducted between 2008–2010, in the Gastroenterology Clinic of the County Emergency Clinical Hospital of Tîrgu Mureş. Our study population consists of 51 patients with proven or suspected BE in white light videoendoscopy. Nine of these patients underwent magnified chromoendoscopy with methylene blue (MB) for confirming and/or monitoring the intestinal metaplasia or for detecting dysplasia. The equipment was composed of an Olympus GIF Q160Z, using an optical magnification up to 115 times. Magnified endoscopy was the standard first-intention procedure to search for spontaneous abnormalities of the oesophageal mucosa and magnified mucosal pit patterns of Barrett epithelium were analyzed and classified into 5 types according to Endo T. classification: Pattern I: round pits, Pattern II: straight type, Pattern III: long oval type, Pattern IV: tubular type and Pattern V: villous type [6]. Then, MB 0.5% was flushed from the upper to the lower portion of the distal oesophagus, followed after 2–3minutes by a water rinse to remove excess dye. Biopsy samples for histopathologic

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Table I. Detection of specialized intestinal metaplasia and dysplasia in sites stained or not stained with methylene blue

	Number of biopsies	Specialized intestinal metaplasia	Gastric metaplasia	Low grade dysplasia	Indefinite for dysplasia
Methylene blue stained sites	19	14 (73.6%)	2 (10.5%)	1 (5.26%)	2 (10.5%)
Methylene blue not stained sites	10	2 (20%)	8 (80%)	0	0
Total	29	16 (55.1%)	10 (34.4%)	1 (3.4%)	2 (6.8%)

Table II. Endo's classification: number of biopsies from regions with particular pitpatterns and frequency of specialized intestinal metaplasia and dysplasia

Pitpattern	Number of biopsies	SIM	Gastric metaplasia	Low grade dysplasia	Indefinite for dysplasia
Small round I	3 (10.3%)	0	3 (100%)	0	0
Straight II	2 (6.8%)	0	2 (100%)	0	0
Long oval III	0	0	0	0	0
Tubular IV	10 (34.4%)	6 (60%)	2 (20%)	1 (10%)	1 (10%)
Villous V	14 (48.2%)	10 (71.4%)	3 (21.4%)	0	1 (7.1%)
Total	29	16 (55.1%)	10 (34.4%)	1 (3.4%)	2 (6.8%)

examination were taken from the regions coloured with MB, from the regions with patterns described by Takao Endo classification, especially from the regions with patterns most often related to SIM, according to Endo's study (tubular and villous).

Results

Our study population was composed of 51 Barrett patients (19 women and 32 men), average age 58 years (range 28–83 years) with histologically confirmed columnar metaplasia after conventional endoscopy. From these patients, 9 (17.6%) underwent magnified chromoendoscopy with MB and we obtained 29 biopsies, with an average of 3 biopsies per patient. None of the patients enrolled in the study had histologically proven dysplasia after conventional endoscopy with random biopsies, but 7 patients have been previously diagnosed with SIM.

The histological examination reported SIM in 16 biopsies out of 29 (55.1%), in eight of the nine patients enrolled in our study. The rest of the biopsies revealed low grade dysplasia (in one biopsy – 3.4%), indefinite for dysplasia (two samples – 6.8%) and gastric metaplasia (10 biopsies – 34.4%).

Three patients had long segment Barrett's esophagus (LSBE) (between 3 and 4 cm) and 6 patients a short segment Barrett's esophagus (SSBE) (below 3 cm); among these, the height was less than 1 cm in 4 patients. The average height of the examined Barrett's esophagus was therefore 1.6 cm (0.5 cm to 4 cm). SIM was found in 2 patients with LSBE (66.6%) and in all patients with SSBE. The patient with low grade dysplasia had SSBE and the biopsies indefinite for dysplasia were found in a patient with LSBE.

Out of 29 biopsies in Barrett's patients, 19 (65.5%) were taken from MB staining mucosa; 14 of them proved SIM (73.6%) and 3 (15.7%) showed low grade dysplasia and indefinite for displasia. Ten biopsies were taken from sites not stained with MB; histology proved SIM in two biopsies (20%); 8 samples from unstained areas were negative for SIM. There was a significant correlation between MB staining and diagnosis of SIM in histology (p=0.005). Sensitivity and specificity of MB staining in detecting SIM was 87% and 66% respectively (Table I).

Of the 29 biopsies, magnified chromoendoscopy reported pattern IV and V in 24 (82.7%) and pattern I and II in 5 biopsies (17.2%) (Table II). No sample with small round and straight patterns according to Endo's classification had SIM or dysplasia; those patterns corresponded to gastric metaplasia. SIM was frequent in sites covered with tubular (60%) and villous (71.4%) patterns. We also found a significant correlation between tubular and villous patterns and the positive histology for SIM (p=0.0004), with a sensitivity of 66%. Among of the 29 studied biopsies, low grade dysplasia was found in one biopsy with tubular pattern; two biopsies showed indefinite for dysplasia and the pitpatterns were tubular and villous. The low grade dysplasia and the indefinite for dysplasia samples were found in two patients; the histological examination in these patients reported only specialized intestinal metaplasia after conventional endoscopy with random biopsies.

Discussion

In a Japanese study, Yagi K et al showed that magnifying endoscopy with methylene blue selectively detects specialized intestinal metaplasia with a sensitivity of 84.8% and a specificity of 91.7% [7]. Canto et al described a very high sensitivity (95%) and specificity (97%) of MB staining in SIM detection [8]. In other studies the method had a sensitivity ranged from 72 to 75% and a specificity from 32 to 46 % [9,10]. In our study magnified endoscopy with MB staining had a sensitivity of 87% and specificity of 66% in detection of SIM. Three samples taken from methylene blue stained sites detected low grade dysplasia and indefinite for dysplasia.

We found differences in the frequency of SIM in relation with particular pitpatterns, with a significant correlation between patterns evaluated according Endo's classification and histology, which can potentially select the biopsies. SIM was found only in tubular and villous pat-

terns with a sensitivity and a specificity of 66% and 100% respectively; small round and straight patterns were characteristic of gastric metaplasia. In Endo's study, SIM was found in tubular (100%) and villous pattern(100%).

Conclusions

In our preliminary study, magnifying chromoendoscopy in methylene blue stained sites had a high sensitivity and specificity in detection specialized intestinal metaplasia in Barrett's esophagus. The magnifying chromoendoscopic patterns indicative of specialized intestinal metaplasia were tubular and villous with diagnostic implications, allowing selection of the site of the biopsy according to pitpattern.

When we compared in our study magnifying chromoendoscopy with methylene blue and conventional endoscopy for the detection of dysplasia, the first biopsy technique proved to be superior. Random biopsies in conventional endoscopy missed both our patients with low grade dysplasia and indefinite for dysplasia.

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