Journal of Gastroenterology, Hepatology and Endoscopy

Case Report
Published: 13 Mar, 2019

Endoscopic Changes in Patients with Barrett's Esophagus and Dysplasia

Anido Escobar V[1], Brizuela Quintanilla R[1], Garcia-Menocal JL[1], Piñol Jimenez F[1], Armenteros Torres M[4], Infante Velázquez M[2] and Betancourt Navarro A[6]*

[1]National Center for Minimally Invasive Surgery, Cuba

[2]Institute of Gastroenterology, Cuba

Abstract

Introduction: Barrett's Esophagus (EB) is the most relevant premalignant condition for the development of esophageal adenocarcinoma and the presence of dysplasia is a marker of progression.

Objectives: To identify the difference in endoscopic findings in a group of patients with BE and dysplasia in its different degrees.

Material and Method: An observational, descriptive, cross-sectional study with 86 patients with a diagnosis of BE treated at the National Center of Minimally Invasive Surgery, between January 2014 and January 2016. There was a comparison between the presence of esophagitis and its grade, hiatal hernia and the length of the segment affected, according to the presence or absence of dysplasia, which was determined by applying a study protocol.

Results: We included 52 male patients (60.5%) and 34 female patients (39.5%), the average age was 49.07 ± 15.5 years. 49 cases had no dysplasia (57%), there was high-grade dysplasia in five cases (5.8%) and low-grade dysplasia in 32 (37.2%). There was a predominance of patients without esophagitis (39.5%) or grade A erosive esophagitis (33.7%), and of these, 16.2% had low grade dysplasia. Barrett's esophagus of short segment was found in 69.7%; 56.9% of the patients had hiatal hernia, 17.4% had low grade dysplasia.

Conclusion: Mild erosive esophagitis and hiatal hernia were related to the presence of dysplasia, especially low grade, after the application of a study protocol during endoscopy.

Keywords: Barrett's esophagus; Dysplasia; Endoscopic diagnosis

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Correspondence:
Anido Escobar V, National Center for Minimally Invasive Surgery, Cuba, E-mail: vivanne@cce.sld.cu

Received Date: *19 Feb 2019*
Accepted Date: *11 Mar 2019*
Published Date: *13 Mar 2019*

Citation:
Anido Escobar V, Brizuela Quintanilla R, Garcia-Menocal JL, Piñol Jimenez F, Armenteros Torres M, Infante Velázquez M, et al. Endoscopic Changes in Patients with Barrett's Esophagus and Dysplasia. J Gastroenterol Hepatol Endosc. 2019; 4(2): 1057.

Introduction

Although in healthcare practice it is common to refer to the changes that occur with the replacement of the epithelium in the distal segment of the esophagus as "Barrett's Esophagus" (BE), in the endoscopic report the term "endoscopic suspicion of esophageal metaplasia" should be used to define these changes [1]. BE has a classic endoscopic appearance of mucosa of "salmon red" color that extends approximately to the esophagogastric junction, almost always in the form of columnar type mucosa. It is also possible to identify islands of columnar mucosa, proximal to the Z line [2]. Measuring the length in cm, of the suspicious BE lesions, from distal to proximal, it is one of the most important elements in the endoscopic description. Most authors consider it useful to classify the BE shorter than or longer than 3 cm, which apparently is associated with a higher risk of progression to adenocarcinoma [3]. The reliable diagnosis of BE depends, first on the effective recognition of the endoscopic characteristics that allow to suspect its presence, followed by an adequate biopsy of esophageal mucosa that makes it possible to diagnose the presence of intestinal metaplasia and dysplasia [4]. The histological samples provide information about the type of columnar epithelium which it is present: gastric, fundic or intestinal type and it is also necessary to define the presence and degree of dysplasia, according to defined histological characteristics [5]. Based on this, therapeutic decisions are made and endoscopic surveillance programs have been established [6]. Endoscopic diagnosis is improved by the application of work protocols that include observation with white light, stains and magnification.

Given that the presence of dysplasia has been related to the probability of developing adenocarcinoma of the esophagus, which is an aggressive and mutilating disease, with a survival rate of only 18% at 5 years [7], the diagnosis of dysplasia constitutes the first step for its subsequent

Table 1: Evaluation of endoscopic features according dysplasia's grades.

Endoscopic features		No dysplasia (n=49)	Low grade dysplasia (n=32)	High grade dysplasia (n=5)	Total (n=86)
Presence of esophagitis	Normal	22 (25.5%)	10 (11.6%)	2 (2.3%)	34 (39.5%)
	Non erosive	0	3 (3.4%)	0	3 (3.4%)
	A Grade	13 (15.1%)	14 (16.2%)	2 (2.3%)	29 (33.7%)
	B Grade	5 (5.8%)	2 (2.3%)	0	7 (8.1%)
	C Grade	1 (1.1%)	3 (3.4%)	0	4 (4.6%)
	D Grade	8 (9.3%)	0	1 (1.1%)	9 (10.4%)
Hiatal Hernia	Yes	32 (37.2%)	15 (17.4%)	2 (2.3%)	49 (56.9%)
	No	17 (19.7%)	17 (19.7%)	3 (3.4%)	37 (43%)
Type of Barrett's esophagus	C 1	6 (6.9%)	9 (10.4%)	0	15 (17.4%)
	M 1-3	35 (40.6%)	20 (23.2%)	5 (5.8%)	60 (69.7%)
	M>3	8 (9.3%)	3 (3.4%)	0	11 (12.7%)

follow-up and endoscopic treatment during the early stages of the development of adenocarcinoma. To contribute to this diagnosis, starting from the endoscopic study, this research has been carried out in order to determine if there are differences in the endoscopic presentation of BE according to the presence or absence of dysplasia and its grades.

Material and Method

An observational, descriptive cross-sectional study was carried out which included all the patients with a diagnosis of BE who were treated in the Endoscopic Department of the National Center for Minimally Access Surgery, in Havana, from January 2014 to January 2016. Patients excluded from the study were those under 18 years old and those with previous treatment, whether surgical for Gastroesophageal Reflux Disease (GERD) or endoscopic for BE or dysplasia. The endoscopic suspicion of intestinal metaplasia was made in the presence of salmon-colored mucosa above the gastroesophageal junction. The endoscopy was performed with an Olympus Evis Lucera Spectrum FQ-260 video endoscope. Erosive esophagitis was diagnosed according to the Los Angeles classification (grades A, B, C and D). Even if the patients did not present erosive lesions in the endoscopy, they were biopsied for histological study in order to determine the presence of non-erosive esophagitis. In all cases of severe esophagitis (grade C-D), a second endoscopy was performed for a new sample after treatment with omeprazole at a double daily dosage for 4 weeks, in order to determine more accurately the degree of dysplasia in BE.

The endoscopic classification of Prague (C & M) was applied [8], according to the length of the circumference and the length of the most apical segment of mucosa, dividing the patients into 2 groups: short segment (C & M less than 3 cm) and long segment (C & M greater than 3 cm). Ultrashort segment was considered when lesions smaller than 1 cm at the level of the Esophagogastric Junction (UEG) were observed, and they were classified as C0M1.

Samples for the histological study were taking according to the Seattle protocol (biopsy in the 4 quadrants, at intervals of 2 cm between the samples) [9]. In this work protocol, the area with suspected BE was first observed with white light. To enhance the lesions and improve the output of the tissue sample collection, approximately 5 ml of 2% acetic acid were instilled, followed by chromoendoscopy observation, electronic (Narrow Band Image System, NBI) or chemical (5 ml of 0.5% blue methylene) or both techniques in patients who were already diagnosed with dysplasia. In the biopsies the existence or not of dysplasia was confirmed, which was classified as High (HGD) or Low Grade (LGD) and indeterminate, as well as esophagitis.

The statistical analysis of the data was performed using the SPSS system, version number 21. Descriptive statistics techniques were used to summarize the data. For the comparisons, the variables were organized in contingency tables according to the groups of types of dysplasia. The comparisons between the groups were established using the Chi square test or the Fisher exact test (provided that the expected frequencies were less than 5). In all cases, the level of statistical significance was 0.05. All patients consented in writing to participate in the research, undergo endoscopic examination and have biopsies taken. The protocol was approved by the Scientific Council of the institution.

Results

A total of 86 patients with BE, confirmed by histology, were included in the study, of them 52 were white males (60.5%), with a mean age of 49.07 ± 15.5 years). The data referring to the epidemiological and clinical characteristics of these patients, where other variables were included, are not part of the objective of this publication, but are analyzed in a different publication.

Fifty-two patients presented endoscopic findings of esophagitis, 29 with grade A esophagitis of Los Angeles and among these, 14 patients also confirmed diagnosis for HGD, although the differences between the groups (no dysplasia/dysplasia) were not statistically significant (X2=16.4; p=0.88).

Hiatal hernia was diagnosed in 49 patients, more frequent among those who did not have dysplasia. The differences between the groups were not significant either (X2=3.3; p=0.19).

More than half of the patients with BE did not have dysplasia (57%) and in those who had it (43%), the low grade prevailed (37.2%). The most frequent endoscopic element in the suspected areas of dysplasia was the elongation of the glandular pattern, unlike the rounded appearance of the cardiac mucosa, as well as the tendency to form micronodules. Each biopsy was labeled independently, with the identification of the segment from which it was taken. In 16 patients, the application of the study protocol allowed to observe suspicious areas of dysplasia that had not been observed with white light. Of these, 14 patients (87.5%) were positive for dysplasia. In 20 of the 32 patients with LGD and in all cases of GAD, it was observed that the

BE lesions had a CM score <3 cm. For this element, there was also no statistical significance in the differences (X2=6.05; p=0.19).

Discussion

By performing the endoscopy as a diagnostic procedure in this study group, it showed that BE under 3 cm turns out to be the predominant form of presentation, almost always without esophagitis, whether in its erosive form in the milder stages (A and B of the Los Angeles classification). The former agrees with most series of research that also diagnose more short BE, than long ones [10,11]. Hiatal hernia turns out to be a finding that often accompanies the endoscopic diagnosis of BE. However, in none of these evaluated aspects there was a predominance of cases with dysplasia, in any of its grades.

The pattern followed by esophagitis means that it is not necessary to have extensive tissue lesions but repeated ones, for modifications of BE and its progression to cancer to happen. In addition, it expresses the resistance of the metaplastic epithelium to the action of the refluxed content [12-14]. Other series of patients with BE and dysplasia with low prevalence of esophagitis have been reported, which highlights the importance of accurate endoscopic observation at the level of the GEJ, even in the absence of esophagitis [12].

The length of BE can be associated with the risk of progression to adenocarcinoma and this can be so important that in 2016, the American College of Gastroenterology generalized the conceptualization of the disease to "columnar epithelium, with goblet cells that extend ≥ 1 cm above the limit of the gastric folds" and named those lesions with goblet cells that do not measure 1 cm in length "specialized intestinal metaplasia of the esophagogastric junction" [15]. The predominance of patients with short BE that was observed in this series is in correspondence with the results that have been observed in comparative studies [14,16]. Although it is known that the prevalence of BE increases with age, the same does not happen for length since, according to the observations, the BE develops to its maximum length quickly, but remains stable for many years. Ishimura and others state that in patients who underwent endoscopy due to GERD [17], the prevalence of segment ranges of less than 3 cm is 5% to 30%, almost 10 times higher than the prevalence of longer BE. In studies that have used esophageal manometry and pH monitoring, it has been confirmed that there are no marked functional differences between patients with short and long BE [18]. However, in a Cuban publication that conducted esophageal manometry studies on more than 30 patients with BE, with greater length in the CM classification, a greater affectation of the resting basal pressure of the Lower Esophageal Sphincter (LES) was recorded [19]. The demographic and pathogenetic aspects of both types were similar and represent the continuity of a single entity [16,20].

In any case, it is a fairly unanimous criterion that the most important risk factor to predict neoplastic progression is the degree of dysplasia, while there is no consensus on the relationship of the length of the segment (dysplasia being defined as a change in the cytological architecture of metaplastic glands) with the development of adenocarcinoma [21]. According to these findings, the neoplastic transformation depends more on the degree of dysplasia than on the length of the BE, although other results make it necessary to consider that the risk of developing dysplasia may be related to the length of the BE segment. In patients with short or ultrashort BE the risk to cancer is unknown and a matter of controversy [22]. In any case, the surveillance strategy should be similar for patients regardless the length of the segment and in accordance with international guidelines for the follow-up of dysplasia, with well- established therapeutic behaviors in the case of HGD, not so unanimous for the LGD [23,24]. Some studies show that the prevalence of dysplasia in long-segment BE is 20% to 35% and 6% to 8% in the short segment, different from the results of this series [25,26]. For other authors, in patients with GERD symptoms, the prevalence of dysplasia in patients with short segment is 5% to 30% [27,28]. Hiatal hernia is a contributing factor for the appearance of GERD in some patients [29,30]. It is not considered a factor that influences the development of the degree of dysplasia but in conjunction with the length of the BE segment, this association is considered a risk factor for progression to ADG or cancer [31-33].

Despite the existence of highly developed observation techniques and classifications that apply to endoscopic studies, the diagnosis of BE dysplasia remains histological, but a rigorous endoscopic examination helps to improve the sensitivity and effectiveness of the diagnosis. The study protocol to identify suspicious areas of dysplasia and conduct targeted biopsies requires that, in order to achieve a good visualization of these mucosal changes, which may suggest the presence of dysplasia; careful and detailed observation is essential, for as long as it is necessary. In order to look for these signs and then perform targeted biopsies, in addition to biopsying the other quadrants, according to the Seattle protocol. Finally, it is necessary to comment on the advantages of the enhancement maneuvers of the lesions with the use of vital dyes.

Investigations carried out by Chaurand found that for the diagnosis of BE and dysplasia, the chromoendoscopy with magnification with previous acetic acid has a sensitivity of 91.6%, with a specificity of 100%. Acetic acid alone increases the contrast between the healthy mucosa and BE: once applied, the normal squamous epithelium becomes white while the BE mucosa becomes white initially and red after 2 or 3 minutes. In those centers where there is no possibility of performing chemical or electronic chromoendoscopy, the use of 2% acetic acid, easy to prepare in hospital pharmacies, improves the possibility of diagnosis of dysplasia. It is a method easy to apply, reproducible and without complications that should be part of the diagnostic routine in these patients.

It is necessary to declare that a limitation of this study is that the histological diagnoses were made by several pathologists, from at least two different institutions, so that there could be interobserver variation in the histological diagnosis. A more complete discussion of this topic is beyond the purposes of this publication.

Conclusion

Only minimal erosive esophagitis and direct hiatal hernia had any value in this investigation to detect the presence of dysplasia in patients with BE during the endoscopic study. The LGD was much more frequent than the HGD. From the endoscopic point of view, the application of a study protocol in these patients with BE allows suspicion of areas of possible dysplasia and to take samples for histological study that will confirm or not, the suspicion of dysplasia.

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