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LONG TERM FOLLOW-UP OF NON-GOBLET CELL AND GOBLET CELL COLUMNAR LINED LOWER END ESOPHAGUS

Poonam Bhaker and Dr. Kim Vaiphei*

Professor, M.D., FUICC, FNAMS, FICP. Departments of Histopathology, Post Graduate Institute of Medical Education and Research, Chandigarh, India.

***Corresponding Author: Dr. Kim Vaiphei**
Professor, M.D., FUICC, FNAMS, FICP. Departments of Histopathology, Post Graduate Institute of Medical Education and Research, Chandigarh, India.

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ABSTRACT

Background: Significance of non goblet (GC) columnar mucosa (CM) present at lower end esophagus (LEE) remains controversial, and there is limited information of the follow-up data. **Aim:** to evaluate outcome of Barrett's mucosa (BM) and NGCM in long term follow-up biopsies. **Methods:** retrospectively evaluated biopsies reported as columnar mucosa (CM) with and without GC and correlated with clinical outcome. **Results:** There were 178 patients, mean age of 52.1±15.6, 7 <20 years, M:F=5:1; 70% had reflux symptom and 30% had dysphagia. Endoscopy: only BM in 130(73%), ulceronodular in 17%, stricture in 5% and small polyps in 5%. Sixty (34%) cases had long segment (LSBM) and 70(54%) short segment (SSBM); 11% had hiatus hernia. Histology: GCs were identified in 83% of the biopsies, 94% with LSBM. Dysplasia was observed in 65 (37%), low grade (LGD) in 68% and high grade (HGD) in 32%, 26(14%) had carcinoma associated with BM and HGD. Thirty (17%) biopsies with no GC showed alcian blue (AB) positive cells, 7(4%) had LGD and 3(2%) had HGD, none had associated carcinoma. Follow-up biopsy showed regression and normalization of mucosa and symptomatic relieve in many. Majority of LGD remained static with few progressing to HGD. Majority of HGD progressed to frank carcinoma over the years. **Conclusion:** high percentage of non-GCCM showed AB positivity and dysplasia. Many of cases with BM, LGD and HGD developed carcinoma. Ulceronodular and stricturous lesions associate frequently with BM and carcinoma. Present study emphasizes equal importance of follow-up biopsy in BM and NGCM.

KEYWORDS: Columnar liner esophageal mucosa, Barrett's esophagus, goblet cell, dysplasia, adenocarcinoma, helicobacter pylori associated gastritis.

INTRODUCTION

In 1950, Norman Barrett[1] described a columnar lined viscus representing the tubular segment of stomach rather than esophagus. In 1957, this columnar lined tubular structure was accepted to be columnar lined esophagus (CLE).[2] Since then there has been better understanding of this metaplastic columnar mucosa that has been termed as Barrett's esophagus (BE).[3] Current definition for BE proposed by American Gastroenterological Association (AGA) is "the condition in which any extent of metaplastic columnar epithelium that predisposes to cancer development replaces the stratified squamous epithelium that normally lines the distal esophagus".[4] Three types of CLE have been described in the setting of BE - i) gastric fundic type, ii) gastric cardia type and iii) intestinal type including goblet cells. The last type has been clearly linked with increased risk of development of adenocarcinoma with annual risk of esophageal adenocarcinoma (EAC) of about 0.5% per year in patients with lower end esophageal intestinal metaplasia (IM).[4-6] AGA and American College of Gastroenterology (ACG) recommend histological confirmation of the presence of IM in CLE recognized during endoscopy.[4,7] Takubo *et al.*[8] examined the mucosa adjacent to EAC treated with endoscopic mucosal resection and observed cardia type mucosa bordering the malignant foci in >70% cases rather than intestinal type mucosa and 56% had no intestinal-type mucosa in the resected specimens. They concluded that a definite relationship between EAC and IM might not be a necessary pre-requisite for the development of EAC. Some recent studies have highlighted demonstration of columnar epithelium to exhibit intestinal character in immunohistochemistry (IHC) and mucin profiles even when goblet cells (GC) were absent.[9,10] Few other studies have demonstrated similar molecular alterations in mucosa with and without GCs.[6,11-13] If in the definition of BE includes all columnar metaplasia in lower end esophagus, there will be substantial social and personal economic impacts as number of patients with columnar metaplasia without GC

is significantly more and conducting surveillance will greatly increase treatment and insurance cost.[14-17] The present study was carried out to analyze lower end esophageal mucosal biopsies.

MATERIALS AND METHODS

The study was included 178 patients (January 2000 to August 2013) that had been reported histologically either as intestinal metaplasia (IM) with GC and columnar cell metaplasia (CCM). Clinical data and endoscopic findings were re-evaluated from the records. All biopsies were stained with hematoxylin and eosin (H&E) and alcian blue periodic acid schiff (AB-PAS). We categorized the biopsies as columnar metaplasia (CM) and BE. Additional histological changes like epithelial regeneration, inflammatory atypia, dysplasia low or high grade or any carcinoma were also commented. Length of abnormal mucosa was measure. Four quadrant biopsies were taken circumferentially and additional biopsies from erosion, ulcer, polypoidal and nodular areas. Repeat endoscopy with biopsy were individualized depending upon the patients' compliance and clinical response to standard treatment and all BE patients. Histopathology features assessed were - IM, columnar cell, cytoplasmic alcian blue (AB) positive columnar cell, lamina propria inflammation, smooth muscle and any mesenchymal component, low (LGD) or high grade (HGD) dysplasia and carcinoma. Gastric antral biopsy if any was also evaluated. Descriptive statistics were used for data analysis and Chi-square test was done for comparative data and *p*-value less than 0.05 was taken as significant.

RESULTS

Male to female ratio (M:F) was 5:1, 147(83%) were males and 31(17%) were females. Age ranged from 8 to 85 years with a mean age of 52.1±15.6 years, 53 (30%) belonged to 5^{th} and 6^{th} decades of life and 7(4%) patients were <20 years. Heartburn, regurgitation and dyspepsia were present in 84(47%) and dysphagia in 54(30%) patients. Durations of complaints were very wide ranging from 6 to 24 months with the mean of 13 months. Observations made at endoscopic examinations (Table 1) were presence of islands of salmon pink to reddish mucosa in 120(67%), reddish pink mucosa along with erosions in 10(6%), polypoidal ulcerated nodular areas in 40(22%) and strictures in 8(5%) patients. Of the 178 patients, abnormal mucosa was documented as long segment BE (LSBE) in 31(17%) and short segment BE (SSBE) in 36(20%) patients; and in the remaining patients, length of abnormal mucosa had not been specified, otherwise all were recorded to have pink or reddish mucosa at lower end of esophagus. Associated hiatus hernia (HH) was observed in 19(11%) patients, 3 of them were documented to have LSBE and 2 with SSBE. All seven younger patients had SSBE of pink mucosa, with erosions in one.

Number of biopsy fragments ranged from 4 to 12 pieces. On histological examination, 148 (83%) biopsies showed demonstrable GCs in H&E stained sections (Figure 1A) whereas the remaining 30 (17%) biopsies showed in AB-PAS staining cells containing acidic mucin in vacuolated but non-goblet columnar cell, which were seen as purplish blue colored cells. GCs were identified in 94% (29 out of 31) of LSBE and 75% (27 out 36) with SSBE. Seven patients who were younger than 20 years of age, GCs were found in three (43%) and the remaining biopsies showed acidic mucin in AB-PAS staining Figure 1B). Altogether, there were 40 (22%) biopsies showing complete IM with presence of absorptive and Paneth cells, 108 (61%) biopsies were incomplete type of IM where GC intermixed with mucous cells. Gastric type of mucosa was seen in 74 (42%) patients, fundic/body type gastric mucosa in 20 (11%) while cardiac / antral type in 54 (30%) patients. Our main interest was to study the biopsies on follow-up endoscopy of these 30(17%) patients which showed AB positive cells containing acidic mucin.

Surface epithelium showed villous configuration in 66 (37%) patients and another 16 (9%) biopsies showed ulceration of the surface epithelium. Surface epithelial cell atypia was noted in 11 (6%) biopsies and all these biopsies were associated with acute mucosal inflammation. Fifty eight (9%) of the biopsies with villiform surface had GCs in H&E stained sections. Stromal inflammation was dominantly chronic in type, and was mild in 32%, moderate in 56% and heavy in 12% patients; 24 (14%) of these biopsies also had neutrophil infiltration (mild in 21%, moderate in 25% and severe in 54%); and 22 (12%) had eosinophil rich infiltration. Mesenchymal changes in the form of splaying and fraying of smooth muscle fibers were noted in 95 (53%) which were associated with variable degree of lamina propria fibrosis in 96 (54%) patients. GCs were present in 78 (82%) of the 95 biopsies with smooth muscle changes and fibrosis.

Dysplastic epithelium was observed in 65(37%) patients (Figure 1C), LGD in 44(25%) and HGD in 21(12%) (Table 2). All HGD were identified in LSBE. BE was present in 37(21%) of LGD and 18(10%) of HGD. Dysplasia was also identified in NGCM - 7(4%) LGD and 3(2%) HGD, none of them had associated carcinoma in entry biopsy. The association between dysplasia and presence of GCs were significant (Qi-square test, $p<0.001$). Endoscopic findings in 65 patients with dysplasia were pink red mucosa in 35(20%), with ulcers in 13(7%), polypoidal/nodular in 10(6%) and erosions in 7(4%) patients. There were 66 biopsies had exhibited villiform surface in histology, 23(13%) with LGD, 17(10%) with HGD and 26(15%) with invasive carcinomas. All 26 patients with carcinomas had associated BE and HGD. Histological types of carcinomas (Table 3) were 22(12%) adenocarcinoma with extracellular mucin production (Figure 1D) and poorly differentiated features in 2 each, one each of signet ring cell carcinoma, papillary adenocarcinoma, adeno-squamous and squamous cell carcinomas.

Endoscopic features in these 26 patients with carcinomas were polypoidal/ulcers/nodular in 18(10%) and strictures in 8(5%). Age of the patients with dysplastic epithelium (i.e. 65 cases) and carcinoma (i.e. 26 cases) ranged from 16 to 85 years with the means of 53 and 59 years respectively. More than half of the patients i.e. 15/26 with carcinoma were in 6th and 7th decades of life. Dysplasia and carcinoma were more frequently documented with LSBE compared to SSBE. All patients who were diagnosed to have frank carcinomas were subjected to esophagectomy, and presence of carcinomas was further confirmed in the resected specimens. Biopsies in 19 patients with HH showed BE with villous surface in 6, HGD in 2 and LGD in 3. Duration of symptoms in these 19 patients ranged from 7 to 24 months, similar to other patients with no HH.

Lamina propria inflammation was dominantly chronic inflammatory cells, mild in 32%, moderate in 56% and heavy in 12% patients; 24(14%) biopsies also had neutrophil infiltration and 22(12%) had eosinophil rich infiltration. Mesenchymal changes in the form of splaying and fraying of smooth muscle were noted in 95(53%) and patchy lamina propria fibrosis in 96(54%) patients. GCs were present in 78/95(82%) biopsies with splayed smooth muscle. Stratified squamous esophageal mucosa included in the biopsies showed features of reflux esophagitis in 59(33%) patients, 47(26%) of them had IM. In the rest of the biopsies, there was no identifiable squamous epithelium included in the biopsies. Superadded infections were found in 8(5%) patients, of which one patient was endoscopically suspected to have esophageal candidiasis. Cellular changes of cytomegalovirus (CMV, Figure 2A) infection were observed in 1(0.6%), herpes simplex virus (HSV, Figure 2B) in 2(1%) and dual infections by HSV and CMV in 2(1%) more patients. One patient with unknown immune status showed infections by multiple organisms consisting of HSV, CMV, Histoplasma, Cryptosporidium (Figure 2C) and Microsporidium. Mucormycosis and actinomycosis were noted in 1(0.6%) each and Helicobacter pylori (HP, Figure 2D) infection was identified in 1(0.6%) patient confining to metaplastic gastric mucosa. This particular patient also had HP related antral gastritis and had received specific treatment for the same. None of these patients were given any specific treatment for the superadded infections. (Table 4) Follow up biopsies in 7/8 did not reveal persistence of any of the infections. The patient who had multiple infections was lost to follow-up.

There were 55(31%) gastric antral biopsies carried out for antral gastritis. Morphological diagnoses in these 55 biopsies are given in Table 4. Atrophic gastritis (AG) was most frequently observed followed by chronic active gastritis (CAG). HP infection was documented in 70% of AG, and 90% of CAG. High degree of association between IM in gastric biopsy with the presence of BE, observed in 93; and 100% of gastric IM had BE (Chi square test, $p<0.001$).

Follow up

All patients were advised symptomatic treatment with life style and dietary modifications. Those who had shown clinical response were on follow up without repeat endoscopic examination. But patients who were diagnosed either with low or high grade dysplasia were on surveillance endoscopy program and follow-up duration ranged 5 months to 11 years (mean duration: 3.3 years). After 3 to 6 months, repeat endoscopic biopsies were carried out in 20/44 LGD and 15/21 HGD. Rests of the patients with dysplasia were lost to follow-up. Follow-up biopsies in 20(11%) patients with LGD, 2 showed reversion to non-dysplastic columnar mucosa at 6 and 12 months. Both had complete clinical response. Outcome in the remaining 18(10%) patients with LGD were - i) remained static in repeat biopsies in 13(7%) patients at 1, 2, 5 and 6 years with partial relieve of clinical symptoms; and ii) 5(4%) patients advanced to HGD at 18 to 24 months of follow-up with persistence of symptoms. Further follow-up biopsies in these 5 patients showed focal lamina propria invasion by carcinoma cells in 3 patients at 24 to 36 months. Ultimately all the 5 patients were resorted to surgical resections and confirmed the presence of HGD with adenocarcinoma in 3 and focal intra-mucosal invasion in 2 patients with HGD. Those 15(8%) patients with HGD in the first entry biopsy, 8(5%) developed invasive carcinoma over 12 months' time and were subjected to esophagectomy. Resected specimens showed features of invasive adenocarcinomas infiltrating into sub-mucosa and beyond, frequently with extra-cellular mucin production in 3 patients. The remaining 7(4%) patients had static disease with no evidence of carcinoma or regression on follow-up at 6, 9, 15, 18, 19, 24 and 36 months.

Eighty three (47%) patients with BE without dysplasia, follow-up information was available in 32(38%) over a period of 6 to 132 months. Follow-up biopsies were carried out whenever they attended out-patient clinics. LGD was detected in 5(3%) after 28 to 60 months after the first biopsy, and subsequently HGD at 60 to 132 months on further follow-up biopsy. Two of the patients aged 54 and 62 years, males, were subjected to surgery and resected specimens showed more than one focus of 1 to 2 cms sized nodulo-ulcerated lesions at lower third esophagus with features of invasive adenocarcinomas. There was no visible remnant of pink mucosa in both the cases. The other three patients aged 68, 72 and 85 were refused surgery on medical grounds. Another 7(4%) patients had foci intermixed of LGD with HGD at 36 to 48 months in follow-up endoscopic biopsies. Three underwent resection and documented presence of HGD; another 3 patients were lost to follow-up, and one 75 years old patient was not operable due to other medical complications. Follow-up period in the remaining 20 patients ranged from 6 to 48 months and there was partial improvement in clinical symptoms in all 20 patients. Follow-up biopsies showed persistence of barrett's mucosa with no dysplasia.

Follow-up information were available in 28/30 patients with NGCM. At the entry point, dysplasia was also identified in NGCM - 7(4%) LGD and 3(2%) HGD, none of them had associated carcinoma in entry biopsy. Three patients had persistent symptom and repeat endoscopic biopsies showed LGD over a period of 6, 8 and 11 months. There were 12 more patients who came for follow-up at 24 to 42 months including the 7 patients who had shown LGD at entry, had responded initially to medical treatment for a period of 2 to 6 months and had recurrence of clinical symptoms. Repeat endoscopy with biopsy at 6 to 19 months of follow-up showed persistence of similar endoscopy and histological features i.e. LGD had persisted in the 7 patients whose initial biopsies had shown LGD and non-dysplastic columnar mucosa in the rest. Another 3 patients had reversal of columnar mucosa to normal squamous mucosa over 16 to 24 months time. Three HGD patients had persistence of the similar type of dyplastic mucosa at 6, 18 and 24 months of follow-up, no carcinoma. Remaining 7 patients initial follow-up at 3 to 5 months showed symptomatic improvements and were advice to continue treatment for reflux esophagitis. But none of them came back for further follow-up. None of the patients in this group developed frank carcinoma during the follow-up period. Seven younger patients including the one with GC metaplasia had shown clinical response at 3 months. Repeat endoscopic biopsy in the one with GCs showed small foci of columnar lined mucosa with no goblet cell.

Table 1: Endoscopic findings of in 178 patients.

Pink mucosa	Number of patients (%)	Total (n=178)
alone	119 (66.8%)	130 (73%)
With erosion	11 (6.2%)	
Polypoidal / ulcerated	40 (22.5%)	48 (27%)
Stricture with or without ulcer	08 (4.5%)	

Table 2: Endoscopic details of patients with dysplasia.

Endoscopy	Dysplasia, low grade (n=44)	Dysplasia, high grade (n=21)	Total
length not available	16	4	20
short segment	5	1	6
long segment	7	2	9
polypoidal ulcers	8	9	17
stricture	5	2	7
nodular lesion (<1cm)	3	3	6
Total	44	21	65

Table 3: Endoscopic details of 26 patients with carcinomas.

Histopathology	Endoscopy
Adenocarcinoma, NOS (n=18)	Pinkish red mucosa (n=4) Growth (polypoidal) (n=8) Growth (ulcerated) (n=3) Nodule (n=1) Stricture (n=2)
Mucinous adenocarcinoma (n=2)	Pinkish red mucosa (n=1) Growth (polypoidal) (n=1)
Papillary adenocarcinoma (n=1)	Growth (polypoidal) (n=1)
Carcinoma, Signet ring (n=1)	Pinkish red mucosa (n=1)
Adenosquamous (n=1)	Pinkish red mucosa (n=1)
Squamous cell carcinoma (n=1)	Growth (ulcerated) (n=1)
Poorly differentiated adenocarcinoma (n=2)	Growth (polypoidal) (n=1) Growth (ulcerated) (n=1)

Table 4. Distribution of histopathological diagnoses on gastric biopsies.

Diagnosis	Number of cases (percentage)
Atrophic gastritis	37 (67.2%)
Chronic active gastritis	19 (34.5%)
Helicobacter Pylori	15 (27.3%)
Intestinal metaplasia	13 (23.6%)
Dysplasia	01 (1.8%)
Adenocarcinoma	01 (1.8%)

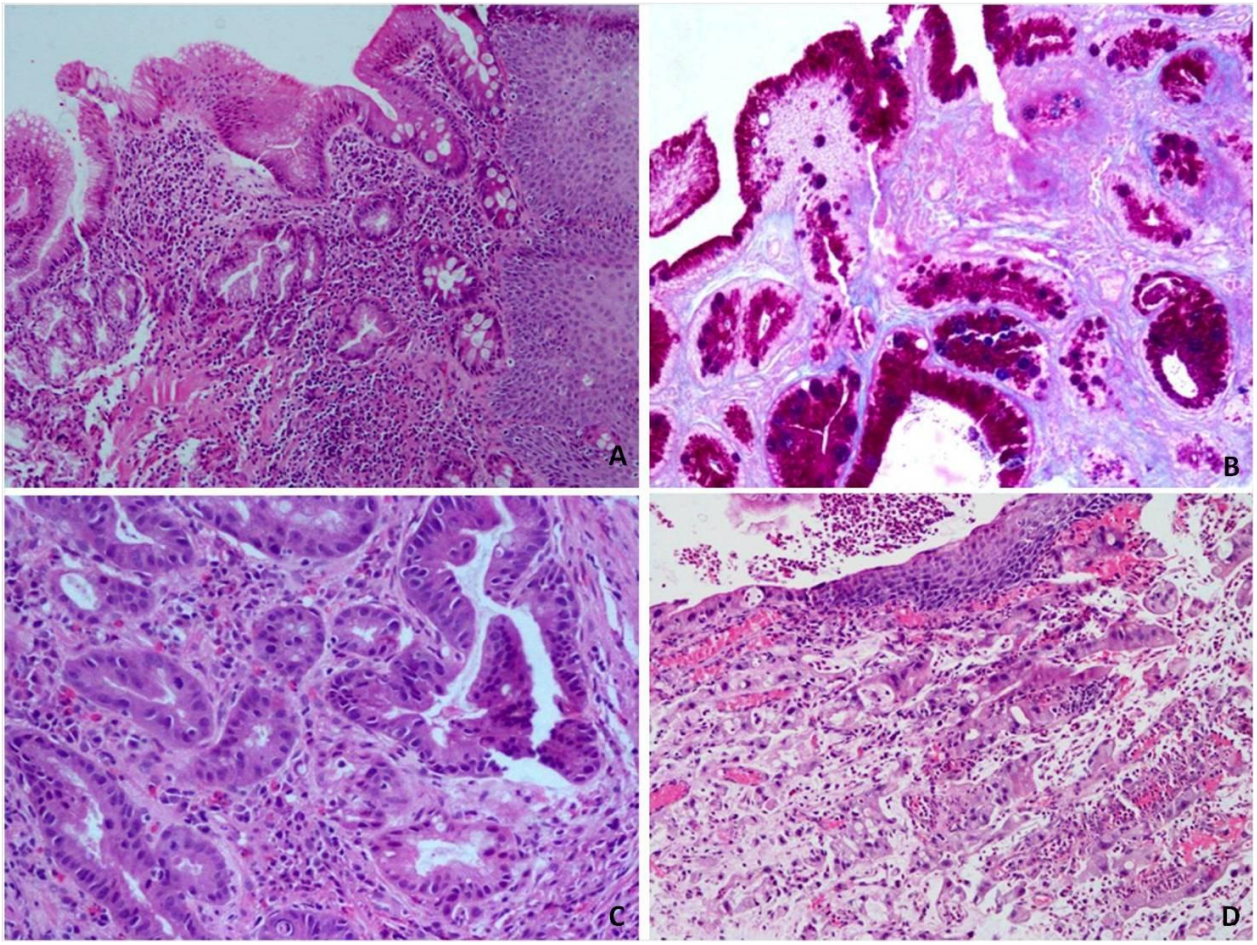

Figure 1: A: low power photomicrograph of lower end esophageal biopsy showing complete intestinal metaplasia with moderately heavy inflammatory cell infiltration in the lamina propria with a patch of fibrosis. (Hematoxelyne and Eosin, x140); B: photomicrograph of alcian blue - periodic acid Schiff stain section highlighting goblet cells in dark purplish blue and magenta coloured gastric type of epithelial cells. (alcian blue-periodic acid Schiff, x240); C: photomicrograph in medium power to show an irregular shape gland showing nuclear stratification and anisonucleosis indicating presence of high grade dysplasia. (Hematoxelyne and Eosin, x240); D: medium power photomicrograph to show partly columnar lining epithelium in continuity with the squamous lining and presence of malignant epithelial cells showing glandular differentiation and with extracellular mucin production. (Hematoxelyne and Eosin, x240).

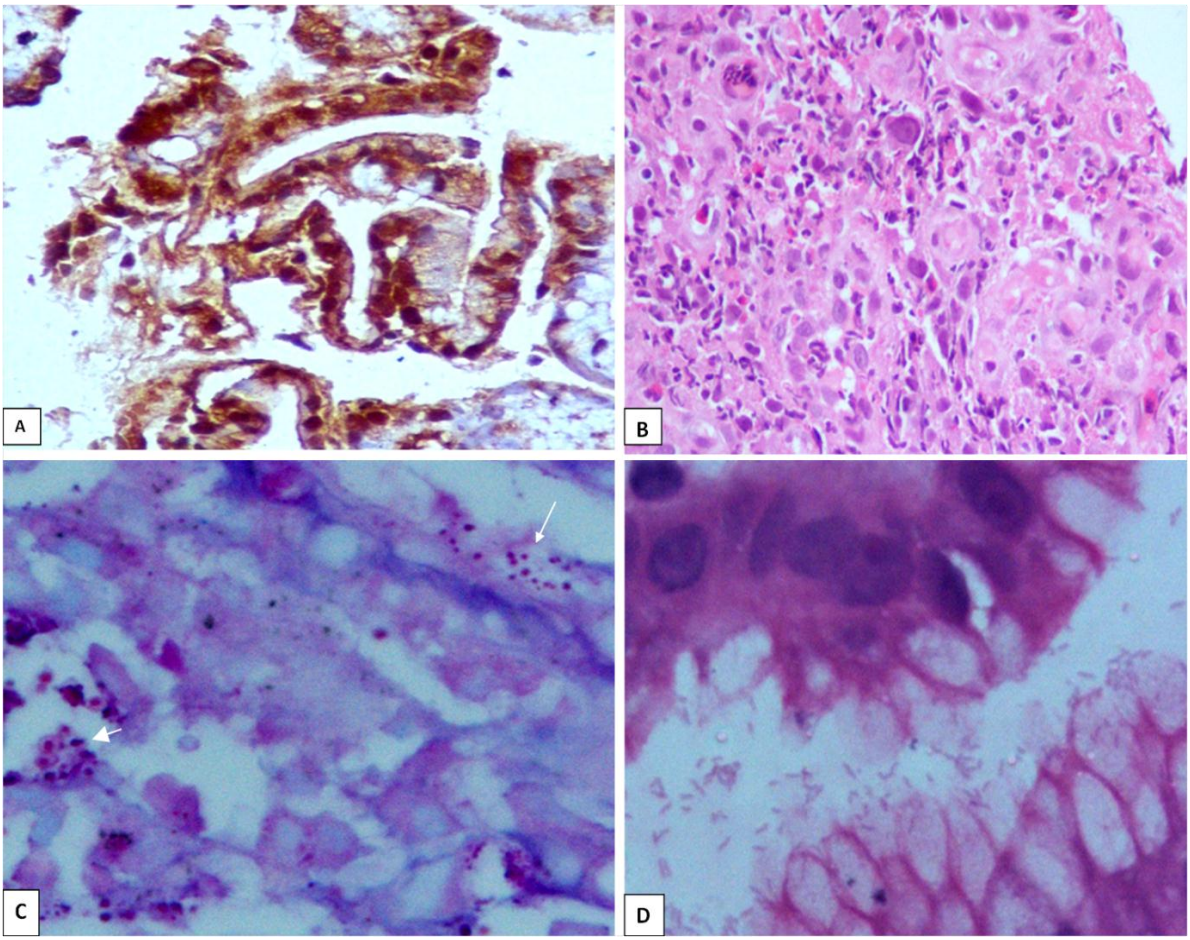

Figure 2: A: Photomicrograph of an esophageal biopsy showing a heavily inflamed granulation tissue with scattered cytomegalic cells with smudged nuclei and intranuclear inclusion. (Hematoxelyne and Eosin, x500). B: Medium power photomicrograph to show dominantly nuclear po`sitivity for Herpes simplex virus. (peroxidase anti-peroxidase, x400). C: High power photomicrograph to show the presence of Histoplasma (arrowhead) and cryptosporidium (arrow) in the same biopsy (alcian blue-periodic acid Schiff, x1000). D: High power photomicrograph of the metaplastic gastric mucosa to show plenty of Helicobacter pylori. (Hematoxelyne and Eosin, x1000).

DISCUSSION

BE is a frequently observed condition in adults and the mean age observed in the present study is similar to reports in the literatures.[18-20] Zhang et al.[19] and Cameron et al.[20] reported higher mean age of 61 and 63 years respectively compared to ours of 52 years. We documented higher mean age of 53.1 and 58.9 years in patients who had dysplastic epithelium and adenocarcinoma respectively, and are similar to the report in population based study conducted in Denmark.[21] Majority of our patients were males, similar to other studies.[22,23] Presenting symptoms were similar to other case series.[19] However, we also observed BE in 8% of our patients who were detected incidentally, similar to 2 other studies.[14,24] Reflux esophagitis is reportedly frequent amongst children but incidence of BE however is low[25] and BE in children has been reported in cystic fibrosis and children who are on chemotherapeutic regimes.[25-27] In the present study, there were seven patients who were younger than 20 years of age and the youngest being 8 years with the median age of 17 years and all were males. BE in children reported median age of 11.7 (2 to 17) years with male predominance.[28,29] Five of our young patients presented with dyspepsia, 2 with dysphagia and in one patient, the pink mucosa was detected incidentally while undergoing endoscopy for chronic liver disease. In 3/7 biopsies in our study had GCs and the gastric biopsies available in two showed loss of antral glands but negative for HP. However, none of the 7 cases had dysplasia or carcinomas. Hoeffel et al.[30] reported esophageal adenocarcinoma associated with BE in 11 and 14 years old children and Hassall et al.[31] also reported another case in a 17 years old boy with multifocal high-grade dysplasia and adenocarcinoma complicating BE.

The classical salmon pink mucosa with reddish coloration was seen in 72% patients and the rest also had in addition to the classic mucosa, polypoidal ulcerations nodular lesions and strictures. Our patients with ulceration showed high percentages of co-existing dysplasia and carcinomas, and 7 of 8 patients with stricture had carcinoma at presentation. Hillman et al.[32] documented similar kind of mucosal changes with the

presence of dysplasia and carcinomas. Hiatus hernia is a known risk factor for BE and the percentage of hiatus hernia documented in our patients were less than the report in a prospective study.[33] We also observed GCs more frequently present in LSBE than SSBE, and similar finding is reported by another study.[34]

Updated guidelines of American College of Gastroenterology in 2008[7] considers presence of GCs on histology to be an essential criterion for BE. Recently published data documented non-goblet metaplastic columnar epithelium having similar risk of development of malignancy.[35-38] Columnar lined esophageal mucosa may be gastric mucosa or intestinal type epithelium purely or admixed with gastric type of mucosa.[39] In the current study, we also observed mixtures of IM and gastric type of mucosa in 42% of the biopsies. Presence of GCs were less frequent in our patients who were less than 50 years of age compared to older individuals who were above 50 years of age, and also with the length of the abnormal mucosa (Chi Square test, $p<0.05$). Similar observations had also been made by others where presence of GCs were related to age of the patient, duration of symptoms and length of abnormal mucosa.[34,40-42] AB-PAS stain had added in identifying non-GC acid mucin containing cells in all 30 (17%) columnar lined mucosa. But the percentages of associated dysplasia or carcinomas were much lesser in this group compared to ones with GCs. Though controversial in some studies,[6,11,12] natural history of columnar and goblet cells however appear to be not always the same, which suggests existence of additional factors for progression to dysplasia and carcinomas.[13] In follow-up, none of the patients with no GC developed frank carcinoma.

In our study, lamina propria showed fraying and duplication of muscularis mucosae (MM) in 53%, which had been reported in up-to 90% by others.[43-45] In our patients, the biopsies which had exhibited duplication or splaying of MM, 44% of these biopsies had associated dysplasia and 5% had associated carcinoma. Histological evidence of reflux esophagitis was seen in 33% of our biopsies and is considered as one important etiological factor for development of BE.[4-6] This low incidence of reflux esophagitis may be related to small tissue bit of stratified squamous mucosa. A recent Italian population had observed smoking to be an important factor for the development of BE.[46] Another interesting finding in our patients was the presence of superadded infections by viruses, fungi and protozoal in eight of the biopsies. These infections may be incidental or may have a potential role in disease pathogenesis. However, authors did not find any data in the English literature to support these hypotheses except for the role of HPV in esophageal carcinogenesis.[47] In the current study, though it was observed only in 4% of the cases, further studies are needed to establish role of infective agents in the development of BE.

In a multi institutional retrospective analysis of BE, dysplasia was documented in 7.2% of patients[48] and the incidence reported is lower than ours. Thirty of the 65 patients with dysplasia in BE exhibited associated polypoidal, ulceration or strictures of the pink mucosa. We observed LGD almost two times higher than HGD. Similar results were also documented in a study by O'Connor et al.[49] Literatures from different parts of the world[48-51] cited 5 to 71% of LGD in BE. Carcinomas observed in 15% of our patients is similar to incidences reported in other studies.[36,52-54] Our study highlights an important observation that mere presence of pink mucosa is not enough indicator for the presence of GC or dysplasia. We also observed important association of columnar lined mucosa with gastritis, which also had been reported by another study[55] supporting the concept of development of lower end esophageal pathology secondary to associated hyperacidity. A few of our patients who had LGD converted to non-dysplastic columnar mucosa, and columnar mucosa to normal mucosa on follow-up. There are studies which had reported regressions of columnar lined mucosa with and without goblet cells.[56,57] A few of our patients had progressed from LGD to HGD and HGD to carcinoma. Similar pattern of progression and regression had been reported by the Cleveland Clinic study group in 136 patients.[49] Another study in 50 patients with BE documented increase frequency of development of dysplasia.[58]

CONCLUSION

The current study documents high percentage of GCs in lower end esophageal pink mucosa. Long segment BE complicated by ulceration and stricture likely to be associated with HGD and carcinoma. Few of the cases with columnar lined alcian blue positive mucosa showed progression to dysplasia suggesting similar malignant potential to goblet cell containing BE. Present study re-emphasizes importance of carrying out multiple follow-up mucosal biopsies, subjecting all tissue fragments to microscopic evaluation at variable time interval of the surveillance program.

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