Original Article

Precursor lesions of gastric carcinoma: A histopathological study

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Abstract

Introduction: Gastric cancer is common human malignant epithelial tumor associated with *Helicobacter pylori* infection. *H. pylori* infection causes chronic active gastritis with progress to precursor lesions such as atrophic gastritis and intestinal metaplasia which can progress to dysplasia and thus carcinoma may develop.

Aim of the Study: To study precursor lesions associated with different types of gastric carcinoma.

Materials and Methods: Eighty cases of gastric carcinoma were included in this study which showed adjacent nonneoplastic gastric fragments. Hematoxylin- and eosin-stained slides were studied.

Results: Intestinal, diffuse, and mixed types of gastric carcinomas were seen in 67.5%, 28.75%, and 3.75% of cases, respectively. *H. pylori*, chronic gastritis, atrophic gastritis, intestinal metaplasia, and dysplasia were seen in 13.75%, 92.5%, 25%, 43.75%, and 22.5%, respectively.

Conclusions: In this study, we have described precursor lesions associated with gastric carcinoma as described in the literature in the Indian population.

Keywords: Atrophic gastritis, dysplasia, gastric carcinoma, *Helicobacter pylori*, intestinal metaplasia

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INTRODUCTION

Gastric carcinoma is a malignant tumor of the stomach and the second- and fourth-most common cancer in males and females, respectively[1] and the third-most common cause of cancer-related mortality.[2] It is a tumor of elderly people and etiologically associated with *Helicobacter pylori* infection (*H. pylori*), dietary habits, smoking, Epstein-Barr virus infection, hypochlorhydria, partial gastrectomy, gastric polyps, and hereditary factors.[3,4] The carcinoma may involve antrum, body, or cardia. Histologically, there are different classification systems for gastric carcinoma but the commonly used Lauren Classification system classifies gastric carcinoma into the intestinal type and diffuse type.[2,5] It is assumed that gastric carcinoma develops through the stepwise progression of certain mucosal lesions such as atrophic gastritis and intestinal metaplasia. Correa suggested a model of gastric carcinogenesis called Correa cascade and according to this model, chronic inflammation leads to atrophic gastritis on which intestinal metaplasia develops which progresses to dysplasia and carcinoma.[6,7] This model fits well with *H. pylori* infection and intestinal type of gastric carcinoma where chronic inflammation induced by *H. pylori* leads to precursor lesions and finally carcinoma. The study by Song *et al.*[8] measured the

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incidence of gastric cancer among patients with precursor lesions and found excess incidence in patients with gastritis, atrophy, intestinal metaplasia, and dysplasia in comparison with normal mucosa.

In this study, we evaluated the nonneoplastic and precursor lesions present near carcinoma fragments.

MATERIALS AND METHODS

A total of 92 cases of gastric biopsies diagnosed as carcinoma were studied (period 2016–2019) in the Department of Pathology, Institute of Medical Sciences, Banaras Hindu University. Of these 92 cases, 80 were included in this study because in these cases fragments of neoplastic tissue (carcinoma) as well as nonneoplastic fragments were available for evaluation.

RESULTS

The study included 55 males and 25 females (M/F 2.2) with the age range of 14–84 years. Majority of patients were in the 6–7 decade of life. Where information was available on the requisition form, site of tumor and presentation as growth or ulcer was noticed. Antrum was involved in 22 cases, 14 of these had presented as ulceroproliferative growth and eight had wall thickening or ulcer. Body region was involved in four cases and cardia in two cases. On histopathological examination, Lauren classification was used to classify gastric carcinoma into the intestinal type and diffuse (signet-ring cell type). Surrounding nonneoplastic fragments were evaluated for chronic gastritis, *H. pylori*, the presence of mucosa-associated lymphoid tissue and precursor lesions such as atrophic gastritis, intestinal metaplasia, and dysplasia. Fifty-four cases (67.5%) were classified as intestinal type [Figure 1], 23 (28.75%) as diffuse type [Figure 2], and 3 (3.75%) were of mixed type. On correlating site with the histopathological type, of the 22 involving the antrum (where information was available) 17 were of intestinal type, three of diffuse type (signet-ring cell type), one mucinous, and one mixed. Of four cases involving the body region, two were of diffuse type and two of intestinal type. On histopathological examination of the nonneoplastic fragments, chronic gastritis was seen in 74 (92.5%, Figure 3) cases with active gastritis in 38 cases (antrum 51, body 18, and both 5). *H. pylori* was seen in 11 cases (13.75%, 9 were of intestinal type and 2 of diffuse type, Figure 4). Chronic active gastritis was seen in all *H. pylori* positive cases. Mucosa-associated lymphoid tissue, atrophic gastritis, intestinal metaplasia, and dysplasia were seen in 3, 4, 3, and 2 cases, respectively in these *H. pylori*-associated cases. Overall, Atrophic gastritis [Figure 5] was seen in 20 cases (25%) associated with carcinoma (11 intestinal type and 9 diffuse type) and involving body region in eight cases, antrum in eight cases, and both antrum and body in four cases. Atrophic gastritis was associated with intestinal metaplasia in eight cases, pseudopyloric metaplasia in two cases, MALT in three cases, and dysplasia in one case.

Intestinal metaplasia [Figure 6] was seen in 35 cases (43.75%, 25 intestinal type, 9 diffuse type, and 1 mixed type) and body, antrum and both regions were involved in eight, 21, and six cases, respectively. Intestinal metaplasia was associated with dysplasia in 10 cases. Further categorization of intestinal metaplasia could not be done. Dysplasia [22.5%, Figure 7] in total was seen in 18 cases (intestinal type 13, diffuse 2, and mixed 3 cases), pseudopyloric metaplasia in five cases (3 intestinal type and 2 diffuse type), and hyperplastic polyp/foveolar hyperplasia was seen in seven cases near the carcinomatous fragments [5 intestinal type and 2 signet-ring cell type, Figure 8].

DISCUSSION

Gastric carcinoma is invasive epithelial tumor of the stomach classified into early gastric cancer and advanced gastric cancer based on infiltration within the wall and into intestinal type and diffuse type histopathologically according to Lauren classification. Gastric carcinoma is associated with *H. pylori* [9,10] which is classified as class I carcinogen by the WHO[11] and is associated with both intestinal and diffuse type of gastric carcinoma.[12,13] *H. pylori* is a Gram-negative spiral-shaped organism and causes chronic active gastritis characterized by superficial plasma cell and lymphocytic infiltrate, lymphoid aggregates, and neutrophilic infiltrate in the epithelium. Chronic inflammation can lead to atrophic gastritis defined as loss of appropriate glands according to topography and replaced by fibrosis or metaplastic epithelium and can be scored and risk prediction can be made by operative link on gastritis assessment staging system (OLGA system).[14,15] Metaplastic epithelium may be of intestinal type or pseudopyloric type (in body region). Intestinal metaplasia may be complete or incomplete based on histology and mucin stains and patients with intestinal metaplasia have increased risk of gastric carcinoma. Bacterial virulence factors such as cagA and vac A lasso play role in this.[16,17] Hence atrophic gastritis and intestinal metaplasia are considered precursor lesions of gastric carcinoma.[2,3,18] It is supposed that in *H. pylori*-associated lesions there is a progressive increased proliferation of the epithelial cell.[16,19,20] In the present study, 80 cases of gastric carcinoma with surrounding nonneoplastic fragments were evaluated. Fifty-four were of intestinal type, 23 were of diffuse

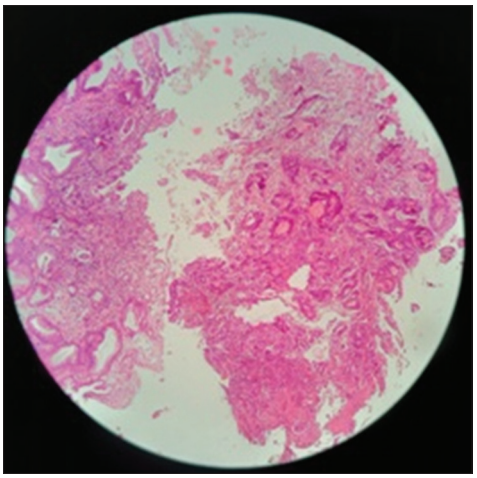

Figure 1: Intestinal type gastric carcinoma (H&E, 10x)

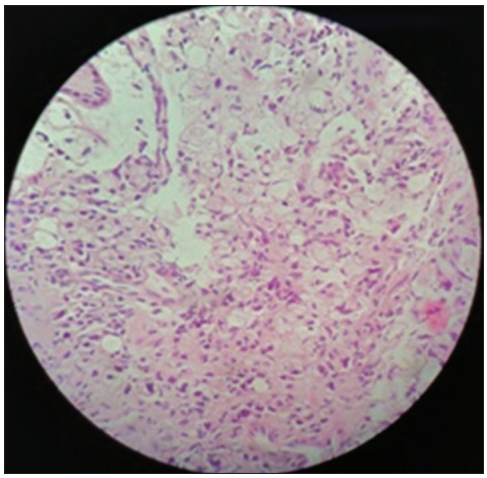

Figure 2: Diffuse (signet ring cell) carcinoma (H&E, 10x)

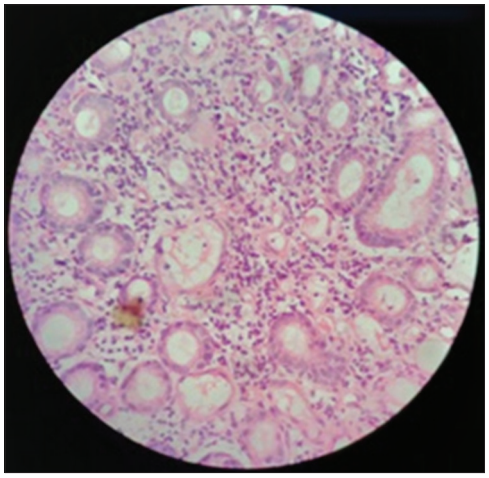

Figure 3: Chronic active gastritis (H&E, 10x)

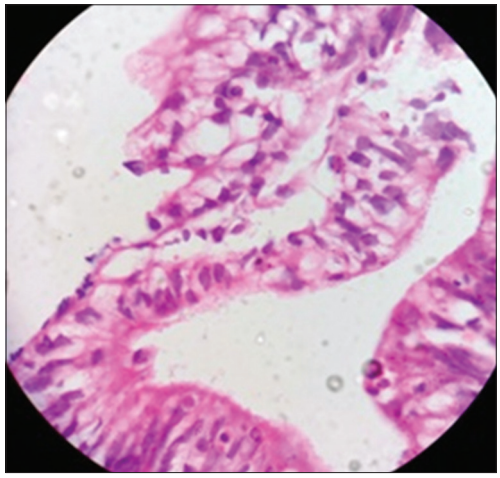

Figure 4: H.pylori (H&E, 100x)

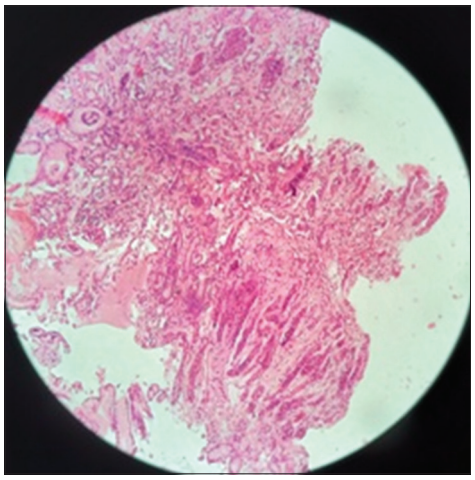

Figure 5: Atrophic gastritis (H&E, 10x)

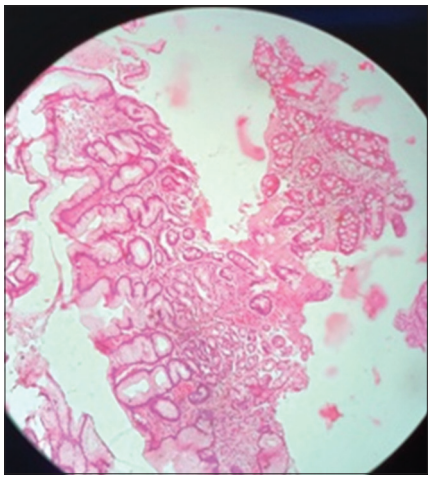

Figure 6: Intestinal metaplasia (H&E, 10x)

type, and three were of mixed type. Of the information available, 22 were in the antrum and four were in the body region. Study by Manasa *et al*.[21] from India found intestinal type to be 78.3% and diffuse type 22.7%. In the present study, *H. pylori* was seen in 11 cases (13.75%). This is low in comparison of other studies because in other studies special stains such as Giemsa and serology were used for the detection of *H. pylori* which was not used in the present

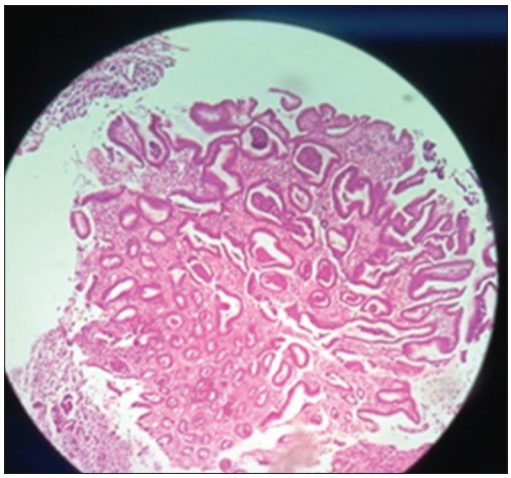

Figure 7: Dysplasia (H&E, 10x)

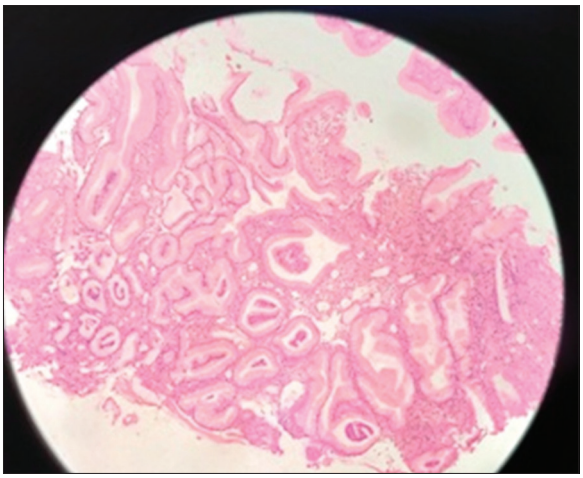

Figure 8: Hyperplastic polyp like areas (H&E, 10x)

study. Atrophic gastritis, intestinal metaplasia, and dysplasia were seen in 20 (25%), 35 (43.75%), and 18 (22.5%) cases, respectively in the present study, whereas other studies have shown more incidence of atrophic gastritis and dysplasia and less incidence of intestinal metaplasia than the present study.[21] The study by Rodrigues *et al*.,[22] 31.7% prevalence rate of *H. pylori* and higher incidence of intestinal metaplasia in *H. pylori* patients than negative patients. Both dysplasia and intestinal metaplasia were seen in 10 cases and all four parameters (*H. pylori*, chronic active gastritis, intestinal metaplasia, and dysplasia were seen in 2 cases. Rarely, the gastric hyperplastic polyp may be associated with carcinoma. In this study, we also found features of hyperplastic polyp/foveolar hyperplasia in seven cases.

Table 1: Distribution of precursor lesions

Precursor lesions	Number (%)
Total number of cases	80
Intestinal-type gastric carcinoma	54 (67.5)
Diffuse-type gastric carcinoma	23 (28.75)
Helicobacter pylori	11 (13.75)
Chronic gastritis	74 (92.5)
Atrophic gastritis	20 (25)
Intestinal metaplasia	35 (43.75)
Dysplasia	18 (22.5)

CONCLUSIONS

In this study, we evaluated precursor lesions associated with gastric carcinoma as described in the literature. Special stains for *H. pylori* and immunohistochemistry could not be done which is a lacunae but this study shows high association of intestinal metaplasia and dysplasia. Hence while evaluating gastric biopsies for dyspeptic symptoms the presence of atrophy and intestinal metaplasia should be carefully sought and if present these patients should be followed up for earlier detection of carcinoma.

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Conflicts of interest
There are no conflicts of interest.

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