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RESEARCH ARTICLE

PATHOLOGIC CHANGES IN THE ADJACENT GASTRIC MUCOSA IN SURGICAL SPECIMENS REMOVED FOR GASTRIC CARCINOMA

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Abstract

This study was undertaken to determine the pathological changes in the gastric mucosa in gastrectomy specimens removed for gastric carcinoma at a tertiary care centre. Sixty four such gastrectomy specimens were received during a six year period between January 2009 and January 2015. There were 47 (73.43%) males and 17 (26.56%) females ranging in age from 31-60 years. The most frequent subtype was the intestinal type (84.32%) followed by the diffuse type (15.6%).

Changes observed in the adjacent mucosa were atrophic gastritis (51 cases), intestinal metaplasia (49 cases), Helicobacter pylori infection (44 cases) and dysplasia (47 cases). There was a high percentage of associated chronic atrophic gastritis in intestinal type of carcinoma (88.18%) as compared to diffuse type (50%).

Intestinal metaplasia was more common and distinct in intestinal type (83.33%) compared to diffuse type (40%). Helicobacter pylori was seen in 79.01% of intestinal type and 40% of diffuse type.

Dysplasia was seen in both the intestinal (75.92%) and diffuse types (60%).

INTRODUCTION

Gastric carcinoma, a leading cause of cancer death worldwide is the second and fourth most common cancer in males and females respectively.[1,2] Its incidence varies widely being high in several countries from Asia, Latin America and Central and Eastern Europe, whereas in North America and in most Western European countries it is no longer a common cancer.[3,4] In India, there are reports of high incidence of gastric cancer from various states.[5,6] In Kashmir, Gastric cancer is the third most common cancer only superseded by esophageal and lung cancer. [7,8]

Histologically as well as prognostically, gastric carcinoma behaves as two distinct diseases. This was first recognized by Lauren (1965) who distinguished an intestinal type of cancer from a diffuse type.[9] The 2010 WHO classification[10] recognizes four major histologic patterns of gastric cancers: tubular, papillary, mucinous and poorly cohesive (including signet ring cell carcinoma), plus uncommon histologic variants.

Many studies have identified a number of morphological precursors of gastric carcinoma. These are chronic gastritis[11], atrophic gastritis[11] and intestinal metaplasia[12] associated with Helicobacter pylori [13], gastric polyps[14], gastric remnants[14], Menetrier's disease[14], chronic peptic ulcer disease[12] and gastric dysplasia.[15] In our state where early detection programmes are in a few centres only, most of the patients with gastric carcinoma are diagnosed at a very late stage. Hence it is very important to recognize the various precursor lesions in gastric biopsies which are significantly associated with increased risk of gastric cancer.

This study identifies some of these precursor lesions in gastrectomy specimens removed for gastric carcinoma. The patients with these precancerous lesions can be followed up for a period of time with repeated endoscopic biopsies to detect gastric carcinoma at an early stage.

Material and methods

This was a prospective study conducted in the Department of Pathology, Sher-i-Kashmir Institute of Medical Sciences- Medical College Bemina over a period of six years. Sixty four surgical specimens of gastric carcinoma were received during this period. The specimens were examined and the gastric mucosa adjacent to the tumor (within 1cm of margin) was studied in great detail grossly. A minimum of two sections each were taken from the tumor and from the adjacent mucosa.

Serial sections 5 microns thick were cut and stained with hematoxylin and eosin stain, periodic acid Schiff with Alcian Blue (pH 2.5) for detecting intestinal metaplasia and modified Giemsa stain for Helicobacter pylori.

Results

Gastric carcinoma was classified according to Lauren's classification into intestinal and diffuse types. Intestinal type was more common than the diffuse type forming 54 cases (84.37%) and 10 cases (15.6%) respectively. Various precursor changes were observed in the adjacent mucosa in both intestinal and diffuse types, being more common in the intestinal type.

The various changes studied were: chronic superficial gastritis, chronic atrophic gastritis, intestinal metaplasia, dysplasia and presence of Helicobacter pylori. Out of these changes, chronic superficial gastritis was seen in only 3.7% of intestinal and 10% of diffuse type and had no significant correlation (p value 0.038) with the tumor suggesting that it is not a precancerous condition.

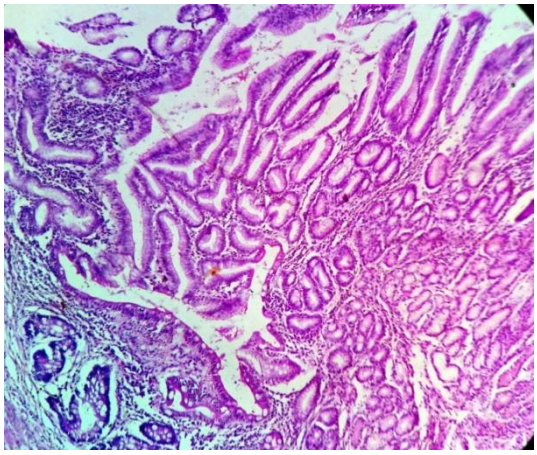
There was a high percentage of chronic atrophic gastritis in intestinal type; 46 cases (85.18%) as compared to diffuse type 5 cases (50%). Microscopically in chronic atrophic gastritis, there was full thickness infiltration of the lamina propria by inflammatory cells, mainly plasma cells, lymphocytes and a variable number of eosinophils accompanied by glandular atrophy. Glandular atrophy was manifested by decrease in glands with increase in the distance between individual glands and condensation of reticulin fibres in the lamina propria. Increasing degree of atrophy was commonly associated with cystic dilatation of glands and metaplasia.

In our study, intestinal metaplasia was more distinct in intestinal type than in diffuse type being 45 cases (83.33%) and 4 cases (40%) respectively. Microscopically, in intestinal metaplasia, there is progressive replacement of gastric mucosa by epithelium having features of intestinal epithelium of either small or large bowel type including globlet cells, absorptive (brush border) cells, Paneth cells, a variety of endocrine cells and occasionally ciliated cells (Fig. 1).Helicobacter pylori were seen in 40 cases (74.07%) of intestinal type and 4 cases (40%) of diffuse type (fig.2). Helicobacter pylori is a gram negative, non sporulated motile spirochete-like bacterium which colonizes the gastric mucosa either lying free in the mucus surface adherent to the surface lining epithelium or within the cells. It is recognized easily in routine Hematoxylin and Eosin stains as thin, wavy, blue rods. However, its detection is facilitated by special stains like modified Giemsa stain which stains it black.

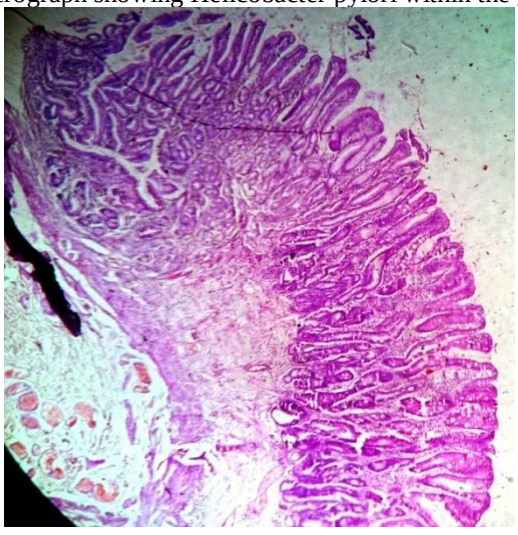
All grades of dysplasia mild – 8 cases (14.81%), moderate – 10cases (18.52%) and severe – 23 cases (42.59%) were seen in intestinal type while as in diffuse type, only two grades mild – 5 cases (50%) and moderate 1 case (10%) were seen(fig. 3). It was recognized by increased cell proliferation accompanied by abnormalities in cell size, configuration and orientation. Mucus secretion was reduced or absent and there was an increase in the nucleocytoplasmic ratio, loss of nuclear polarity and pseudostratification. Mitosis was increased and some atypical mitotic figures were seen. There was a statistical highly significant correlation (p value=0.014) between dysplasia

and tumor (especially intestinal type) and hence this is considered as a precancerous lesions for the development of gastric adenocarcinoma especially the intestinal type. Finally, the distribution of various precancerous lesions was studied in both intestinal and diffuse types of gastric carcinoma. In intestinal type, out of 54 cases, 26 showed four precancerous lesions in the adjacent mucosa, 18 showed three lesions, 4 showed two lesions and 6 cases showed one lesion only. There was a statistically significant difference (p=0.000) in the number of lesions in intestinal type and these lesions have an additive effect and a direct casual role in the etiopathogenesis of gastric carcinoma, especially intestinal type. In diffuse type of carcinoma, the precancerous lesions are less common and do not have a significant association with the tumor.

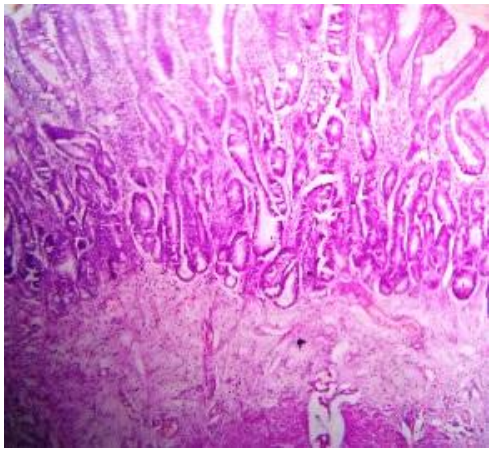
1. Photomicrograph showing intestinalization of gastric surface epithelium (H&E 100X).



2. Photomicrograph showing Helicobacter pylori within the gastric epithelium (Modified Giemsa 400X).



3. Photomicrograph showing high grade dysplasia in the adjacent mucosa (H&E 400X).



Discussion

Gastric carcinoma is a major health problem throughout the world. In India, there are reports of high incidence of gastric cancer from various states like North Kerala[16] and Mizoram[17]. In view of the high incidence of gastric carcinoma in Kashmiri people established in earlier studies[5], the present study was carried out to identify various precursor/precancerous lesions which may play a role in the pathogenesis of gastric carcinoma.

Majority of the gastric tumors (84.37%) were of the intestinal type while as 15.6% were of the diffuse type. This was slightly different from the study done by Sethi et al[18] who reported a higher incidence of the diffuse type (31.1%). Of these, 74.07% of intestinal type gastric carcinoma were males and only 14% females.

The mean age in males was 54.16 years and in females 48.46 years, hence females are affected at a younger age. The gastric mucosa in the immediate vicinity of mostly intestinal type cancers showed a number of morphological changes. There was a high percentage of chronic atrophic gastritis especially in intestinal (85.18%) as compared to diffuse type. Hence the association between chronic atrophic gastritis and carcinoma of stomach is well recognized in our study. Our findings correlate well with those of Lauren[9], Imai et al[19] and Seema Sethi[18].

Intestinal metaplasia in the surrounding mucosa was distinctly more common and widespread in the intestinal type carcinoma (83.33%) than in diffuse type (40%) as has also been shown by Lauren[9] and Bhat et al[20].

Regarding the presence of Helicobacter pylori in the adjacent mucosa, 74.07% of intestinal type and 40% of diffuse type showed Helicobacter pylori positivity. This is in agreement with similar results by Khanna et al. [21] Dysplastic changes in the adjacent mucosa were more pronounced in the intestinal type (75.92%) than diffuse type (60%). In intestinal type, all the three grades of dysplasia were seen with severe dysplasia forming a large proportion (42.59%). Various studies which support our findings include study done by Gregerio et al[22] and Rugge et al.[23].

Thus various precussor changes observed in the adjacent mucosa in this study include chronic atrophic gastritis, intestinal metaplasia, Helicobacter pylori and dysplasia. These changes are more pronounced in the intestinal type than in the diffuse type of gastric carcinoma.

Conclusion

In our state, where the incidence of gastric carcinoma is very high and the patients usually present at a late stage, study of precursor lesions of gastric carcinoma can be helpful in identifying the patients at a very early stage. By recognizing various precancerous changes in gastric biopsies, the patients can be followed up for a period of time with repeat biopsies. Such an approach allows gastric carcinoma to be detected at an early stage thereby increasing the overall survival of the patients.

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