Mucin Histochemistry of the Upper Gastrointestinal Tract

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Abstract

Histochemically differentiated mucins have been studied in the mucosal lining of the esophagus and stomach. Acid mucin was differentiated from neutral mucin by the alcian blue-PAS technique and sulphomucin by the high iron diamine/alcian blue technique. Neutral mucin secreted normally by the stomach mucosa was replaced by acid mucin in 17 of the 19 mucin secreting adenocarcinomas involving the lower third of the esophagus, and in 24 of the 28 mucin secreting gastric adenocarcinomas studied. The intestinal metaplasia (IM) seen in the gastric mucosa associated with adenocarcinoma, chronic gastric ulcer and chronic gastritis was classified according to the type of mucin secreted by the goblet cells. IM secreting sulphomucins was seen to be associated with gastric adenocarcinoma.

Key words: Intestinal metaplasia, adenocarcinoma.

Introduction

Gastrointestinal mucins have been classified histochemically into neutral mucins, sialomucins and sulphomucins.1,2 The purpose of this study was to observe the alterations in the chemical structure of mucin in the normal and affected mucosa in carcinomatous lesions of the upper gastrointestinal tract. The adjacent normal mucosa was also studied to detect changes in the mucin secretion pattern and to determine whether these changes can be considered as premalignant. These changes were compared with changes in the mucin secretion pattern associated with benign lesions.

Material and Methods

The material studied was obtained from surgically resected specimens of the stomach and lower third of the esophagus, in patients with carcinomatous lesions (61 cases) and benign peptic lesions (17). Multiple sections of tissues were studied from the lesion, and from areas adjacent to and distant from the lesion. The carcinomas included 31 gastric adenocarcinomas and 20 carcinomas involving the cardio-esophageal junction. The control cases (12) were selected from individuals presenting with clinical symptoms of acid peptic disease, but the mucosa was found to be endoscopically and histologically normal. The mucosa in these cases was studied from material obtained by endoscopic biopsy.

The various histochemical techniques carried out besides the routine haematoxylin and eosin stains were: (1) alcian blue (pH 2-5) followed by PAS (AB/ PAS) to differentiate acid mucin (blue) from neutral mucin (pink); (2) high iron diamine followed by alcian blue (pH 2-5) (HID/AB) to differentiate sulphomucins (brown/black) from sialomucins (blue); and (3) phloxine tartrazine (PT) to demonstrate mucus cells (red).

Results

Normal mucosa

Normal mucosa was studied from the control cases, and from the mucosa distant from the lesion in resected specimens.

The foveolar cells, the mucus neck cells and glands in the pyloric zone showed ample amounts of neutral mucin, which stained very strongly pink by the AB/PAS technique. A few mucous neck cells and the deep foveolar cells in the fundic zone showed mild AB positivity by the HID/AB technique, denoting the presence of sialomucins. The esophageal submucous glands secreted ample amounts of sulphomucins with moderate amounts of neutral mucins and sialomucins.

Neoplastic mucosa

Gastric: 24 of the 31 gastric carcinomas were located in the pyloric antrum. Histologically, those included moderately differentiated adenocarcinoma (9), poorly differentiated carcinoma (5), intermediate type of carcinoma (1), and undifferentiated carcinoma (1). Of the 28 mucin secreting adenocarcinomas, 24 secreted mixtures of acid mucins, with sulphomucins and sialomucins predominating in 12 cases each. Four mucin secreting adenocarcinomas secreted predominantly neutral mucins.

Cardio-esophageal junction: Histologically, the 20 adenocarcinomas studied were moderately differentiated (10), poorly differentiated (9) and undifferentiated (1). Of the 19 mucin secreting adenocarcinomas, 17 secreted mixtures of acid mucins, with sulphomucins predominating in ten and sialomucins in seven cases. Two mucin secreting adenocarcinomas secreted predominantly neutral mucins.

Intestinal metaplasia (IM): IM was seen in 28 cases with gastric adenocarcinoma. Of these, colonic type of IM was seen in 18 cases, where the goblet cells secreted mainly sulphomucins along with sialomucins. The other 10 cases showed IM which resembled small intestinal mucosa with the presence of mucus cells; the goblet cells secreted sialomucins with no sulphomucins.

Two cases with carcinoma localized to the pyloric antrum, with previous clinical history suggestive of acid-peptic disease for a prolonged period, showed colonic type of IM around the lesion.

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There was no relation between the type of mucus secreted by the tumour and the type of IM seen.

IM was seen in only three of the 20 cases with adenocarcinoma involving the cardio-esophageal junction. Colonic IM was seen in one of these three cases.

**Benign Lesions**

IM was seen in 6 of 14 cases with chronic gastric ulcer studied; colonic IM was seen in one of these cases. IM was seen extensively in two of the three cases of chronic gastritis. Colonic IM was not observed in either of the cases. There was a marked decrease in mucus production in the areas of inflammation.

**Discussion**

The mucus secretion pattern in the normal gastric mucosa observed in this study is consistent with other studies. Trace amounts of sulphomucins were seen in the neck cells and occasionally in the foveolar epithelium. Since the sulphated mucins secreted by the goblet cells and the tumours are stained very prominently in tissues fixed in formalin, the sulphomucin, if present in the normal gastric mucosa in vivo, must be of a different type. The sulphate radical in this mucin may have a very weak binding to the rest of the molecule.

The mucus secretion pattern in the gastric adenocarcinomas in this study has shown predominance of acid mucins, which is similar to the observations of others. This observation led us to investigate the possible role of intestinal metaplasia in the histogenesis of malignancy in the stomach. A close association of IM with gastric adenocarcinomas has been shown in this study. Morson studied IM in detail, and reported a significant association of IM with gastric carcinoma which arose from metaplastic epithelium.

IM was also observed in the mucosa adjacent to benign gastric ulcers. However, two gastric adenocarcinomas in this series, occurring in patients with a long-standing history suggestive of acid-peptic disease, showed the presence of colonic IM around the lesion. Repeated attacks of gastritis may lead to faulty cell regeneration and the development of intestinal types of cells which probably have a low grade of differentiation as compared to the gastric epithelium. This IM has a precancerous potential.

Intestinal metaplasia has been classified into 'intestinal' and 'colonic' types. The latter type denotes incomplete metaplasia with greater instability and a potential to transform into a neoplasm, and is significantly associated with tumours. The association of sulphomucin secreting IM with gastric adenocarcinomas has been reported.

Neutral mucins form a barrier to protect the gastric epithelium from its acidic juices. This function is drastically disturbed by the metaplastic transformation of the mucosa. The sulphate radical is more acidic than the carboxyl radical. Thus the presence of the sulphomucin secreting IM in the associated with gastric carcinoma may be greater. Another suggestive evidence for the neoplastic nature of colonic IM is the fact that colonic adenocarcinomas were seen very frequently in the surface small intestinal carcinomas.

IM has been observed less frequently in the fundic mucosa. Hence it is not possible to associate IM with the adenocarcinomas involving the cardio-esophageal region. These carcinomas showed a predominance of sulphomucin secretion which is consistent with the normal esophageal esophageal glands. Thus we may hypothesize that some of the carcinomas may be arising from these glands rather than from the gastric mucosa. The prognosis of these tumours needs to be evaluated.

**References**