

Mucin profile of Upper Gastrointestinal Tract Lesions

Prathima S, Harendra Kumar M L

Department of Pathology
Sri Devaraj Urs Medical College, Kolar

ABSTRACT

Background: Mucin secretions reflect the composition changes in the functional state of the mucosa in health and disease of the upper gastrointestinal tract.

Objectives: To study the different types of upper gastrointestinal tract lesions and to determine the role of mucin histochemistry in the interpretation of lesions of upper gastrointestinal tract.

Methods: A prospective study from September 2006 to August 2007 was carried out. 60 endoscopic biopsy specimens obtained from upper gastrointestinal tract lesions from the department of Gastroenterology at R.L. Jalappa Hospital & Research Centre was sent for histopathological examination. All the sections were stained by routine Haematoxylin and Eosin stain followed by special stains for mucins i.e Alcian blue pH 2.5 / PAS and Hale's Colloidal Iron.

Results: Age of presentation of various upper gastrointestinal lesions was between 26-90 years. Females dominated the study group i.e. 39 (65%) when compared to males i.e. 21 (35%). Alcian Blue/Periodic Acid Schiff (AB/PAS) staining in oesophageal lesions could detect mixture of acidic mucins & neutral mucins and sulphomucins in Barrett's oesophagus. In gastritis, predominantly mixture of acidic and neutral mucins and in one case, sulphomucins were detected. Adenocarcinoma of stomach showed combination of acidic and neutral mucins. Duodenitis showed acidic, neutral and sialomucins. Adenocarcinoma of duodenum showed combination of acidic & neutral mucins. Hale's Colloidal Iron (HCl) stain in inflammatory & neoplastic lesions of stomach & duodenum, could detect only acidic mucins.

Conclusion: In neoplastic condition of stomach this study suggests that those tumours which secrete neutral and mixed mucins probably arise from gastric epithelium and neck cells of the gastric glands. In those cases where the tumour produces acidic mucins it is possible the tumour arose from areas of intestinal metaplasia.

Key words: Mucins, Histochemistry, Alcian Blue / Periodic Acid Schiff, Hale's Colloidal Iron

Corresponding author:

Dr. Prathima.S,
Assistant Professor,
Department of Pathology,
Sri Devaraj Urs Medical College,
Tamaka, Kolar 563 101.
Email: parianil@gmail.com
Mobile: +918050976979

INTRODUCTION

The upper gastrointestinal tract comprises of the oesophagus, stomach and the first part of the duodenum.^[1] The epithelial cells of the gastrointestinal mucosa are rich in main carbohydrate-protein component of the secretory mucus and cell membranes.^[2] The original term 'Mucin' was mentioned by an

American worker named Carpenter as long ago as 1846.^[3] Mucins can be classified by their histochemical properties into neutral mucins detected by Periodic acid Schiff [PAS] stain, sialic acid containing mucins (Sialomucins) detected by Alcian blue [AB] stain and sulphate containing mucins [Sulphomucins] detected by High iron diamine [HID] stain.^[2]

Mucus glycoproteins are high molecular weight compounds with large numbers of carbohydrate side chains attached to the proteins core through an O-glycosidic bond between N-acetyl galactosamine and serine or threonine.^[2] The physiochemical properties of mucus depend on the composition and structure of its glycoprotein constituents. These mucins not only form a viscoelastic mucus gel layer that protects and lubricates the underlying epithelium but also generates a protective diffusion barrier from the underlying epithelium. It also acts as a free radical scavenger partly as a consequence of its ability to bind with lipids.^[2]

The present knowledge of the composition of mucins in the various mucus secretory cells throughout the body and its alterations in disease owes much to its histochemistry. Hence this study has been taken up to study the role of mucin histochemistry in diagnosis of upper gastrointestinal lesions.

AIMS AND OBJECTIVES

1. To study the different types of upper gastrointestinal tract lesions.
2. To determine the role of mucin histochemistry in the interpretation of lesions of upper gastrointestinal tract.

MATERIALS AND METHODS

A prospective study was carried out in the department of pathology for a period from September 2006 to August 2007. Endoscopic biopsy specimens obtained from 60 patients with upper gastrointestinal lesions were included for the study. Lower gastrointestinal tract biopsy specimens were excluded. The demographic data of patients were recorded at the time of collection. Specimens were fixed in 10% formalin, processed and embedded according to standard protocol. All the cut sections were stained by Hematoxylin and Eosin (H&E) followed by special histochemical stains i.e. Alcian Blue/Periodic acid Schiff (AB/PAS) at 2.5 and 1.0 pH and Hale's Colloidal Iron (HCl) stain. The data was analysed using SPSS package. Tests of significance were employed and value of 0.05 was taken as critical level of significance.

RESULTS

In our study 60 cases of upper gastrointestinal endoscopic lesions were considered, comprising of 12 cases from oesophagus, 44 cases from the stomach and 4 cases from the duodenum. Age of presentation of various upper gastrointestinal lesions was between 26-90 years. Maximum number of cases i.e., 19 (31.67%) were among the age group of 61-70 years and the least were 4 (6.67%), belonging to ≤ 30 years of age showing a significant association $p < 0.05$ [Table-1]. The Mean age of cases was 59.2 years. Females dominated the study group i.e., 39 (65%) when compared to males i.e., 21 (35%). The Male: Female ratio was 1:1.8.

AB/PAS at 1.0 pH staining in oesophageal lesions could detect mixture of acidic & neutral mucins and sulphomucins in Barrett's oesophagus only. In stomach lesions, AB/PAS stain at 2.5pH could detect predominantly neutral mucins, mixture of acidic and neutral mucins in gastritis and acidic mucins, neutral mucins and mixture of acidic and neutral mucins in adenocarcinoma of stomach [Figure 1]. One case of chronic gastritis



Figure 1: Photomicrograph of Adenocarcinoma stomach showing predominantly neutral mucins within signet ring cells.(AB/PAS at pH 2.5, 400x)



Figure 2: Photomicrograph of Intestinal metaplasia of stomach showing goblet cells with acidic mucins. (AB/PAS at pH 1.0, 400x)

with intestinal metaplasia showed goblet cells positive for sulphomucins [Figure-2]. Duodenitis showed acidic, neutral, sialomucins and sulphomucins and well differentiated adenocarcinoma showed mixture of acidic and neutral mucins and sulphomucins by AB/PAS stain at 1.0 and 2.5 pH [Table-2]. HCl staining could not detect any mucins in oesophageal lesions. In stomach and duodenal lesions, HCl detected only acidic mucins. [Table-3]

DISCUSSION

The distribution and amount of mucins varies in different regions of the upper gastrointestinal tract. Mucosa of the stomach, oesophagus and duodenum has been found to have some qualitative as well as quantitative changes in the non-neoplastic and neoplastic lesions compared to normal mucosa by mucin histochemistry.^[3]

Silva S et al in their study on gastric mucins noted that the maximum number of cases were between 45-60 years and the mean age was 55.7 years.^[4] In the present study maximum number of cases i.e., 19 (31.61%) were among the age group of 61-70 years and the mean age being 59.2 years.

In our study females dominated the study group i.e. 39 (65%) when compared to males i.e. 21 (35%). The Male: Female ratio was 1:1.8. But study by Rothery et al and Silva S et al observed male preponderance with Male: Female ratio of 1.5:1 and 1.23:1 respectively.^[4,5] High spicy diet, tobacco chewing in females contribute to the female preponderance of upper gastrointestinal lesions and risk for upper gastrointestinal cancer in Kolar in a study by Kalyani et al.^[6]

Suvarna N et al in their study on lesions

Table 1: Age-wise distribution of cases

Age (Yrs)	No	%
≤30	4	6.67
31-40	7	11.67
41-50	5	8.33
51-60	14	23.33
61-70	19	31.67
>70	11	18.33
Total	60	100.00

$$\chi^2 = 16.8, p < 0.05$$

Table 2: Alcian Blue/PAS at pH 2.5 and 1.0 staining-wise distribution of cases

SITE	HISTOPATHOLOGICAL DIAGNOSIS	ALCIAN BLUE/PAS				
		+ve Acid Mucin	+ve Neutral Mucin	+ve Acid & Neutral Mucin	+ve Sialo- mucin	+ve Sulpho- mucin
Oesophagus	Normal Glands (n=12)	0	0	0	0	0
	Oesophagitis (n=2)	0	0	0	0	0
	Barrett's oesophagus (n=1)	0	0	1	0	1
	Well Differentiated SCC (n=3)	0	0	0	0	0
	Moderately Differentiated SCC (n=5)	0	0	0	0	0
	Poorly Differentiated SCC (n=1)	0	0	0	0	0
Stomach	Normal Glands (n=44)	0	26	1	0	0
	Gastritis (n=16)	0	3	13	0	1
	Polyp (n=1)	0	0	1	0	0
	Well Differentiated ADC (n=12)	4	1	7	0	0
	Moderately Differentiated ADC (n=10)	1	1	8	0	0
	Poorly Differentiated ADC (n=5)	0	1	4	0	0
	Normal Glands (n=4)	0	1	0	0	0
Duodenum	Duodentitis (n=2)	1	1	0	1	1
	Polyp (n=1)	0	0	1	0	0
	Well Differentiated ADC (n=1)	0	0	1	0	1

Table 3: Hale's colloidal Iron staining-wise distribution of cases

HALE'S COLLOIDAL IRON						
SITE	HISTOPATHOLOGICAL DIAGNOSIS	+ve Acid Mucin	+ve Neutral Mucin	+ve Acid & Neutral Mucin	+ve Sialo- mucin	+ve Sulpho- mucin
Oesophagus	Normal Glands (n=12)	0	0	0	0	0
	Oesophagitis (n=2)	0	0	0	0	0
	Barrett's oesophagus (n=1)	0	0	0	0	0
	Well Differentiated SCC (n=3)	0	0	0	0	0
	Moderately Differentiated SCC (n=5)	0	0	0	0	0
	Poorly Differentiated SCC (n=1)	0	0	0	0	0
Stomach	Normal Glands (n=44)	1	0	0	0	0
	Gastritis (n=16)	14	0	0	0	0
	Polyp (n=1)	1	0	0	0	0
	Well Differentiated ADC (n=12)	12	0	0	0	0
	Mod Differentiated ADC (n=10)	8	0	0	0	0
	Poorly Differentiated ADC (n=5)	5	0	0	0	0
Duodenum	Normal Glands (n=4)	0	0	0	0	0
	Duodentitis (n=2)	1	0	0	0	0
	Polyp (n=1)	1	0	0	0	0
	Well Differentiated ADC (n=1)	1	0	0	0	0

of stomach observed that 37 (52.85%) cases were from antrum followed by fundus 8 (11.42%) and body 9 (12.85%) similar to findings of the current study.^[7]

Jass JR, in his study of mucin histochemistry of the columnar epithelium of the oesophagus showed that intestinal metaplasia was characterised by barrel shaped goblet cells secreting acidic mucins.^[8] In our study in

Barrett's oesophagitis, sulphomucins were detected in intestinal metaplastic cells by AB/PAS at 1.0 pH which is consistent with Intestinal metaplasia Type III. Sandick JW et al in their study observed sulfomucin positivity tended to be less frequent in Intestinal Metaplasia at an endoscopically normal appearing esophagogastric junction than in Intestinal Metaplasia in a columnar cells lined

esophagus, traditionally called Barrett esophagus.^[9]

Meenakshi GI et al, in their study showed that neutral mucins predominated in normal gastric epithelium which was also seen in the present study.^[10]

Wabinga HR, in his study of mucin secretion by gastric carcinoma cells by AB/PAS stain in 30 cases found that in 84% cases the tumour cell secreted either neutral or mixed mucins and acidic mucins were demonstrated in 5% of the cases.^[11] In the present study out of 27 (45%) cases of carcinoma stomach, in 19 (31.7%) cases tumour cells secreted neutral mucins and acidic mucins. Long standing chronic gastritis leads to significant loss of parietal cell mass and associated with intestinal metaplasia recognised by the presence of goblet cells showing positivity for acidic mucins and is strongly associated with increased risk of gastric adenocarcinoma.^[12] In cases where tumour cells produce acidic mucins it is possible that tumour arises from the areas of intestinal metaplasia which was observed in the present study. However *Helicobacter pylori* status was not established in this study.

In our study mucin histochemistry of gastric polyp detected mixture of acidic and neutral mucins but studies by Lev R and Goldman H et al, neutral mucins were detected.^[13,14]

In the present study duodenitis showed acidic, neutral, sialomucin and sulphomucins. Duodenal polyp showed mixture of acidic and neutral mucins. Adenocarcinoma of duodenum showed combination of acidic & neutral mucins and sulphomucins. Filipe MI, in his study

observed that in normal duodenum and cases of duodenitis neutral mucins predominated and also showed that sulphomucins were absent from normal duodenum but, in adenocarcinoma of duodenum he observed a mixture of acidic and neutral mucins, sialomucins and sulphomucins.^[2]

In stomach lesions i.e. gastritis, gastric polyp and gastric adenocarcinoma, HCl could detect only acidic mucins. In duodenitis, duodenal polyp and adenocarcinoma of the duodenum it could detect only acidic mucins. Belanger et al, in his study observed that fundic stomach, pit cells and some cells of the isthmus and mucous neck cells of the stomach are Hale's positive.^[15] He also observed some acidic mucins in brunner's gland of the duodenum.

In view of the multiple cell types individually contributing to the oesophagus, gastric and duodenum mucinous secretions, not much variation was observed when compared to other studies which can be attributed to mucosal structure and function. A large sample study needs to be carried out to establish the histogenic link and clarify the various relationships with confidence.

CONCLUSION

Neutral mucins and a mixture of acidic and neutral mucins predominated in inflammatory lesions of the stomach and duodenum. In neoplastic conditions of stomach and duodenum neutral mucins were found along with mixture of acidic and neutral mucins detected by AB / PAS at 2.5 pH. In neoplastic condition of stomach this study suggests that those tumours which secrete neutral and mixed

mucin probably arise from gastric epithelium, neck cells of the gastric glands. In those cases where the tumour produces acidic mucins it is possible the tumour arose from areas of intestinal metaplasia.

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