SHORT REPORTS

Mucin histochemistry of esophagus in health and malignancy

TANUJA SHET, SANGEETA DESAI, SUHASINI PRABHU, DEEPAK AMARAPURKAR

Departments of Pathology and *Gastroenterology, T N Medical College and B Y L Nair Ch Hospital, Mumbai 400 008

Aims: To study mucin histochemistry of the normal esophagus, esophageal adenocarcinoma, and carcinoma exhibiting glandular and squamous elements, to ascertain the origin of these tumors. **Methods:** Mucin histochemistry was studied in sections of the normal cardiosophageal junction obtained from 25 post-mortem specimens and in 12 mucin-secreting esophageal carcinomas. **Results:** The normal submucosal esophageal glands and three adenocarcinomas secreted predominantly sulfomucins; a mixture of neutral and sialomucins was seen in the nine carcinomas with squamous and glandular traits. Barrett's metaplasia was not encountered. **Conclusions:** In the absence of Barrett's metaplasia, esophageal adenocarcinoma probably arises from the submucosal glands, whereas squamous carcinomas with mucin-secreting component could arise from metaplastic change in squamous epithelium, cardiac glands, or multipotent stem cells in the epithelium. [Indian J Gastroenterol 1997; 16: 140-141]

Key words: Esophageal adenocarcinoma

Most esophageal adenocarcinomas develop in areas of Barrett's metaplasia, although a few may arise from submucosal glands and heterotopic gastric mucosa. Since Barrett's metaplasia is rare in Asians, origin from the latter two sites seems likely in Indians. The character of mucosa secreted could provide a clue to this. We compared the types of mucin secreted in 12 esophageal carcinomas with that in the normal esophagus with a view to find the probable site of origin.

**Methods**

Of 84 esophageal carcinomas seen in our institution from January 1991 to January 1993, nine with squamous and glandular (adenoc) elements (SA) and three adenocarcinomas showed mucin secretion. Adequate biopsy tissue was available from seven SA; two were resected specimens. Biopsy tissue from the three adenocarcinomas was also analyzed.

Biopsies or sections were taken from the tumor, adjacent mucosa, cardiosophageal (CE) junction and, in tumors close to the CE junction, from cardiac mucosa. These were stained with H & E, mucicarmine, periodic acid Schiff (PAS) with alcian blue at pH 2.5, and high iron diamine-alcian blue (HID-AB). We also studied 6 cm of the lower esophagus along with the CE junction and 2 cm of cardiac mucosa from 25 post-mortem specimens.

**Results**

Six SA were in the lower third of the esophagus and three involved the lower and middle thirds. Eight were confined to the esophagus; one had a satellite nodule at the cardia. The adenocarcinomas were situated in the lower third; one tumor extended less than 1 cm into the cardia.

The mucin-producing element occupied more than 5% of the tumor in all cases. The squamous component was moderately differentiated in all the SA. The mucin-secreting component was in the form of glands clearly demarcated from the squamous component in six cases (Fig 1); in two cases biopsies showed islands of cells (few with clear cytoplasm) with central lumina containing mucin. In one case a mixture of the above patterns was seen. The squamous component was at the periphery and was the locally invading one, whereas the glandular component was more submucosal and central. In one case the primary lesion had more squamous elements but the nodal metastasis showed the glandular trait. The adjacent epithelium showed moderate dysplasia in one case and dysplasia with in situ carcinoma in two SA cases, along with changes of reflux esophagitis in one of the latter.

Of the three adenocarcinomas, two showed well-formed glands (Fig 2); one showed poor differentiation with signtet-ring cells. The adjacent epithelium was normal. Cardiosophageal mucosa was normal in the two adenocarcinomas restricted to the esophagus.

The post-mortem sections showed normal squamous epithelium; features of Barrett's metaplasia were not seen.

Fig 1: Glandular element showing acidic mucin (arrow) clearly demarcated from squamous component (arrowheads) (PAS with alcian blue, 40X)
Eosophageal mucon histochemistry

In the post-mortem sections, submucosal esophageal glands contained 90% or more sulfomucins in 18 cases (Fig 2); in seven cases variable mixture of sialo- and sulfomucins was seen, though the latter predominated (60%-70% of total mucin). The cardiac glands showed predominant neutral mucin and variable sulfomucin in five cases.

The normal submucosal glands in the two resection specimens with SA showed predominantly sulfomucins. Six SA showed more than 90% sialomucin and scanty neutral mucin (Fig 1), whereas three showed approximately 60% sialomucin and 40% neutral mucin, along with sparse sulfomucin in two cases.

In the two moderately differentiated adenocarcinomas, there was a mixture of mucins with predominance of sulfomucin (75%-60%) (Fig 2); the poorly differentiated signet-ring adenocarcinoma expressed scant sulfomucin.

Discussion

Esophageal adenocarcinomas probably arise from embryonic columnar epithelium, submucosal glands or Barrett’s epithelium. In view of the rarity of Barrett’s metaplasia in Asians, adenocarcinomas in Indians could originate from the first two. Bell-Thomson et al. proposed that the subepithelial nature of adenocarcinomas and noncancerous overlying epithelium suggest origin from submucosal glands. This was noted in the three adenocarcinomas in our study; their mucin histochemistry had mainly sulfomucins, which was the mucin found in the normal submucosal glands. Also, the adjacent mucosa and CE junction did not show specialized columnar epithelium; however, Barrett’s metaplasia cannot be ruled out as there may have been sampling errors. Though one tumor straddled the CE junction, gastric origin is less likely as the tumor had a dominant intraesophageal mass. Some workers believe that tumors of the cardia behave akin to esophageal carcinomas and should be grouped with them.

The origin of mucin-secreting adenosquamous carcinomas is more controversial. Lam et al. postulated that SA arise from submucosal glands as mucin produced by them and the glands is similar. Western studies reported a mixture of neutral mucin, sialomucin and sulfomucin in the submucosal glands. In our series the submucosal glands showed sulfomucins; this was also reported in another Indian study. The SA showed a preponderance of sialomucins; this suggests that they arise from glandular metaplasia of the squamous cells. Also, the adjacent mucosa often shows dysplasia in situ squamous carcinoma, suggesting a squamous cell origin of these tumors.

Another possible site of origin is cardiac glands. We found that CE junction glands secreted neutral mucin and variable sulfomucin. Sialomucin and less frequently sulfomucin have been demonstrated in these glands in reflux esophagitis. Thus, cardiac glands altered by reflux esophagitis could be progenitors for SA. Finally, multipotent stem cells in the esophageal mucosa, capable of differentiating along squamous and glandular lines, could also give rise to SA.

Thus, esophageal adenocarcinomas unaccompanied by Barrett’s metaplasia could arise from submucosal glands. Mucin-secreting adenosquamous carcinomas could arise from metaplastic change in the squamous epithelium, or from cardiac glands or multipotent stem cells in the mucosa.

References


Correspondence to: Dr. Shet, 398, Building 31, Prabhudas, Swatentry Sainik Nagar, Amboli, Andheri(W), Mumbai 400 058
Received July 9, 1996. Received in final revised form April 16, 1997. Accepted April 18, 1997.

Indian Journal of Gastroenterology 1997 Vol 16