

“Glassy” Cells in Barrett’s Mucosa

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Abstract. *Background:* In 1991 we detected glandular cells with “glassy” cytoplasm (GCs) in human gastric mucosa having intestinal metaplasia (IM). GCs were subsequently found in the gastric mucosa of baboons. *Materials and Methods:* The frequency of GCs (defined as glandular cells with a homogeneously pale, eosinophilic cytoplasm having a ground-glass appearance) was assessed in 403 human esophageal biopsies with columnar-lined esophagus. GCs may be in one gland or in a group of glands in metaplastic mucosa. *Results:* Out of the 403 esophageal biopsies, 176 had cardiac glands with or without oxytic cells (glandular metaplasia type 1 and 2, respectively) and the remaining 227 cases additionally had goblet cells (that is IM), glandular metaplasia type 3 (namely, Barrett’s mucosa). Four out of the 403 cases (0.99%) had glands with GCs; all four cases were recorded among the 227 cases having glandular metaplasia type 3. Thus, GCs were detected in 1.8% of the cases with Barrett’s mucosa. *Conclusion:* Previous studies showed that GCs were present in the gastric mucosa of specimens harbouring a gastric carcinoma. The present study showed that GCs are also present in Barrett’s mucosa, a lesion often preceding epithelial dysplasia and carcinoma. The association between GCs and Barrett’s mucosa deserves further investigation.

In 1991 we reported the existence of a novel glandular phenotype in the human gastric mucosa characterized by cells with a homogeneously pale, eosinophilic cytoplasm having a ground-glass appearance (1, 2). The occurrence of these gastric cells was subsequently confirmed in other studies (3-6), and they were given the trivial working name of “glassy” cells (GCs). Notably, GCs were also found in the gastric mucosa of non-human primates (7, 8).

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Recently, while examining esophageal biopsies with columnar-lined epithelium in humans, we noticed the presence of glands displaying GCs.

The purpose of the present work was to audit the frequency of cases with GCs in a cohort of esophageal biopsies in humans, having at histological examination, columnar-lined mucosa.

Materials and Methods

From the files of the Department of Pathology, 403 consecutive biopsies having columnar-lined esophageal mucosa were retrieved.

Definitions. Three phenotypes of glands with columnar-lined mucosa may occur in the esophageal metaplastic mucosa: with cardiac or with fundic glands (referred to as glandular mucosa type 1 and 2, respectively) and with intestinal metaplastic glands (referred to as glandular mucosa type 3). There is a prevailing consensus to call Barrett’s esophagus those cases having glandular mucosa type 3, as dysplasia or cancer are associated with this mucosa phenotype and not with glandular mucosa types 1 or 2. The American Gastroenterological Association defines Barrett’s esophagus as the displacement of the squamocolumnar junction (SCJ) proximal to the gastroesophageal junction (GEJ). When the metaplastic transformation displays glands with mucus-producing goblet cells, it is referred to as intestinal metaplasia (IM).

GCs may be found in one gland or in a group of glands in esophageal metaplastic mucosa (Figures 1 and 2). In order to disclose the presence of GCs, hematoxylin and eosin (H&E) stained sections were scrutinized at x200.

Results

Out of the 403 consecutive esophageal biopsies showing columnar-lined mucosa, 176 (98 male and 78 female) had cardiac glands with or without oxytic cells (that is glandular metaplasia type 1 and 2, respectively). The remaining 227 cases (154 male and 73 female) had, in addition, goblet cells (that is glandular metaplasia type 3, known as Barrett’s mucosa). The glassy material was not found in the cytoplasm of the goblet cells. Out of the 403 biopsies, four (0.99%) had glands with GCs; all four cases were recorded among the 227 cases having glandular metaplasia type 3. Thus, GCs were detected in 1.8% of the cases with Barrett’s mucosa.

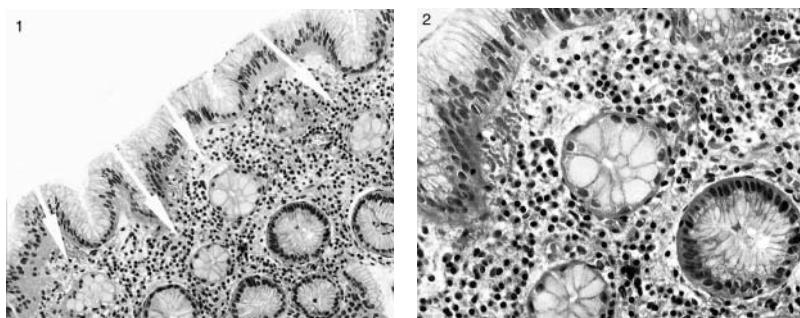


Figure 1. Columnar-lined human esophagus showing several groups of glands having cells with "glassy" cytoplasm (arrows, $\times 10$, H&E, Barrett's esophagus).

Figure 2. Detail from Figure 1, showing a gland built of cells with "glassy" cytoplasm ($\times 20$, H&E, Barrett's esophagus).

Discussion

The results demonstrated that esophageal biopsies showing Barrett's mucosa at histological examination might contain glands with GCs.

The proteinaceous, glassy material secreted by GC-organelles is, for unknown reason(s), retained in the cytoplasm of the cells of the metaplastic mucosa. Kopito and Sitia (9) claim that all cells are equipped with a proteolytic apparatus that eliminates misfolded and damaged proteins. The 26S proteasome, the principal engine of cytoplasmic proteolysis, requires unfolded substrates but is ineffective at degrading aggregated proteins. When the production of aggregated proteins exceeds the cell's capacity to eliminate them, a phenomenon of cellular indigestion of the endoplasmic reticulum (ER) occurs. The condensation of non-secreted products suggests that the mechanism of protein transport in the ER is incompetent and that the proteins are neither degraded nor secreted and, thus, remain stored in dilated cisternae (9). This mechanism might explain the accumulation of intracellular glassy material in metaplastic esophageal glands.

The glands with GCs were found to be surrounded by well-preserved connective tissue amidst other well-preserved metaplastic esophageal glands, implying that GCs are not a structural artifact conveyed by poor fixation or by other causes, but a genuine morphological phenomenon. Despite GCs being easily recognized in H&E stained sections, the histochemical and/or immunohistochemical nature of the glassy material remains unidentified (3, 6).

GCs were first detected in the glands of the gastric mucosa (1-6). In a subsequent comparative survey of 3,203 gastrectomy specimens (10), we found GCs in 2.1% of the 1,261 patients living in the Pacific basin, but only in 0.6% of the 1,942 patients residing in the Atlantic basin ($p < 0.05$). These results suggested that GCs might be evoked by dissimilar environmental exposures in the two basins. Since environmental factors have been suggested to influence the presence of GCs in the gastric mucosa (10), the possibility that environmental factors might also have contributed to evoke GCs in the Barrett's mucosa cannot be totally rejected. This possibility will be tested on patients dwelling in disparate geographical regions. Recently, GCs were identified in the Barrett's mucosa of baboons (11) and in the gastric mucosa of H/K-ATPase-

deficient (Atp4a $(-/-)$) mice (12). The latter findings are a new indication that asserts the identity of GCs.

A previous study showed that GCs were present in the gastric mucosa of specimens harbouring a gastric carcinoma (10). The present study showed that GCs are also found in the Barrett's mucosa, a lesion often preceding epithelial dysplasia and carcinoma. Hence, the association between GCs and Barrett's esophagus (as well as gastric carcinoma) deserves further investigation.

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