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Abstract:

Undifferentiated cells in gastrointestinal mucosa inferring an association between carcinoma of the colon and intestinal type gastric cancer*

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Clusters of abnormal columnar cells have been observed within surface epithelium in gastric mucosa (fig 1). Computerised image analysis confirmed that they were taller than normal gastric foveolar cells with centrally situated, round, or ovoid nuclei and prominent nucleoli. The cytoplasm appeared clear and contained no demonstrable mucin. There was abrupt transition between the cell clusters and adjacent normal epithelium and no evidence of a brush border to suggest intestinal differentiation. Immunohistochemical analysis showed expression of p62 *c-myc* oncogene product by the cells. In a study of the abnormal cells in 200 routine gastric biopsy specimens they were most frequently associated with atrophic gastritis and type 3 intestinal metaplasia ($n = 164$, 82%), compared with atrophic gastritis, and types 1 and 2 metaplasia ($n = 70$, 35%), and chronic superficial gastritis ($n = 8$, 4%). They were not seen in normal mucosa.¹

In a further study of colorectal mucosa, cells morphologically identical with those described in gastric mucosa were seen within surface epithelium in 25 of 130 adenomatous polyps, and in the non-polypoid and polypoid mucosa in 10 out of 10 cases of familial adenomatous polyposis.² Some of the cells were in mitosis, and none showed evidence of mucin secretion or a brush border. As in the stomach the cells occurred in clusters and were easily identifiable within

both neoplastic epithelium in adenomatous polyps (fig 2) and histologically normal epithelium in non-polypoid mucosa in familial adenomatous polyposis (fig 3).

Fig 1 Cluster of undifferentiated cells (between large arrows) within surface epithelium in a case of atrophic gastritis. A small group of intermingled normal columnar cells are present (small arrow). (Haematoxylin and eosin.)

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Fig 2 Undifferentiated cells surrounded by typical basophilic neoplastic epithelium on the luminal surface of a non-hereditary tubulovillous adenoma. There is a sharp border between the two cell types (arrows).

These cells have not been previously described in histological sections, although a similar cell was noted in an ultrastructural study of non-polypoid mucosa in familial adenomatous polyposis.³ They show no light microscopic evidence of gastric or intestinal differentiation, and the nuclear appearance, presence of mitotic figures, and staining for *c-myc* product suggest that at least some of the cells are proliferating. The presence of immature, dividing cells on the gastrointestinal mucosal surface is abnormal and may represent extension of the proliferative compartment from the glandular neck region in the stomach and the crypt base in the colon and rectum to the mucosal surface. This is supported by cell kinetic studies using thymidine labelling which have shown surface proliferative activity in atrophic gastritis,⁴ and in the colon before the formation of hereditary adenomatous polyps,⁵ and by a morphological study showing that non-hereditary colonic adenomas arise in surface epithelium.⁶

It is proposed that the appearance of undifferentiated cells on the mucosal surface may be an important step in the histogenesis of type 3 intestinal metaplasia in the stomach and adenomatous polyps in the colon and rectum. Cells with capacity for differentiation would be uniquely susceptible at this site to influence by substances within the gastrointestinal lumen. Type 3 intestinal metaplasia is characterised by

Fig 3 Groups of undifferentiated cells (between arrows) on the mucosal surface of non-polypoid mucosa in familial adenomatous polyposis. The surrounding epithelium seems to be normal. (Haematoxylin and eosin.)

production of sulphomucin, normally found in the colon, and is associated with intestinal type gastric carcinoma.⁷ This variant of gastric carcinoma may share a common histogenesis with colorectal adenomas and carcinomas.

References

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