RAPID COMMUNICATION Jpn. J. Cancer Res. 84, 493–494, May 1993

Atypical Mitosis in Gastric Intestinal Metaplasia in Japanese Patients

Carlos A. Rubio,[1] Yo Kato and Tomoyuki Kitagawa

Department of Pathology, Cancer Institute, Kami-Ikebukuro 1-37-1, Toshima-ku, Tokyo 170

The characteristics of the mitotic figures occurring in intestinal metaplasia of the gastric mucosa were investigated in 50 consecutive gastrectomy specimens. The specimens contained, in addition, early gastric cancer of intestinal type (n=38) or of diffuse type (n=12). One hundred or more consecutive mitoses/specimen were studied by high-power microscopy (×1000). Of the 5,140 mitoses, 1,030 (i.e. 20.0%, range 8–34%) were considered as atypical according to a previous classification. The presence of atypical mitosis was not influenced by the gender or age of the patient, or the histological type of the tumor present in the specimen. Studies of gastrectomy specimens from Swedish patients with early gastric cancer showed a much lower frequency of mitotic figures/specimen and occasional atypical mitosis. The high frequency of atypical mitosis in intestinal metaplasia in the gastric mucosa of Japanese nationals may mirror a profound genetic instability in that mucosa, and suggests that intestinal metaplasia with atypical mitosis may be a precancerous lesion in the Japanese.

Key words: Gastric mucosa — Intestinal metaplasia — Atypical mitosis

While reviewing gastrectomy specimens from Japanese patients having early gastric cancer, to assess the frequency of intramucosal cysts[1] of ciliated cells[2] and of intestinal metaplastic mucosa,[3] we noticed a high frequency of mitotic figures in areas with intestinal metaplasia (IM). The purpose of the present work was to study in more detail the morphologic characteristics of those dividing cells. Hematoxylin and eosin-stained sections from 50 gastrectomy specimens were analyzed. Areas with IM (frequent in the gastric mucosa of the Japanese carrying a gastric carcinoma[4]) were screened for the presence of mitotic figures at low magnification (×25). Mitotic figures were subsequently analyzed by high-power microscopy (×1000). A total of 100 or more consecutive mitoses were analyzed. In a previous report, we described the characteristics of the various phases (prophase, prometaphase, metaphase, anaphase and telophase) of normal mitosis (in areas with chronic gastritis) and of atypical mitosis (in areas with gastric adenoma[5]). Atypical mitoses were considered those having giant prophases, segregated chromosomes, irregular chromosome arrangement with angularity of the metaphasal plate, oblique or horizontal metaphases, semicircular or quasi-semicircular metaphases, three or four polar mitoses, asymmetric migrating chromosomes, chromosomal bridging and asymmetric daughter cells. Examples of those anomalies are shown in Fig. 1.

A total of 5,140 mitoses were recorded in the 50 gastrectomy specimens (mean 104.1 mitoses/case, range 100–117). Of the 5,140 mitoses, 1,030 (i.e. 20.0%, range 8–34%) were considered as atypical. Of the 50 cases, 38 were males and 12 females. No significant difference in the percentage of atypical mitosis was found between males (20.3%) and females (19.8%). The percent of atypical mitosis was not influenced by the age of the patient or by the histological type of the tumor present in the specimen. The sections obtained for this study were obtained from the various regions of the stomach (i.e. corpus and antrum). The results demonstrated no trend concerning the presence of atypical mitoses and their topographical localization (antrum, corpus or tumor proximity). Study of 8 additional gastrectomy specimens carrying a benign peptic ulcer revealed only a few mitoses in areas with IM and consequently did not meet the criterion for inclusion in the present series (i.e., specimens with 100 or more mitoses).

Previous work in Japanese subjects[5] indicated that the percentage of atypical mitosis in areas with chronic gastritis was 1.4%. It should be pointed out that the total number of mitoses recorded in those specimens was only about 30. The occurrence of atypical mitosis in tumors of the gastrointestinal tract has been previously reported not only in the esophagus,[6] stomach,[5] and colon,[7] but also in the atrophic mucosa of pediatric patients with celiac disease.[8] The percentage of atypical mitosis in atrophic (non-neoplastic) intestinal mucosa from pediatric patients was 1.2%.[8] On the other hand, up to 81.3%[7] of the mitoses in gastrointestinal tumors were shown to be atypical.

The high frequency of atypical mitosis in IM from Japanese patients contrasts with the low percent of atypical mitosis found in 18 gastrectomy specimens with early gastric cancer in Swedish patients.[9] While 16 of the 18

[1] Present address: Karolinska Institute, 104 01 Stockholm, Sweden.

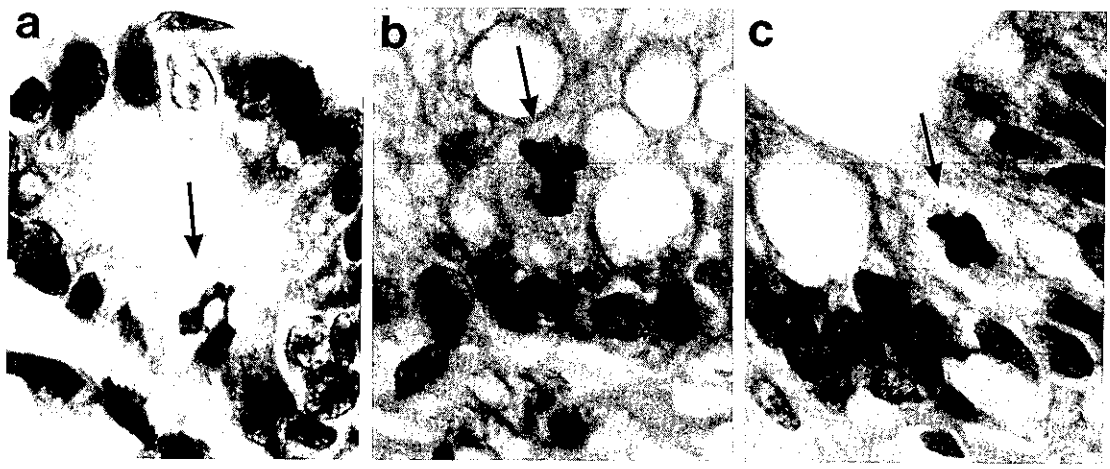

Fig. 1. Examples of atypical mitosis in intestinal metaplasia in gastrectomy specimens from Japanese patients (at arrows). a) Ring-shaped prometaphase with asymmetric chromosomal distribution. b) Three-polar mitosis. c) Four-polar mitosis. (All sections stained with H&E, ×1000).

gastrectomies contained only a few mitoses in IM, 2 specimens had >100 mitoses. In these 2 specimens, the frequency of atypical mitosis in areas with IM was 1.3% and 1.6% respectively (Rubio, unpublished data). The difference in mitotic frequency as well as in the percent of atypical mitosis in areas with IM between the two ethnic groups was unexpected. The findings, however, appear to substantiate the suggestion that environmental factors may influence the gastric mucosa of Japanese subjects.[3] Moreover, the high frequency of atypical mitosis in IM in the gastric mucosa of Japanese nationals with adenocarcinoma may mirror a profound genetic instability in that metaplastic mucosa and suggests that IM with atypical mitosis in Japanese may be a precancerous lesion.

This study was supported by grants from the Cancer Society, Stockholm and the Karolinska Institute, Stockholm.

(Received December 11, 1992/Accepted March 2, 1993)

REFERENCES

1) Rubio, C. A., Kato, Y., Kitagawa, T., Sugano, H. and Grimelius, L. Intramucosal cysts of the stomach. VIII: Histochemical studies. *Acta Pathol. Microbiol. Immunol. Scand.*, **96**, 627–634 (1988).
2) Rubio, C. A., Stemmermann, G. N. and Hayashi, T. Ciliated gastric cells among Japanese living in Hawaii. *Jpn. J. Cancer Res.*, **82**, 86–89 (1991).
3) Rubio, C. A., Hirota, T., Itabashi, M., Hirohashi, S. and Kato, Y. Quantitation of gastric intestinal metaplasia by morphometry in Japanese patients. *Jpn. J. Cancer Res.*, **83**, 495–498 (1992).
4) Rubio, C. A. and Jessurun, J. Low frequency of intestinal metaplasia in gastric biopsies from Mexican patients: a comparison with Japanese and Swedish patients. *Jpn. J. Cancer Res.*, **83**, 491–494 (1992).
5) Rubio, C. A., Hirota, T. and Itsbashi, T. Atypical mitoses in elevated dysplasias of the stomach. *Pathol. Res. Pract.*, **180**, 372–376 (1985).
6) Rubio, C. A. and Riddell, R. H. Atypical mitoses in dysplasias of the Barrett's mucosa. *Pathol. Res. Pract.*, **184**, 1–5 (1989).
7) Rubio, C. A. Atypical mitoses in colorectal adenomas. *Pathol. Res. Pract.*, **187**, 508–513 (1991).
8) Rubio, C. A., Theorell, M., Befrits, R. and Uribe, A. The characteristics of mitotic figures in jejunal mucosa of patients with celiac disease. *Am. J. Clin. Pathol.*, **98**, 575–578 (1992).
9) Rubio, C. A., Slezak, P., Öhman, U. and Emås, S. The histological classification of early gastric cancer (microinvasive carcinoma of the stomach). *Acta Pathol. Microbiol. Immunol. Scand.*, **90**, 311–316 (1982).