ORIGINAL PAPER

Early gastric carcinoma diagnosed on endobiopsic and surgical specimens

MARIA-SULTANA MIHAILOVICI[1)], M. DANCIU[1)], LUMINIŢA IVAN[2)], D. FERARIU[3)]

[1)]*Pathology Department,*
„Gr. T. Popa" University of Medicine and Pharmacy, Iassy
[2)]*Pathology Department, Military Hospital, Iassy*
[3)]*Pathology Department, „St. Spiridon" Emergency Hospital, Iassy*

Abstract

Early gastric carcinoma (EGC) is difficult to diagnose without a screening program. *Aims*. In this study, we reveal the importance of endobiopsy in EGC diagnosis. *Material and methods*. We examined multiple gastric endobiopsies from 1 201 patients with or without symptoms and endoscopical aspect for gastric carcinoma. All specimens were fixed in 15% buffered neutral pH formaldehyde and paraffin embedded. Histological sections were stained using current techniques: Hematoxylin–Eosin, trichromic van Gieson, Giemsa (for *Helicobacter pylori*) and Alcian blue, pH 1 and 2.5 (for acid and sulfated mucins). We used Laurén histological classification with two main types of gastric carcinoma: intestinal and diffuse. *Results*. From 1 201 gastric endobiopsies, we diagnosed gastric carcinoma in 257 patients (21.3%) and only four of them were EGCs, although their endoscopical examination was negative for gastric tumor. Among these malignant proliferations, three cases showed intestinal type EGC and one case was diffuse type EGC. The additional endobiopsies fragments presented chronic atrophic gastritis with *H. pylori* infection, intestinal metaplasia and dysplasia. *Conclusions*. EGC had an incidence of 0.34%, which is very low because the lack of an endoscopical screening program favors the diagnosis of gastric cancer in advanced stages. Both histological types – intestinal and diffuse, were present in EGC, associated with *H. pylori* chronic gastritis, intestinal metaplasia and dysplasia. The presence of dysplasia recommends the endoscopical surveillance of these patients.

***Keywords*:** early gastric carcinoma, dysplasia, endobiopsy.

Introduction

Diagnosed by classical methods, early gastric cancer (EGC) represents 16–24% from all gastric cancers, while using endoscopical screening methods, the incidence raises to 30–50% [1–3].

In this study, we present four cases of EGCs diagnosed by endobiopsy and confirmed after gastric surgical resection.

Histopathological changes in the surrounding gastric mucosa are analyzed.

Material and methods

The study included 1 201 gastric endobiopsies and four specimens of total gastric surgical resection.

The patients were adults aged between 23 and 89 year-old; the sex ratio was M/F – 2.37/1.

All tissue specimens were fixed in 10% formalin, neutral pH and paraffin-embedded.

Thin sections (4–6 microns) were stained with Hematoxylin–Eosin, van Gieson (trichromic), and special histochemical techniques: Giemsa (for *Helicobacter pylori*), and Alcian blue, pH 1 and pH 2.5 (for acid mucins as sialomucins / hyaluronic acid and sulphomucins).

The sections were evaluated using the Laurén classification and according to the *World Health Organisation 2000 Guidelines* [4].

Results

After analyzing the 1 201 cases, 257 (21.3%) were diagnosed with gastric adenocarcinoma. Only in four of them (0.34%) we found aspects of EGC, although the endoscopical examination of these cases wasn't suggestive for gastric cancer. The evaluation of the surgical resection specimens from these patients revealed three cases of intramucosal adenocarcinoma and only one of submucosal adenocarcinoma.

According to Laurén classification, intestinal type adenocarcinoma was diagnosed in three endobiopsies and confirmed on corresponding surgical specimens ($pT_1N_0M_xG_1$). Microscopically, intestinal type adenocarcinomas were well differentiated, with atypical cells arranged in a tubular pattern, similar with intestinal metaplasia (Figures 1 and 2).

Only one case was diffuse type adenocarcinoma, which, on surgical resection specimen, proved to be a poorly differentiated adenocarcinoma, mucus secreting, invading the submucosa by penetrating the muscularis mucosae ($pT_1N_0M_xG_3$). Atypical tumor cells were isolated or in cords and strands, and most of them were positive for Alcian blue (Figures 3 and 4).

Both in endobiopsies with multiple tissue samples, and in surgical specimens we noticed chronic gastritis with *H. pylori* or atrophic gastritis. Gastric mucosa adjacent to intramucosal carcinoma presented high grade dysplasia in native epithelium or in intestinal

metaplasia areas. Histologically, high-grade dysplasia is characterized by distorted glands, arranged in a "back to back" pattern, lined by atypical cells often with irregular, stratified nuclei, but preserved polarity. Mitosis is present. Neoplastic cells are confined to the glandular structures, inside the basement membrane. (Figures 5 and 6).

Discussions

Early gastric cancer is a carcinoma invading only the mucoasa or the mucosa and the submucosa, irrespective of the presence of lymph node metastasis [4]. Countries with an operational screening program for early detection of gastric cancer (e.g. Japan), EGC incidence is high (30–50%) [3].

In our study group, the EGC incidence was very low (0.33%), as a result of routine endoscopy practice and not of a screening program.

Endoscopically, EGC is classified as protrusive (type I), elevated (type IIa), flat (type IIb) or ulcerated (type IIc), and excavated (type III). With regard to the dimensions, carcinomas limited to mucosa can be divided in: intramucosal carcinoma if it is smaller than 4 cm (M) and superficial carcinoma if it is larger than 4 cm (SUPER-M). Similarly, submucosal carcinomas will be SM, and SUPER-SM, respectively.

In addition, penetrating carcinomas have two subtypes: PenA – when tumor cells invade into the submucosa in a large front, and PenB – characterized by multiple foci of invasion beneath the muscularis mucosae [4].

Upon correlation between endoscopical and pathological data, one can conclude that protrusive (type I) and elevated (type IIa) EGCs present a papillary or glandular pattern, well to moderately differentiated, while depressed / ulcerated (type IIc) carcinomas are often poorly differentiated. Excavated (type III) carcinomas may be intestinal or diffuse type [4, 5].

None of the above mentioned endoscopical aspects was observed in the four cases of EGC diagnosed in our study group. Histologically, three of them were well differentiated, intestinal type adenocarcinomas, the fourth being poorly differentiated, diffuse type, mucin producing adenocarcinoma. Laurén classification also has a prognostic value, as the intestinal type has a better five year-survival ratio than the diffuse type, mucin producing, for the same clinical stage [6].

Goseki classification adds the histopathological factor to the TNM classification [7]. Many other classification systems have been proposed in order to improve the prognostic evaluation correlated with histopathological type [8, 9].

We could evaluate changes in the surrounding gastric mucosa, due to multiple biopsies from the same patient. This way, we increased the odds to diagnose EGCs. All EGCs presented intestinal metaplasia and dysplasia.

Originating either in native gastric epithelium and/or in areas with intestinal metaplasia *WHO 2000* describes low-grade intraepithelial neoplasia, and high-grade intraepithelial neoplasia [10, 11].

Follow-up studies of gastric dysplasia proved that histological grade correlates with progression ratio and duration to cancer [4, 12].

Therefore, low- or high-grade gastric dysplasia recommends endoscopical reevaluation of the patient with multiple gastric biopsies every 6–12 months. Gastric dysplasia may progress to carcinoma or may favor its' diagnosis. Eighty percent of high grade intraepithelial dysplasia progress to carcinoma within the next four to 17 months. The risk is increased if the dysplasia associates intestinal metaplasia (type II or III, incomplete), with sulphomucins secretion.

In our study, atrophic chronic gastritis with *H. pylori* was associated with intestinal metaplasia in the mucosa surrounding the intestinal type adenocarcinomas. These observations are in accordance with other studies [13], demonstrating the role of *H. pylori* and intestinal metaplasia in gastric carcinogenesis.

Conclusions

In summary, low incidence of EGC is a consequence of the lacking of a screening program for early detection of gastric cancer. Gastric dysplasia recommends endoscopical surveillance of the patient. EGC presented both histological types of Laurén classification, and were associated with chronic gastritis with *H. pylori*, intestinal metaplasia and dysplasia.

Abbreviations

EGC – early gastric cancer; *H. pylori – Helicobacter pylori*.

References

[1] GREEN P. H, O'TOOLE K. M, WEINBERG L. M, GOLDFARB J. P, *Early gastric cancer*, Gastroenterol, 1981, 81:247–256.

[2] CARTER K. J., SCHAFFER H. A., RITCHIE W. P. J., *Early gastric cancer*, Ann Surg, 1984, 199:604–609.

[3] OHTA J., NOGUCHI Y., TAKAGI K. *et al., Early gastric carcinoma with special reference to macroscopic classification*, Cancer, 1987, 60:1099–1106.

[4] FENOGLIO-PREISER C., CARNEIRO F., CORREA P. *et al*., Gastric carcinoma. In: HAMILTON S. R., AALTONEN L. A. (eds), *Pathology and genetics tumours of the digestive system. The OMS Classification*, IARC Press, Lyon, 2000, 39–52.

[5] KODAMA Y., INOKUCHI K., SOEJIMA K. *et al., Growth patterns and prognosis in early gastric carcinoma. Superficially spreading and penetrating growth types,* Cancer, 1983, 51:320–326.

[6] MIHAILOVICI M. S., DANCIU M., TELEMAN S. *et al., Aplicarea clasificării OMS în evaluarea carcinomului gastric diagnosticat pe endobiopsie*, Rev Med Chir Soc Med Nat, 2002, 106(4):725–730.

[7] GOSEKI N., TAKIZAWE T., KOIKE M., *Differences in the mode of the extension of gastric cancer classified by histological type: new histological classification of gastric carcinoma*, Gut, 1992, 33:606–612.

[8] CARNEIRO F., *The distinction between dysplasia and truly invasive cancer. Classification of gastric carcinomas*, Curr Diagn Pathol, 1997, 4:51–59.

[9] CARNEIRO F., AMADO M., LAGO P. *et al*., *Helicobacter pylori infection and blood groups*, Am J Gastroenterol, 1996, 91:2646–2647.

[10] RUGGE M., LEANDRO G., FARINATI F. *et al., Gastric epithelial dysplasia. How clinicopathologic background relates to management*, Cancer, 1995, 76:376–382.

[11] RUGGE M., CORREA P., DIXON M. F. *et al., Gastric dysplasia: the Padova international classification*, Am J Surg Pathol, 2000, 24:167–176.

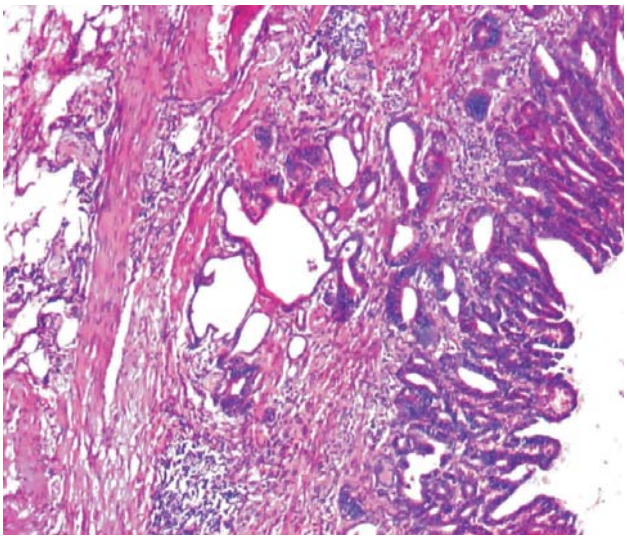

Figure 1 – ***Intramucosal intestinal type adenocarcinoma (HE, ob. ×4)***

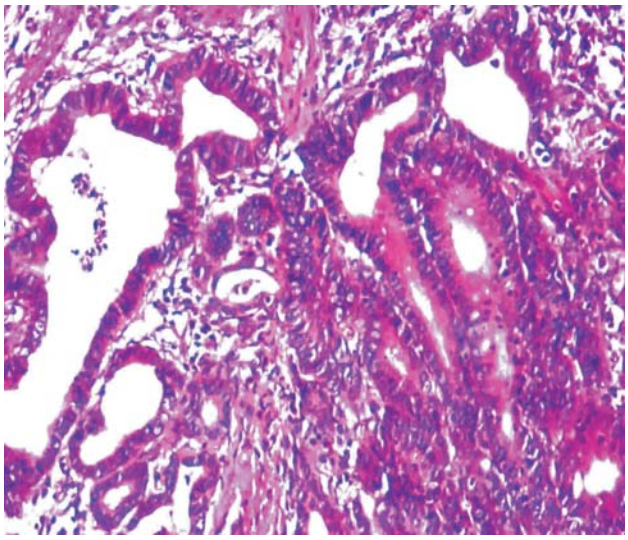

Figure 2 – ***Intramucosal intestinal type adenocarcinoma, detail (HE, ob. ×20)***

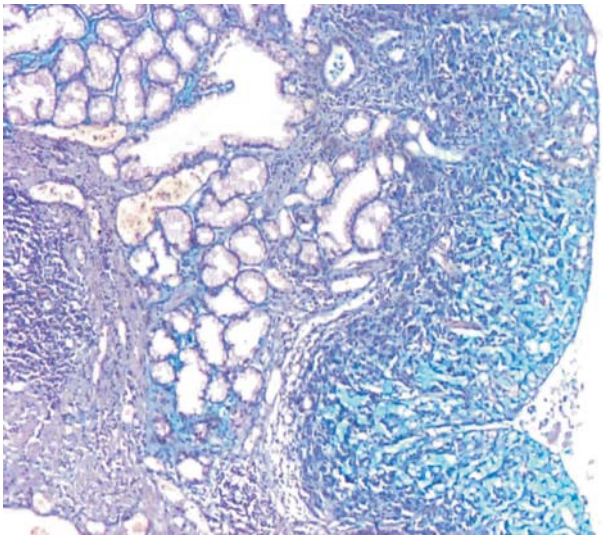

Figure 3 – ***Intramucosal diffuse type adenocarcinoma, mucin-producing (Alcian blue, ob. ×4)***

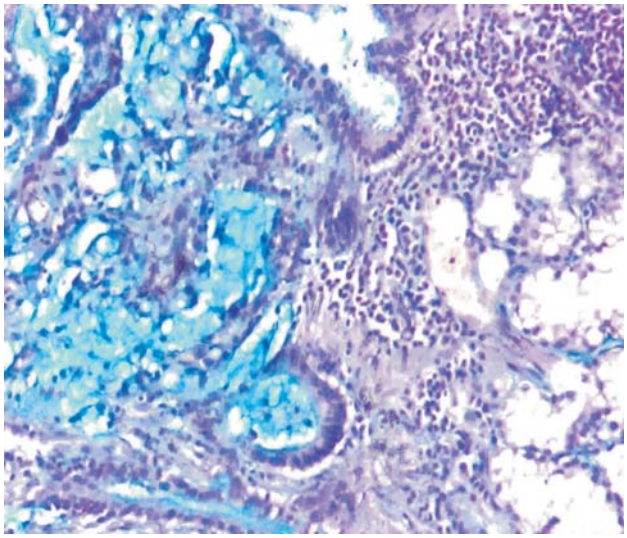

Figure 4 – ***Intramucosal diffuse type adenocarcinoma, mucin-producing, colloid (Alcian blue, ob. ×20)***

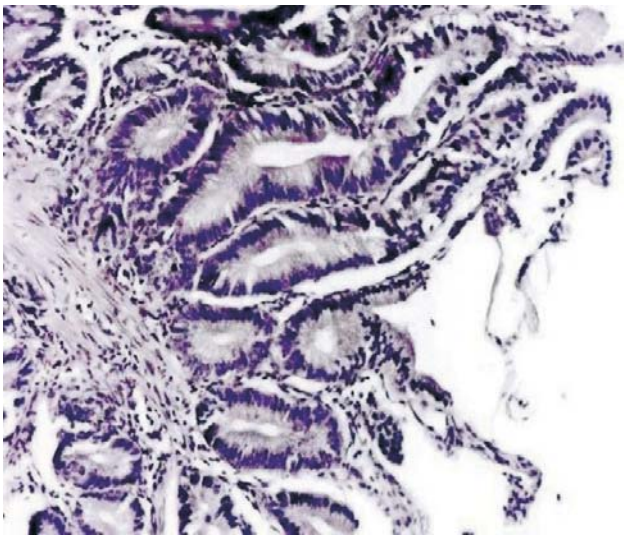

Figure 5 – ***High-grade dysplasia in gastric epithelium surrounding intramucosal carcinoma (HE, ob. ×10)***

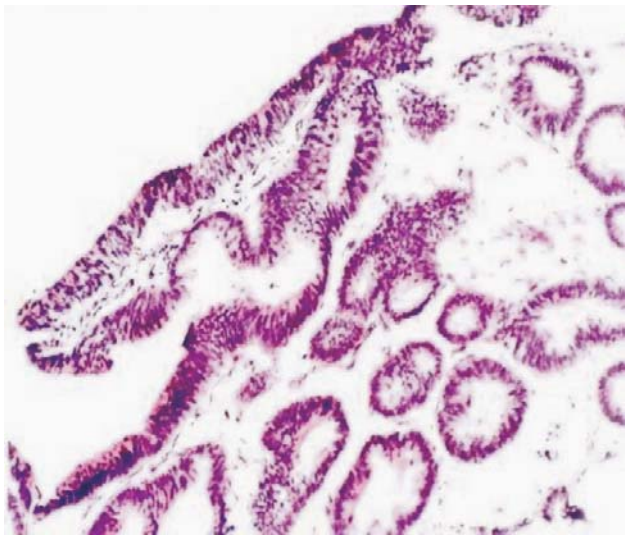

Figure 6 – ***High-grade dysplasia in superficial gastric mucosa; endobiopsy (HE, ob. ×10)***

[12] CAMPBELL F., BAGOMOLETZ W. V., WILLIAMS G. T., Tumors of the esophagus and stomach. In: FLETCHER C. D. M. (ed), *Diagnostic histopathology of tumors*, volume I, Churchill Livingstone, Edinburgh, 1995, 193–242.

[13] GRIGIONI E. F., D'ERRICO A., MILANI M. *et al*., *Early gastric cancer. Clinico-pathological analysis of 125 cases of early gastric cancer (EGC)*, Acta Pathol Jpn, 1984, 34:979–989.

Corresponding author
Maria-Sultana Mihailovici, Professor, MD, PhD, MIAC, Head of Pathology Department, „Gr. T. Popa" University of Medicine and Pharmacy, 16 University Street, 700 115 Iassy, Romania; Phone/Fax +40232–314 080, E-mail: msmihailovici@yahoo.com

Received: December 22nd, 2006

Accepted: January 20th, 2007