The Role of Gastric Mucosal Dysplasia in the Development of Gastric Carcinoma*

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It is widely acknowledged that most stomach carcinomas developed from dysplastic lesions of gastric mucosa. They can be found in known precancerous conditions as chronic gastritis, gastric adenoma, giant rugal hypertrophy, chronic peptic ulcer, gastric stumps after partial resection and pernicious anemia. Several grading systems of gastric dysplasia have been suggested. Nagayo’s or the ISGDC classification was applied to 367 biopsy specimens of 258 patients between 1979-1995. The frequency of moderate and severe dysplasia was 0.84% regarding all gastric endoscopies in the same period of time. Follow-up studies were performed in 56 cases in a period of 1–7 ys. In this group cancer developed during 14 patients. The authors' recommendation is to follow up the patients gastric dysplasia for least 10 ys after with diagnosis. (Pathology Oncology Research Vol 4, No 4, 297–300, 1998)

Key words: gastric dysplasia, gastric cancer

Introduction

Dysplastic epithelium (Figure 1.) replacing the normal stomach glands is thought to be the precursor lesion for most tubular adenocarcinomas and so for the so-called intestinal type of gastric carcinomas. Nakamura et al1 were the first in 1966 to call attention to the atypical epithelium of the stomach and to its probable pathogenetic role in the natural history of gastric cancers. Since its introduction several decades ago into gastric pathology, the term of gastric dysplasia has become step by step more and more complex as well as confusing. Different grading systems and nomenclature have been elaborated for evaluation of dysplastic changes in gastric epithelium based on their endoscopic, macro- and microscopic resp. cytological features.

These efforts have resulted in such terms as simple dysplasia, “adenoma” or recently “flat” and “depressed adenoma”. Sometimes the simple reactive atypical changes (Figure 2.) are also included under the term “gastric dysplasia”.

Materials and Methods

In our material (collected from Department of Pathology, Haynal Imre University of Health Sciences; Department of Pathology, Uzsoki Municipal Hospital; and Gastroenterology Unit, Town Council Hospital, Jászberény, Hungary) gastric dysplasia was found in 367 biopsy specimens obtained from 258 patients between 1979–1995. Both Nagayo’s and the ISGDC’s classification have been applied to grade each sample. The former one has been applied and, on the other hand, a gastric lesion has been accepted as a gastric dysplasia only according to the ISGDC’s recommendations (Table 1.). The number of cases mentioned above represents a frequency of 0.84% of the total number of gastroscopies in the same period of time. The yearly frequency varied between 0.46 and 1.27% (Figure 1.). This prevalence of gastric dysplasia corresponds generally to the data reported by Farini et al.10

Results

Nagayo’s grade III. dysplasia was found in 208 patients and grade IV. dysplasia in 50 ones. The macroscopic picture distributes into three groups as follows: a.) a protruded lesion was present in 50 patients, b.) excavated changes in 128 patients and c.) flat lesions in 80 cases. The distribution

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of the three types was the same in the groups of two different grades of dysplasia. The excavated form was the most frequent (49.6%). It is also very remarkable that the flat lesion (i.e. when the endoscopist couldn’t reveal any well defined mucosal change) occurred in 80 patients (31%).

In the group of patients with gastric dysplasia during the period of our investigation gastric carcinoma was detected in 39 patients (15%). 18 of them belonged to the grade III. dysplasia group and other 21 to the grade IV. dysplasia group.

During the period of time of our examinations only 56 patients could be followed by endoscopic examinations. In this latter group, 16 patients had to be submitted to surgery. Amongst them, the final histological diagnosis of removed surgical specimens was as follows: gastric carcinoma was the result in 14 patients, chronic peptic ulcer in the stomach with adjacent grade III. dysplasia in 1 case and chronic duodenal peptic ulcer in 1 case.

In the carcinomatous group, 10 patients were found with true Early Gastric Carcinoma (EGC): 3 cases were had advanced cancer. In one patient a double cancer was found, i.e. an advanced cancer in the antrum and an EGC in the corpus.

Among the 56 followed-up patients, stomach carcinoma developed during a period of time of 1–7 ys. Therefore, the authors’ recommendation is to follow up the patients bearing true gastric dysplasia for at least following 10 ys diagnosis.

Discussion

The first specific histological criteria of atypical gastric epithelium were reported by Nakamura et al\(^1\) in 1966. Nagaya\(^2\) has subdivided the atypical mucosal changes of the stomach in five categories. These are as follows (Table 1.): normal or benign without cellular atypia, benign with slight atypia, borderline-lesion (a very important grade analogons to gynecological pathology), probable carcinoma and true cancer. The term “dysplasia” was not yet used in this grading system.

Ming\(^3\) has divided the dysplastic lesions of gastric mucosa into four grades (Table 1.). Grundmann and Schlake,\(^4\) also in 1979, were the first to apply the term “dysplasia”. They and Oehlert et al\(^5\) have distinguished three forms of gastric dysplasia, respectively (Table 1.).
An International Reference Center for Histological Classification of Precancerous Lesions of the Stomach set up by the World Health Organization (WHO) has recommended terming the presumed precancerous lesions of the stomach mucosa “dysplasia” and that the term “intra-mucosal carcinoma” should replace “in situ carcinoma” for lesions that have invasive malignant cells confirmed to the lamina propria.7

The International Study Group on Gastric Cancer (ISGOC) founded in 1976 in Mexico by M Crespi and Si-Chun Ming, has performed a wide-spread study on the classification of gastric dysplasias. At the Consensus Meeting held in San Miniato in 1982, the pathological panel classified gastric lesions as simple hyperplasia, atypical hyperplasia and dysplasia, distinguished a simple and a “borderline” form (Figure 3.) of the latest group (Table 1.).8 (One of the authors was a participant at the pathological panel and the Consensus Meeting).

A recent report on this field of stomach pathology was published by Goldstein and Lewin9 this year. The very comprehensive summary of gastric dysplasia was given in this article detailed the history of this phenomenon and also analyzed the most important classifications. Their final conclusion was that the term “dysplasia” has to be restricted to neoplastic epithelium in the gastric mucosa. These changes could be classified into two categories:

### Table 1. Different classification for gastric dysplasia

<table>
<thead>
<tr>
<th>Nagayo (1971)</th>
<th>Normal mucosa; benign hyperplasia (grade I.)</th>
<th>Benign lesion with mild atypia (grade II.)</th>
<th>“Borderline lesion” (grade III.)</th>
<th>Probably carcinoma (grade IV.)</th>
<th>Gastric cancer (grade V.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grundmann and Schlake (1997)</td>
<td>Inflammatory hyperplasia</td>
<td>I. Mild dysplasia</td>
<td>II. Moderate dysplasia</td>
<td>III. Severe dysplasia</td>
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<tr>
<td>Oehlert (1979)</td>
<td>–</td>
<td>Grade I. dysplasia</td>
<td>Grade II. dysplasia</td>
<td>Grade III.</td>
<td>–</td>
</tr>
<tr>
<td>Ming (1979)</td>
<td>Grade I. dysplasia</td>
<td>Grade II. dysplasia</td>
<td>Grade III. dysplasia</td>
<td>Grade IV.</td>
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<tr>
<td></td>
<td>Hyperplastic dysplasia</td>
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<td></td>
<td>Adenomatous dysplasia</td>
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<tr>
<td>Cuello et al. (1979)</td>
<td>Mild</td>
<td>Severe</td>
<td>Mild</td>
<td>Severe</td>
<td>–</td>
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<tr>
<td>WHO (1980)</td>
<td>Inflammatory or regenerative changes</td>
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<td>Serck-Hanssen</td>
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<tr>
<td>Nagayo</td>
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<td>Grundmann</td>
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<tr>
<td>Morson</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
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<td>Sobin</td>
<td>dysplasia</td>
<td>dysplasia</td>
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<tr>
<td>ISGOC (Florence, 1982)</td>
<td>Simple</td>
<td>Atypical</td>
<td>“Borderline lesion”</td>
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<td>–</td>
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<tr>
<td></td>
<td>hyperplasia</td>
<td>hyperplasia</td>
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</table>
adenoma (Figure 4.) for raised lesions and Gastric Epithelial Dysplasia (GED) for non-raised alteration or when the shape cannot be ascertained.

What does the mucosal dysplasia mean in pathological practice in terms of macroscopic appearance? It is not characteristic. It may be protruded, fl at or depressed as well as a deeply excavated mucosal defect. Of course, the macroscopic picture doesn’t reveal any specific features for the extension or degree of severity of dysplasia. On the other hand, the pathological process itself in which the mucosal dysplasia occurs alters the macroscopic features of dysplastic mucosa (e.g. gastric adenoma or chronic peptic ulcer).

The histological features of the dysplastic glands are more important. According to the WHO’s recommendations these most characteristic microscopic characteristics are as follows: 1. cellular atypia, 2. the abnormal differentiation and 3. the pathological architecture of mucous membrane.

The most important components of the abovementioned characteristics are summarized as follows:

1. Cellular atypia:
   - nuclear pleomorphism
   - hyperchromasia
   - nuclear stratification
   - increased N/P ratio
   - sometimes increased cytoplasmic basophilia
   - loss of cellular and nuclear polarity

2. Abnormal differentiation:
   - lack or reduced numbers of goblet cells and Paneth cells in the metaplastic intestinal epithelium
   - reduction, alteration or disappearance of secretory products from the gastric epithelium

3. Disorganized mucosal architecture
   - irregularity of crypt structure
   - back-to-back gland formation
   - budding and branching of crypts
   - intraluminal and surface papillary growth

Table 1. summarizes the different dysplasia classifications.

Nowadays, more and more operative endoscopic interventions are performed. So endoscopic polypectomy is also very frequent to remove the protruded lesions of the stomach. A new method of operative endoscopic interventions is mucosectomy which may also be an adequate tool to remove protruded and sessile fold of dysplastic mucosa. It is very advantageous, but because these dysplastic changes may be multifocal, the endoscopic follow-up of such patients is still necessary.

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References*


*Only selected references are listed; please request the full list from the authors.