Gastric adenocarcinoma of fundic gland type. A new entity

Takashi Yao
Department of Human Pathology,
Juntendo University Graduate School of Medicine
Memory of St. Mark's Hospital in 1994-1995

Morson, Talbot, Ilias (Latch)
We published and proposed a new entity of GA-FG.

Gastric Adenocarcinoma of Fundic Gland Type (Chief Cell Predominant Type): Proposal for a New Entity of Gastric Adenocarcinoma

Hiroya Ueyama, MD,*† Takashi Yao, MD,* Yutaka Nakashima,‡ Katsuya Hirakawa,§ Yumi Oshiro,‖ Minako Hirasashi,¶ Akinori Iwashita,# and Sumio Watanabe†

Ueyama H, Yao T, et al.
Gastric adenocarcinoma of fundic gland type (GA-FG).
A new entity

1. Process of establishing the entity and clinicopathological features of GA-FG
2. Progressive variant of GA-FG
3. Genetic events of GA-FG
4. Differential diagnosis
In 2005, the biopsy was sent to me for consultation.

My report at that time was "Atypical (or immature) chief cell hyperplasia, MUC6(+) / pepsinogen I(+)".
Gastric lesion with chief cell differentiation

  Chief cell proliferation of the gastric mucosa mimicking early gastric cancer: an unusual variant of fundic gland polyp.

  Chief cell hyperplasia with structural and nuclear atypia: a variant of fundic gland polyp.
  Pathol Res Pract 200: 817-821, 2005

Only by biopsy, the diagnosis of carcinoma was not confirmed, although its possibility was suggested in these reports.
The first report of gastric adenocarcinoma with chief cell differentiation


Case Report
Gastric adenocarcinoma with chief cell differentiation

Tetsuya Tsukamoto,1,2 Takio Yokoi,2 Shinya Maruta,3 Masakazu Kitamura,2 Tsuyoshi Yamamoto,3 Hisayo Ban1 and Masae Tatematsu1

1Division of Oncological Pathology, Aichi Cancer Center Research Institute, 2Department of Pathology and Molecular Diagnostics, Aichi Cancer Center Hospital and 3Department of Internal Medicine, Tokai Hospital, Nagoya, Japan

Only one case report had been reported before our report.
We collected 6 cases of GA-FG from 2007

Case 1

Case 2

Case 3

Case 4

Case 5

Case 6

Flatly elevated lesion with or without a shallow depression
The definition of GA-FG

GA-FG is defined as neoplastic lesions mainly composed of highly differentiated columnar cells mimicking the fundic gland and having differentiation toward the fundic gland, confirmed by immunohistochemical stains by pepsinogen I (chief cell) and H+/K+-ATPase (parietal cell)
## Clinicopathological features of GA-FG (10 cases)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>42-79 (average: 65.5)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>M : F = 6 : 4</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Upper : Middle : Lower = 10 : 0 : 0</td>
</tr>
<tr>
<td><strong>Size</strong></td>
<td>4-20 (average: 8.6) mm</td>
</tr>
<tr>
<td><strong>Macroscopic</strong></td>
<td>IIa : IIb : IIc = 5 : 0 : 5</td>
</tr>
<tr>
<td><strong>Depth of invasion</strong></td>
<td>M : SM = 1 : 9</td>
</tr>
<tr>
<td><strong>Lymphatic invasion</strong></td>
<td>(-)</td>
</tr>
<tr>
<td><strong>Venous invasion</strong></td>
<td>(-)</td>
</tr>
<tr>
<td><strong>Lymph node metastasis</strong></td>
<td>0/1 (not examined in 9)</td>
</tr>
</tbody>
</table>

### Immunohistochemical results of GA-FG

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>MUC2</td>
<td>0/10</td>
</tr>
<tr>
<td>MUC5AC</td>
<td>1/10</td>
</tr>
<tr>
<td><strong>MUC6</strong></td>
<td>10/10</td>
</tr>
<tr>
<td>CD10</td>
<td>0/10</td>
</tr>
<tr>
<td><strong>Pepsinogen-I</strong></td>
<td>10/10</td>
</tr>
<tr>
<td>H⁺/K⁺-ATPase</td>
<td>4/9 (*)</td>
</tr>
<tr>
<td>Chromogranin A</td>
<td>0/10</td>
</tr>
</tbody>
</table>

* not diffusely positive, less than 20%

<table>
<thead>
<tr>
<th>Protein</th>
<th>GA-FG Predominant Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>MUC2 (-)</td>
<td>CD10 (-)</td>
</tr>
<tr>
<td>MUC5AC (-)</td>
<td>pepsinogen-I (+)</td>
</tr>
<tr>
<td>MUC6 (+)</td>
<td>H⁺/K⁺-ATPase (+)</td>
</tr>
<tr>
<td>Chromogranin-A (-)</td>
<td>All GA-FG differentiated mainly toward immature chief cell * and partly toward parietal cell, which were named as GA-FG-chief cell predominant type</td>
</tr>
</tbody>
</table>

* Ota et al. Pathology International 2015; 65: 202-204
Differentiation of fundic gland mucosa

- Foveolar cell
  - MUC5AC
- Stem cell
  - GA-FG
- Parietal cell
  - H.K-ATPase (proton pump)
  - PG1
- Mucous neck cell
  - MUC6
  - Immature chief cells
- Chief cell
Cytological features of GA-FG
【Case presentation of GA-FG】

75y.o. Female, In the gastric body
15mm, flatly elevated lesion with vague margin

Conventional view

Indigocarmine dye
【Histopathological diagnosis】

GA-FG, 15mm, pT1b/SM1(200μm), ly(-), v(-), Ul(-), HM(-), VM(-)
The tumor grows mainly in the deep mucosal layer, covered by non-neoplastic mucosa.