Foveolar Gastric Metaplasia of the Duodenum: A Frequent, so far Neglected Type of Duodenal Polyp

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Foveolare gastrale Metaplasie des Duodenums: Eine häufige, bislang nicht beachtete Form der Duodenalpolypen

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Schlüsselwörter
- Duodenum
- Polyp
- Metaplasie
- Dünndarmblutung
- intraepitheliale Neoplasie
- kolorektales Adenom
- gastro-entero-pankreatische Tumoren

Key words
- duodenum
- polyps
- metaplasia
- small intestinal bleeding
- intraepithelial neoplasia
- colorectal adenoma
- gastro-entero-pancreatic tumours

Zusammenfassung

Abstract
Foveolar gastric metaplasia of the duodenum (FGM) is considered as imperfect mucosal healing in the context of H. pylori gastritis and intake of NSAIDs or ASS. Typical endoscopic findings are redness of the mucosa, erosion/ulcer and loss of mucosal folds. During diagnostic histological examinations we observed a frequent so far not described association of FGM with endoscopically observed duodenal polyps. The archives of two institutes of pathology with high gastroenterological workload (approximately 100 000 patients per year) were investigated for an association between “duodenal polyp” and “foveolar gastric metaplasia”. In Institute 1, of 481 duodenal polyps 41 % were classified as FGM, 9 % as adenoma and 2 % as heterotopic gastric mucosa. In 48 % no histological correlate was present. In Institute 2, 217 cases of FGM were diagnosed. Of these, in 69 cases the endoscopic finding was “polyp” (32 %). In the other cases, the endoscopic findings were mucosal defect (18 %), redness/inflammation (16 %), suspicion for gastric heterotopia (5 %) and scar (3 %). In 26 % of cases no pathologic endoscopic finding was reported. Both groups of patients with FGM showed a similar distribution of age ranges (24 – 83 years and 16 – 88 years), median age (62 years and 61 years, respectively) and a dominance of male sex (both 1:5:1). In conclusion, foveolar gastric metaplasia is a frequent, so far neglected correlate of endoscopically detected duodenal polyps.

Introduction
Sporadic duodenal polyps are found in about 1 – 5 % of patients who undergo an endoscopic examination of the upper GI tract. In the majority of cases these are incidental and asymptomatic findings [1 – 4]. The most important benign epithelial neoplasias of the duodenum are tubular or tubu-

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lo villous adenomas which are most frequently found in the periampullary region. Other frequent histological correlates of duodenal polyps are gastric heterotopia and hyperplasia of Brunner’s glands. The frequency of these entities in different diagnostic series show marked variations, most probably because of differences in diagnostic criteria (Table 1). Foveolar gastric metaplasia of the duodenum (FGM) is not considered in the publications listed in Table 1 or in current textbooks of gastrointestinal pathology as a correlate of duodenal polyps. Histologically, FGM is defined as mucus secreting cells with gastric differentiation which resemble the superficial epithelium of the stomach (foveolar cells). These cells with gastric differentiation show cytoplasmatic PAS-positive mucin and no apical brush border by light microscopy. FGM is considered as an acquired lesion connected with the impact of gastric acid and gastric H. pylori infection. Additionally it can be a complication of a drug-induced lesion of the duodenal mucosa, of an endoscopic resection and even of a forceps biopsy. FGM can be found in the duodenal bulb, in the descending part of the duodenum and at the papilla of Vater. In the context of increased gastric acid secretion as it is found in antrum-dominant H. pylori gastritis additionally duodenitis as well as Brunner’s glands hyperplasia can be found [5]. During our routine diagnostic examination of upper gastrointestinal biopsies we observed a frequent so far not described association of FGM with endoscopically detectable duodenal polyps. This observation formed the starting point of this retrospective investigation.

**Material and Methods**

The association between the “FGM” and “duodenal polyp” was investigated in the archives of two institutes of pathology with large gastroenterological work load (approximately 100 000 patients per year) in the period between January 1, 2011 and December 31, 2011. Differences in coding of diagnoses and structure of data bases resulted in different search strategies between Institute 1 and Institute 2. In Institute 1 (Pathologie München Nord) all duodenal polyps as well as the associated histopathological diagnoses in the period of interest were considered. In Institute 2 (Pathologie Ansbach) the data base search focused on the term “gastric metaplasia of the duodenum”. Subsequently in these cases the related endoscopic findings were retrieved.

**Results**

In the period under investigation, in Institute 1 a total of 481 duodenal polyps were retrieved among 27 587 endoscopies of the upper GI tract. This corresponds to a prevalence of 1.88%. Of these, 195 (41 %) were classified as FGM (Fig. 2), 41 cases were classified as adenoma (9 %) and 11 as gastric heterotopia (2 %). In 234 cases no histological correlation for the endoscopic finding of a polyp was present (48 %). In Institute 2, 217 cases of FGM were found. Of these, 69 (32 %) were correlated with the endoscopic finding of a polyp. The other endoscopic findings were mucosal

**Table 1** Frequency and distribution of polyps of the duodenum (modified according to [2]).

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>number of biopsied polyps (n=)</td>
<td>378</td>
<td>45</td>
<td>44</td>
<td>27</td>
<td>698</td>
</tr>
<tr>
<td>prevalence %</td>
<td>1.5</td>
<td>1</td>
<td>0.3</td>
<td>0.7</td>
<td>1.88</td>
</tr>
<tr>
<td>no histology performed %</td>
<td>6</td>
<td>16</td>
<td>0</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>normal mucosa %</td>
<td>0</td>
<td>42</td>
<td>0</td>
<td>15</td>
<td>48</td>
</tr>
<tr>
<td>inflammation %</td>
<td>35</td>
<td>0</td>
<td>0</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>gastric mucosa heterotopia %</td>
<td>36</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>adenoma/adenocarcinoma %</td>
<td>7</td>
<td>31</td>
<td>55</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Brunner’s gland hyperplasia %</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>lipoma %</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>hamartoma %</td>
<td>1</td>
<td>0</td>
<td>25</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>others %</td>
<td>5</td>
<td>2</td>
<td>9</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>foveolar gastric metaplasia %</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>41</td>
</tr>
</tbody>
</table>

![Fig. 1](Image312x468) Mucosa and submucosa of the duodenum separated by the muscularis mucosae present from bottom right to center left. Brunner’s glands hyperplasia according to the criteria in materials and methods. Discernible mucous glands in the mucosa in nearly the whole biopsy (H&E, magnification × 4).

Additionally the original slides of FGM in Institute 1 were revised and analyzed regarding any findings not described in the original pathology report. Especially it was evaluated whether there was a coincidence between FGM and Brunner’s glands hyperplasia. The diagnosis of Brunner’s glands hyperplasia in endoscopically obtained biopsies is not well defined so far. In the current investigation a Brunner’s glands hyperplasia was diagnosed when Brunner’s glands were found in the mucosa in at least 50 % of the length of the biopsy particles with foveolar gastric metaplasia ([6], Fig. 1). Moreover in a subset of cases (n=11) an additional immunohistochemical investigation for the expression of the mucin MUC5AC which is characteristic for gastric foveolar cells [7] was performed.
showed an additional hyperplasia of Brunner glands in 34 of 195 cases (17.4 %) as defined in the Materials and Methods section. The adherent gastric mucous layer is composed of alternating layers of MUC5AC and MUC6 mucin proteins.

Both cohorts of patients show a similar age range (24 – 83 years and 16 – 88 years, respectively) and median age (62 and 61 years, respectively). Furthermore a dominance of the male sex of 1.5:1.0 was present in both cohorts.

The histological revision of the FGM slides from Institute 1 showed an additional hyperplasia of Brunner’s glands in 34 of 195 cases (17.4 %) as defined in the Materials and Methods section. FGM was always characterized by areas of superficially located mucous secreting cells which resembled gastric foveolar cells (Fig. 3). These cells with gastric differentiation were always located in the villi and not in the crypts. Furthermore, there was no spatial association between foveolar cells and goblet cells. The immunohistochemical investigation of 11 randomly selected FGM cases for the mucin antigen MUC5AC (Novocastra; clone CLH 2, dilution 1:200) showed a constant MUC5AC expression in cells of foveolar gastric metaplasia whereas preexistent cells (enterocytes, goblet cells, neuroendocrine cells, stroma cells) were negative for MUC5AC (Fig. 4).

Discussion

The present investigation shows that foveolar gastric metaplasia of the duodenum is a frequent so far not considered correlate of endoscopically detected duodenal polyps. A comparison with previous investigations on the frequency and histological correlation of duodenal polyps (Table 1) shows a reasonable plausibility in terms of representativity for the patients’ recruitment in the series of Institute 1. Thus, the prevalence of duodenal polyps in this group of patients (1.88) is well comparable to the so far published data (range: 0.3 – 1.5). Further hints of plausibility of case selection and subsequent histological investigations are possible by comparison with further data from the literature. Regarding duodenal adenoma (carcinoma) the prevalence found in our series (9 %) is close to the data published by Höchter et al. [1] (7 %) and Jepsen et al. [2] (15 %) whereas Reddy et al. [3] and Ghazi et al. [4] report significantly higher prevalences. A marked deviation of our results from the data in the literature is found regarding the diagnosis of gastric heterotopia which was reported much more frequently by Jepsen et al. [2] and Höchter et al. [1] (26 % and, respectively, 36 %) than in our series (2.28 %). This is most probably the case because in older publications the congenital gastric heterotopia was not differentiated from acquired foveolar gastric metaplasia (Fig. 1). The plausibility of our results is further strengthened by the high similarity of FGM prevalence in connection with duodenal polyps in two different Institutes of pathology.

It is astonishing why such a frequent finding as FGM is neither quoted in original publications nor in current text books of pathology as a correlate of duodenal polyps. Although the clinical significance of the of FGM may be limited, consideration and use of this diagnostic term may help to reduce the so far high percentage of cases in which the endoscopic finding of a polyp is not correlated with a pathological histological finding.

References