Endoscopic features, pathological correlates and possible origin of foveolar gastric metaplasia presenting as a duodenal polyp

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Abstract

It has recently been shown that duodenal foveolar gastric metaplasia (FGM) sometimes presents as a polyp. The mechanism by which FGM develops into a polypoid lesion is unknown and it is unclear whether this form of FGM is indistinguishable from other polypoid lesions or whether endoscopists do not recognize it because they are unfamiliar with it.

We identified and retrieved archival cases of FGM endoscopically suspicious for adenomatous polyp and examined their pathological, clinical and endoscopic features.

Endoscopic features of the 13 identified FGMs presenting as polyps were heterogeneous and overlapping with those of adenomatous polyps. FGM was frequently associated with mucosal and submucosal Brunner's glands, but defining and recognizing hyperplasia of these glands remains difficult. Other pathological features could not explain the development of a polypoid lesion.

The endoscopic features of FGM polyps are non-specific, overlapping with those of adenomatous polyps. FGM polyps probably acquire their polypoid aspect due to association with Brunner's gland hyperplasia (BGH), which also arises due to chronic inflammation and damage. Because BGH is ill-defined and difficult to recognize, while FGM is diagnosed easily, this type of polypoid lesions has until now only been recognized based on the presence of FGM, although FGM is most likely a secondary phenomenon and not the primary cause of the polyp. (Acta gastroenterol. belg., **2019**, 82, **257-260**).

Key words : Foveolar gastric metaplasia, duodenal polyp, Brunner's gland hyperplasia, endoscopic features.

Introduction

Foveolar gastric metaplasia (FGM) in the duodenum is a phenomenon **that has been known** for several decades. It occurs mainly in the upper part of the duodenum. Studies have shown that chronic inflammation of and damage to the intestinal epithelium due to Helicobacter Pylori infection, acid or medications such as NSAIDs play an important role in its pathogenesis (1). **Although FGM has generally been considered a benign process, it has recently been shown that a significant portion of FGM lesions are associated with genetic alterations such as GNAS and KRAS mutations, which are known to be associated different types of tumors including duodenal adenocarcinoma. This suggests that FGM could be a precursor lesion for adenocarcinoma and thus merits more clinical attention; although the frequency of FGM compared to the rare occurrence of duodenal adenocarcinoma suggests that cancerous transformation of FGM is a rare event. (2)**

The endoscopic aspects of FGM have been described several decades ago (3). However, only in recent years **has it** become clear that duodenal FGM can present as a protruding lesion. Using a clinico-pathological database analysis, Sarbia et al. (4) showed that FGM is a frequent and so far neglected cause of duodenal polyp. In our daily practice we may be confronted with situations where the endoscopists submits a duodenal polyp to the pathologists, suspecting an adenomatous polyp, while the pathologists **report** FGM as the sole significant abnormal finding. Since Sarbia et al (4) did not report in detail on the endoscopic features of FGM polyps, it is currently not clear whether these polyps have a specific presentation upon endoscopy or whether they are most often suggestive of being adenomatous polyps simply because endoscopists are not acquainted with FGM polyps as an entity. Moreover, it remains unclear how FGM by itself can lead to the endoscopic impression of a polyp.

In order to investigate these issues, we performed an endoscopic and histopathological study of a series of duodenal polyps encountered in our daily practice that were endoscopically suspicious for adenoma and were subsequently diagnosed as FGM by the pathologists.

Materials and methods

To identify cases of FGM presenting as a duodenal polyp, we performed a search in the pathological database of the Saint-Luc University Hospitals, covering the period from 01/2015 to 10/2018. The laboratory information and management system of the pathology department enables Boolean searches on words in the pathological report, so cases could be identified based on the words "adenoma" in the clinical information field and "foveolar gastric metaplasia" in the conclusion. For all identified cases, the slides were retrieved and the diagnosis of FGM was confirmed. The presence or absence of the following variables was evaluated: submucosa, Brunner's glands in the mucosa and submucosa, chronic inflammation revealed by an increase of the lamina propria mononuclear infiltrate, active inflammation identified by neutrophils in the stroma or epithelium, stromal edema, regenerative aspect of the non-metaplastic intestinal epithelium and erosion/ulceration.

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Next, we retrieved the corresponding endoscopic images. When no images were available, the case was not included. We evaluated each case for the following endoscopic criteria: localization (bulb or second duodenum), Paris classification (5), size and color. Gender, age at presentation and relevant previous history of duodenal lesions were retrieved from the clinical files.

Results

We identified 13 cases of suspected duodenal polyp labeled FGM by the pathologist between 03/2015 and 09/2018. One had to be excluded due to the lack of endoscopic images. **Patients' mean age** was 63 years old (range 51-80). There were 7 women and 5 men. One patient **was diagnosed with** Lynch syndrome and Lynch syndrome was also suspected in another patient.

Six lesions (50%) were located in the duodenal bulb, 2 (17%) in the upper duodenal flexure and 4 (33%) in the second part of the duodenum. Their size ranged from 2 to 40mm with a mean size of 9.4 mm. 8 (66%) lesions were sessile (Paris 0-Is), 1 (8%) was pedunculated (Paris 0-Ip) and 4 (33%) were flat, slightly elevated lesions (Paris 0-IIa). Figure 1 shows the only Paris 0-Ip lesion. Regarding color, 4 (33%) lesions had the same color as the surrounding mucosa, 2 (17%) were a reddish color darker than the surrounding mucosa, 3 (25%) were paler than the surrounding mucosa and 3 (25%) were isochromatic or slightly red but with milk-white fringes. Figure 2 shows a representative example.

Furthermore, we noticed that some patients had a history of other duodenal lesions: **2 had** a history of endoscopic resections of adenomatous polyps in the duodenum and 3 had a history of duodenal peptic ulcer. One patient had a history of pancreatoduodenectomy with conservation of the duodenal bulb.

Regarding the histopathological features, there were no signs of active inflammation in any of the 12 cases, but signs of chronic inflammation were found in all of them. The non-metaplastic part of the duodenal epithelium

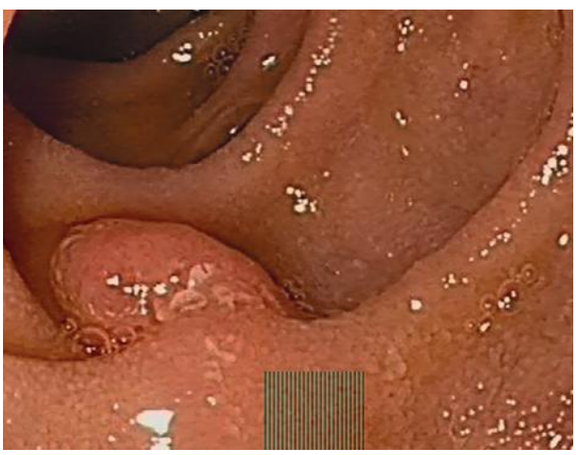

Figure 1. — Endoscopic image of a pedunculated polypoid lesion (Paris 0-Ip) in the second portion of the duodenum.

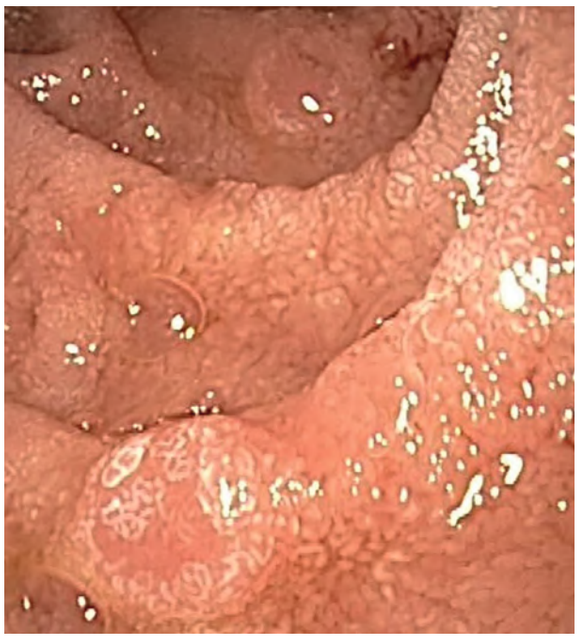

Figure 2. — Endoscopic image of two lesions in the second duodenum with milky white signs as seen in duodenal adenomas

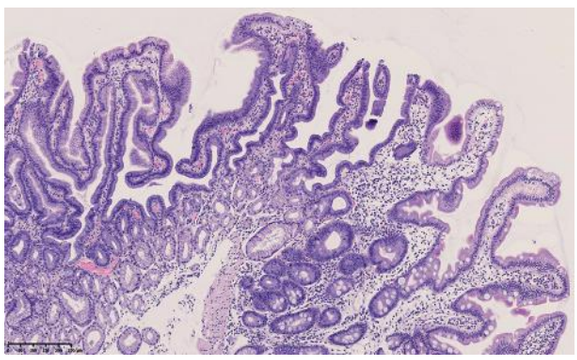

Figure 3. — **Hematoxylin-eosin staining of a FGM polyp magnified 80 times (X80)**, showing normal intestinal epithelium (right), regenerative epithelium (middle) and foveolar metaplastic epithelium (left). Brunner's glands are present in the mucosa, immediately below the area with regenerative and metaplastic epithelium.

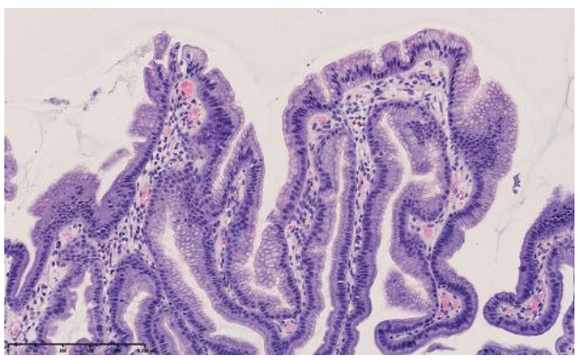

Figure 4. — Higher magnification **(X150)** of figure 3, showing the area with regenerative and foveolar metaplastic epithelium.

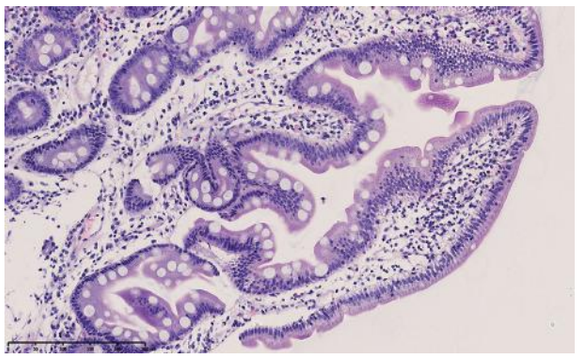

Figure 5. — Higher magnification **(X150)** of figure 3, showing the area with non-metaplastic intestinal epithelium.

showed a regenerative aspect in 8 cases (66%). There were no signs of active erosion or ulceration in any of the samples. Edema was present in 2 cases (17%). Brunner's glands were present in the mucosa in 9 out of the 12 cases (75%). Only 3 (25%) samples contained submucosa and in all of them we observed Brunner's glands; all 3 cases were lesions in the duodenal bulb. A representative example is **shown** in figures 3-5. In line with the original pathology reports, the morphological examination of the samples yielded no clear evidence for a polyp, since the fragments had not a clear polypoid aspect. Hence, the endoscopic aspect of a polyp could not be reproduced at the microscopical histopathology level.

Discussion

Presentation of FGM as a duodenal polyp is a recently recognized entity that previously attained little attention (4). At endoscopic examination, polyps with FGM are frequently considered adenomatous and it is not clear whether this is due to the endoscopist's insufficient familiarity with this entity or whether it is endoscopically indistinguishable from adenomas or other polypoid lesions of the duodenum. Although our series is rather small and retrospective, also meaning that narrow band imaging and magnifying endoscopy images were not always available, our data clearly show that the endoscopic aspect of FGM polyps is very heterogenous and shows no specific features enabling to distinguish them from other lesions, especially adenomatous polyps. Some FGM polyps showed milk-white fringes, which is endoscopic feature that is considered as an argument for adenomatous polyps (6).

Regarding the possible origin of these polyps, our findings show that phenomena such as edema and active inflammation are rarely present, so this cannot account for the polypoid aspect of the lesion. The frequent presence of a regenerative aspect of the non-metaplastic intestinal epithelium is not surprising, since this lies at the origin of the foveolar metaplasia. In the large majority of cases, **we noticed** the presence of **Brunner's glands** in the mucosa. **And in the few cases in which submucosa was contained in the sample, there were always Brunner's glands contained in that submucosa**. Sarbia et al. (4) noted that 17% of FGM polyps also showed Brunner's gland hyperplasia, which was defined as presence of mucosal Brunner's glands in at least 50% of the length of the biopsy fragments containing FGM. However, older studies have clearly shown that Brunner's glands often extend through the muscularis mucosae into the deep portions of the mucosa in normal epithelium, with about one third of the gland population residing in the mucosa (7,8). Moreover, there does not exist a clear definition of Brunner's gland hyperplasia; only vague definitions have been used, defining Brunner's gland hyperplasia as "excessive number of Brunner's glands" and as "a lesion with prominent Brunner's gland proliferation" (9). Hence, in small and mainly mucosal biopsies, it is very difficult or even virtually impossible to determine whether Brunner's gland hyperplasia is present. The situation is made even more complicated by the fact that different terminologies have been used for probably similar or identical lesions, leading to a plethora of terms, including Brunner's gland hyperplasia, Brunner's gland hamartoma and Brunner's gland adenoma (8). Nevertheless, our study shows that there are no arguments for other possible phenomena that could cause the arising of a polypoid lesion associated with the FGM, such as edema in the setting of acute inflammation. So, using a *per exclusionem* reasoning in combination with the very frequent presence of mucosal Brunner's gland in our cases, we propose that it is logical to assume that Brunner's gland hyperplasia is associated with the FGM and that the hyperplasia of the Brunner's glands **causes** the polypoid aspect, leading to an indirect correlation between FGM and the presence of a polyp. Indeed, chronic damage and inflammation do not only lie at the basis of FGM but can also lead to the development of Brunner's gland hyperplasia (10). We do not have a clear explanation for the finding that the endoscopic aspect of a polyp could not be reproduced at the level of the pathology examination.

In conclusion, our findings show that the endoscopic features of FGM polyps are not specific and overlap with those of adenomatous polyps, preventing the distinction of FGM polyps from adenomatous polyps solely on the endoscopic aspect. Furthermore, we propose that FGM polyps acquire their polypoid aspect due to their association with Brunner's gland hyperplasia, which also arises, like FGM, due to chronic inflammation and damage. Because Brunner's gland hyperplasia is ill-defined and difficult to recognize, while FGM is straightforward and easy to diagnose, this type of polypoid lesions has until now only been recognized based on the presence of FGM, although FGM is most likely not the primary cause of the polyp, but rather a secondary phenomenon.

Conflicts of interest

We have no conflicts of interest to disclose.

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