

A Report of Gastric Fundic Gland Polyps

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Fundic gland polyps (FGPs) are currently the most common type of gastric polyps found on upper endoscopy. These polyps can be sporadic or can be associated with an inherited polyposis syndrome. The prevalence of FGPs appears to be on the rise. This has partly been attributed to the expanded use of upper endoscopy, the increasing use of acid suppressive medications, and the decreasing prevalence of *Helicobacter pylori* infection. This case report begins with the case of a patient found to have FGPs and then outlines the features, prevalence, pathogenesis, and management of FGPs.

Case Report

A 65-year-old woman, who had never previously undergone upper endoscopy, underwent the procedure for the evaluation of chronic gastroesophageal reflux disease. The patient was taking rabeprazole 20 mg daily and had been on chronic proton pump inhibitor (PPI) therapy for 10 years, with predominantly effective symptom control. She denied having dysphagia, anorexia, weight loss, abdominal pain, cough, shortness of breath, or chest pain. Upper endoscopy revealed innumerable large polyps in the cardia, fundus, and body of the stomach (Figure 1). The gastric antrum was free of polyps and appeared normal. Biopsies from the gastric body and antrum were negative for *H. pylori* infection. Three of the largest seen polyps (ranging in size from 15 mm to 30 mm) were removed via hot snare polypectomy. Steady retraction with cold biopsy forceps allowed for the successful removal of a fourth 8-mm polyp completely intact at its base (Figure 2). Histology of all 4 polyps demonstrated cystically dilated fundic glands lined by normal gastric corpus-type epithelium arranged in a mildly disordered and microcystic configuration (Figure 3). There was no evidence of dysplasia. Histologic findings were consistent with gastric FGPs.

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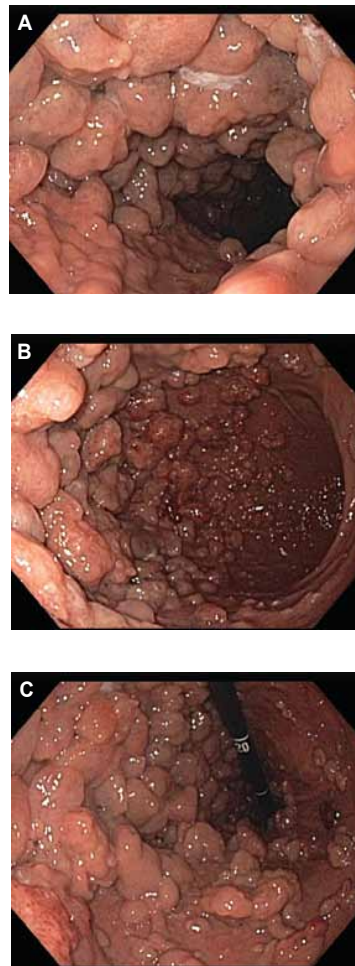


Figure 1. Proximal stomach (A). Midgastric body (B). Gastric cardia and fundus (C).

The patient had undergone a normal colonoscopy with an excellent bowel preparation 1 year earlier. She had no family history of gastrointestinal malignancy or polyposis syndromes. Her PPI therapy was discontinued. When her reflux symptoms returned, a histamine blocker



Figure 2. Entire polyp removed cleanly with biopsy forceps (“chunking-off” sign).

was initiated, with good symptom relief. A repeat surveillance upper endoscopy was planned for 1 year later. The patient’s final diagnosis was sporadic giant fundic gland polyposis.

Discussion

Sporadic FGPs are the most common type of gastric polyps found in middle-aged adults of both genders undergoing upper endoscopy. FGPs are usually discovered incidentally at endoscopy and are typically asymptomatic. They account for 50–77% of all gastric polyps and are found in up to 1.9% of the general population.^{1–3} FGPs also occur in up to 84% of patients with familial adenomatous polyposis (FAP) and attenuated familial adenomatous polyposis (AFAP) and, in this setting, are more commonly observed at a much younger age compared to sporadic polyps.⁴ FGPs may be found individually, though they are more often found in groups, and always develop in the acid-secreting mucosa of the gastric body and fundus.¹ FGPs are usually 1–5 mm in size, though larger polyps have been found. FGPs are typically sessile, shiny, translucent, pale to pinkish in color (resembling the surrounding mucosa), and often exhibit tiny surface blood vessels (Figure 4). These polyps have characteristically been observed to “chunk off” or detach entirely at the base when removed with cold forceps, in contrast to other types of gastric polyps.¹ This trait is most evident when the polyp base is grasped with forceps and the scope is slowly retracted. The number and size of both sporadic and FAP-associated FGPs may slowly increase, remain the same, or decrease over time.²

Histologically, FGPs are characterized by cystically dilated and irregularly budded fundic glands, which are lined by normal parietal cells, chief cells, or mucous neck cells.⁴ The surrounding mucosa is typically normal, without any inflammatory changes.

The pathogenesis and cancer risk of FGPs are not well understood. FGPs in FAP arise from mutational inactiva-

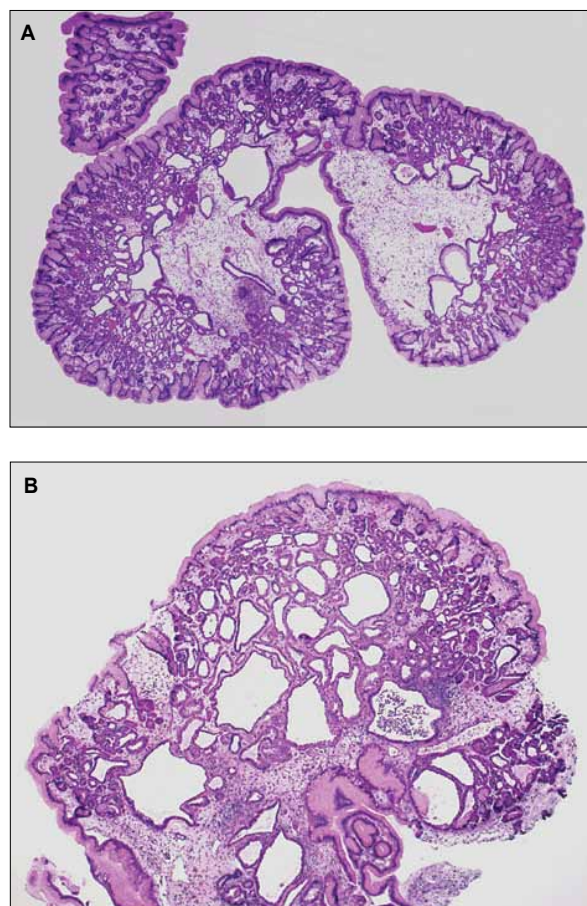


Figure 3. Fundic gland polyp (hematoxylin and eosin stain, 4× [A] and 10× [B]).

tion of the *adenomatous polyposis coli* gene, whereas sporadic FGPs are usually caused by activating mutations of the β -*catenin* gene.⁴ Dysplasia is found in up to 41% of FAP- or AFAP-associated FGPs.⁵ The incidence of gastric cancer is increased in patients with FAP and FGPs.⁶ The lifetime risk of gastric cancer in FAP is estimated to be 0.6–4.2%.^{7–9} Sporadic FGPs have typically been regarded as benign lesions with no risk of malignant transformation; however, some reports have described sporadic FGPs containing low-grade dysplasia.^{3,10,11} One case in the literature has reported a 68-year-old man on chronic PPIs with FGPs containing high-grade dysplasia in whom FAP and AFAP were excluded.¹² There are no reports of gastric cancer arising from sporadic FGPs.

A variety of factors have been associated with FGPs. A negative correlation exists between FGPs and *H. pylori* infection, as the latter is rarely observed in the presence of FGPs. In addition, regression of sporadic polyps has been observed to coincide with the acquisition of *H. pylori*



Figure 4. Characteristic appearance of fundic gland polyps.

infection.^{13,14} A positive association between FGPs and acid suppression was first reported in 1992.¹⁵ One study observed a 7.3% incidence of FGPs after a mean PPI treatment duration of 32.5 months, and polyp regression was noted following discontinuation of acid suppression therapy.¹⁶ Another study demonstrated a 4-fold increase in the risk of developing FGPs with long-term PPI use.¹⁷

Most patients on chronic PPI therapy will not develop FGPs, and it is unclear why some do develop them with chronic PPI use. A small subset of patients are thought to be highly susceptible to developing FGPs with acid suppression. These patients often display greater numbers of polyps than typically observed in sporadic cases.² One theory possibly explaining the correlation between acid suppression and FGPs is that PPIs elevate serum gastrin, which is a growth factor for oxyntic mucosa and a downstream target of Wnt signaling.^{18,19} The development of hyperplasia and protrusion of parietal cells is thought to be one of the initial steps in FGP development.²⁰ These protrusions are thought to develop secondary to PPI impairment of hydrochloric acid secretion within secretory canaliculi.²¹ Fundic gland cyst formation secondary to dilated glands is thought to be the second step in FGP formation, and as the fundic gland cysts enlarge, they develop into FGPs.²¹

The most important consideration in a patient with FGPs is the potential presence of a familial polyposis syndrome such as FAP or AFAP. This importance relates to the risk of FGP dysplasia, gastric cancer, and the significant risk of other malignancies such as colorectal, ampullary, small bowel, pancreatic, thyroid, and central nervous system cancer in patients (and their families) with FAP or AFAP. Therefore, determining whether the patient has an inherited polyposis condition is paramount for the facilitation of appropriate screening and surveillance. A detailed and extended family history (including endoscopic examinations) should be

obtained from all patients with FGPs. Colonoscopy will typically demonstrate a predominance of colonic polyps in patients with concomitant FAP and serves as a useful screening test. Patients with AFAP, in contrast to FAP, may have a more variable presentation and may manifest only a few colonic adenomas even at older ages. This can lead to confusion regarding the presence of a polyposis syndrome versus sporadic colon adenomas or sporadic cancer. If FAP or AFAP is suspected based upon colonoscopic examination findings, genetic testing to confirm the diagnosis should be undertaken. Genetic testing should also be performed in those suspected of having FAP or AFAP despite an inconclusive colonoscopy.

The utility of discontinuing acid suppressive therapy to promote sporadic FGP regression is unclear. Although it is interesting from a mechanistic point of view, there appear to be several clinical implications of the association between long-term PPI therapy and sporadic FGP development. Several studies have demonstrated regression of FGPs upon discontinuation of acid suppression therapy; however, this finding has not been consistently observed, and the clinical benefit of FGP regression is unclear, as sporadic FGPs are thought to be benign lesions without malignant potential. It is unclear whether any benefits from sporadic polyp regression outweigh potential adverse effects from disruption of antisecretory therapy. A recent study reported a significantly lower rate of FGP dysplasia in FAP patients taking acid suppressive medications (histamine antagonist or PPI) versus patients not using these medications.⁵ This inverse relationship was thought to be related to the induction of differentiation and impairment of cellular proliferation of surface epithelial and foveolar cells of FGPs by acid suppressive medication.⁵ It was unclear whether this effect was found equally with both H2 blocker and PPI therapy. The authors proceeded to recommend chemoprevention with a PPI for FAP patients with FGPs and high-grade dysplasia.

Two unique features of our case were the large size and the enormous number of FGPs. Case reports have documented isolated giant FGPs ranging from 5 cm to 8 cm in size.²²⁻²⁴ Our case appears to be the first report of innumerable giant sporadic FGPs. In our patient, we elected to discontinue the PPI in the hope that this would promote sporadic FGP regression. We also elected to repeat a surveillance upper endoscopy in 1 year. Due to the large polyp burden and size, we decided to proceed with a surveillance approach in our patient in order to document polyp regression and/or stability and monitor for the development of dysplasia. We were confident that we were not dealing with an inherited polyposis syndrome, based upon the patient's age, negative family history, and a recent normal colonoscopy.

Summary

Gastric FGPs are the most common type of gastric polyps found in middle-aged adults undergoing upper endoscopy. FGPs have typical and characteristic endoscopic and histologic hallmarks. A positive association between FGPs and acid suppression has been noted. Why certain patients are more likely to develop FGPs in the setting of acid suppression remains unclear. FGPs can be sporadic, or they can be associated with an inherited polyposis syndrome such as FAP or AFAP. Patient age, history of acid suppression, family history, and prior colonoscopy results should be evaluated to determine the possible presence of an inherited syndrome. Ultimately, genetic testing may be necessary to establish the diagnosis and facilitate subsequent screening and surveillance of the patient and family members. The role of surveillance for sporadic FGPs is controversial, as these polyps have typically been regarded as benign lesions without malignant potential. There is a clear role for surveillance of FGPs in patients with an inherited polyposis syndrome due to the increased risk of dysplasia and cancer. Finally, FAP patients may benefit from chemoprevention with acid suppressive therapy to prevent FGP dysplasia and cancer.

References

- Weston BR, Helper DJ, Rex DK. Positive predictive value of endoscopic features deemed typical of gastric fundic gland polyps. *J Clin Gastroenterol*. 2003;36:399-402.
- Burt RW. Gastric fundic gland polyps. *Gastroenterology*. 2003;125:1462-1469.
- Carmack SW, Genta RM, Schuler CM, Saboorian MH. The current spectrum of gastric polyps: A 1-year national study of over 120,000 patients. *Am J Gastroenterol*. 2009;104:1524-1532.
- Abraham SC, Nobukawa B, Giardiello FM, Hamilton SR, Wu TT. Sporadic fundic gland polyps: common gastric polyps arising through activating mutations in the beta-catenin gene. *Am J Pathol*. 2001;158:1005-1010.
- Bianchi LK, Burke CA, Bennett AE, Lopez R, Hasson H, Church JM. Fundic gland polyp dysplasia is common in familial adenomatous polyposis. *Clin Gastroenterol Hepatol*. 2008;6:180-185.
- Zwick A, Munir M, Ryan CK, Gian J, Burt RW, et al. Gastric adenocarcinoma and dysplasia in fundic gland polyps of a patient with attenuated adenomatous polyposis coli. *Gastroenterology*. 1997;113:659-663.
- Offerhaus GJ, Giardiello FM, Krush AJ, Booker SV, Tersmette AC, et al. The risk of upper gastrointestinal cancer in familial adenomatous polyposis. *Gastroenterology*. 1992;102:1980-1982.
- Jagelman DG, DeCosse JJ, Bussey HJ. Upper gastrointestinal cancer in familial adenomatous polyposis. *Lancet*. 1988;1:1149-1151.
- Park JG, Park KJ, Ahn YO, Song IS, Choi KW, et al. Risk of gastric cancer among Korean familial adenomatous polyposis patients. Report of three cases. *Dis Colon Rectum*. 1992;35:996-998.
- Wu TT, Kornacki S, Rashid A, Yardley JH, Hamilton SR. Dysplasia and dysregulation of proliferation in foveolar and surface epithelia of fundic gland polyps from patients with familial adenomatous polyposis. *Am J Surg Pathol*. 1998;22:293-298.
- Lakshman V, Shah AN, Ryan CK. The presence of dysplasia and carcinoma in gastric fundic gland polyps in patients with familial adenomatous polyposis. *Gastroenterology*. 1997;112:A599.
- Jalving M, Koornstra JJ, Gotz JM, van der Waaij LA, de Jong S, et al. High-grade dysplasia in sporadic fundic gland polyps: a case report and review of the literature. *Eur J Gastroenterol Hepatol*. 2003;15:1229-1233.
- Bertoni G, Sassatelli R, Nigrisoli E, Pennazio M, Tansini P, et al. Dysplastic changes in gastric fundic gland polyps of patients with familial adenomatous polyposis. *Ital J Gastroenterol Hepatol*. 1999;31:192-197.
- Watanabe N, Seno H, Nakajima T, Yazumi S, Miyamoto S, et al. Regression of fundic gland polyps following acquisition of *Helicobacter pylori*. *Gut*. 2002;51:742-745.
- Graham JR. Gastric polyposis: onset during long-term therapy with omeprazole. *Med J Aust*. 1992;157:287-288.
- Choudhry U, Boyce HW Jr, Coppola D. Proton pump inhibitor associated gastric polyps: a retrospective analysis of their frequency, and endoscopic, histologic, and ultrastructural characteristics. *Am J Clin Pathol*. 1998;110:615-621.
- Jalving M, Koornstra JJ, Wesseling J, Boezen HM, DE Jong S, Kleibeuker JH. Increased risk of fundic gland polyps during long-term proton pump inhibitor therapy. *Aliment Pharmacol Ther*. 2006;24:1341-1348.
- Koh TJ, Bulitta CJ, Fleming JV, Dockray GJ, Varro A, Wang TC. Gastrin is a target of the beta-catenin/TCF-4 growth signaling pathway in a model of intestinal polyposis. *J Clin Invest*. 2000;106:533-539.
- Koh TJ, Chen D. Gastrin as a growth factor in the gastrointestinal tract. *Regul Pept*. 2000;93:37-44.
- Driman DK, Wright C, Tougas G, Riddell RH. Omeprazole produces parietal cell hypertrophy and hyperplasia in humans. *Dig Dis Sci*. 1996;41:2039-2047.
- Cats A, Schenk BE, Bloemena E, Roosendaal R, Lindeman J, et al. Parietal cell protrusions and fundic gland cysts during omeprazole maintenance treatment. *Hum Pathol*. 2000;31:684-690.
- El Hajj II, Hawchar M, Sowaid A, Maasri K, Tawil A, Barada KA. Giant sporadic fundic gland polyp: endoscopic and endosonographic features and management. *World J Gastroenterol*. 2008;14:6593-6595.
- McGarrity TJ, Ruggiero FM, Chey WY, Bajaj R, Kelly JE, Kauffman GL Jr. Giant fundic polyp complicating attenuated familial adenomatous polyposis. *Am J Gastroenterol*. 2000;95:1824-1828.
- Winkler A, Hinterleitner TA, Langner C. Giant fundic gland polyp mimicking a gastric malignancy. *Endoscopy*. 2007;39(suppl 1):E34.

Review

Fundic Gland Polyps: Common and Occasionally Problematic Lesions

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Given the relative frequency of fundic gland polyps (FGPs) in upper endoscopic examinations, nearly every gastroenterologist encounters patients with one (or more) of these lesions. In most patients, FGPs are an incidental finding of little clinical significance—indeed, they are more common in gastric mucosa without gastritis, *Helicobacter pylori* infection, or glandular atrophy.¹ This is in

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sharp contrast to other gastric polyps such as adenomas and hyperplastic polyps, which are linked to a background of mucosal injury, antral and/or fundic gland atrophy, and intestinal metaplasia.² As noted by Spiegel and colleagues, most FGPs are small (<5 mm) and their histologic appearance is innocuous.³ Composed of cystically dilated fundic glands beneath a normal gastric foveolar epithelium, FGPs do not appear to be neoplastic and have at times been regarded as retention cysts or hamartomas.⁴

However, there are still occasional cases in which FGPs pose significant clinical and management issues. This scenario is aptly illustrated by the patient treated by Spiegel and associates, a middle-aged woman on chronic proton pump inhibitor therapy who underwent upper endoscopy for esophageal reflux.³ During the procedure, she was found, incidentally, to have fundic gland polyposis carpeting the gastric body, fundus, and cardia, with the largest polyps measuring up to 3 cm. In this type of patient, three main questions arise: What is the etiology of the polyposis? Do these FGPs have neoplastic potential? Finally, and, most importantly, how should they be managed? Although it may not be possible to reach a definitive answer regarding management, some insight into this issue can be gained by addressing the first two questions.

FGPs arise in two settings: sporadic (possibly linked to proton pump inhibitor use) and familial adenomatous polyposis syndrome (FAP)-associated settings. FGPs are the most common gastric polyps in both groups, as they are found in up to 5.9% of adults undergoing upper endoscopy and 53–84% of adults with FAP.¹ As FAP is estimated to occur in only 1 per 6,000–18,000 births, it follows that most FGPs are nonsyndromic. In comparison to sporadic FGPs, FAP-associated FGPs are more likely to be multiple and to occur at a younger age. In an 18-year review of pediatric gastric polyps, Attard and coworkers found that FAP accounted for 81% of FGPs in children and the polyps were multifocal in 85% of children with FAP-associated FGPs.⁵ Sporadic fundic gland polyposis is occasionally also observed in the non-FAP population.⁶ Two recent reports of giant FGPs in the sporadic setting described a 63-year-old man with an 8-cm FGP and a 67-year-old man with a FGP that covered large areas of the gastric body.^{7,8} The latter case mimicked gastric carcinoma, with endosonography suggesting irregular thickening of the first three layers of the stomach.⁸

FAP or attenuated FAP, therefore, needs to be excluded in patients with numerous large or dysplastic FGPs. The patient reported by Spiegel and colleagues had a negative family history and had undergone a normal colonoscopy the previous year, supporting the final impression of sporadic giant fundic gland polyposis. Her age was also more typical of the age associated with sporadic FGPs, which has a median of 59 years of age.⁹ However, family

history and patient age are not entirely reliable factors in excluding FAP. Approximately 25% of patients with FAP have no relevant family history and presumably represent *de novo* mutations in the *adenomatous polyposis coli (APC)* gene. In patients with FGPs plus colonic adenomas (who have fewer than 100), attenuated FAP is a consideration. In these cases, genetic testing for germline mutations in the *APC* gene can be undertaken. Genetic testing using a combination of DNA sequencing and protein truncation assay will identify most, but not all, such mutations. In negative cases, further testing can be performed to evaluate for germline mutations in the *MYH* gene.

Understanding the genetics of sporadic and FAP-associated FGPs also opens an alternative method for ruling out FAP or attenuated FAP in patients with fundic gland polyposis. In the setting of FAP, FGPs arise through “second-hit” alterations (somatic mutations or allelic loss on chromosome 5q) in the *APC* tumor suppressor gene, the same mechanism responsible for colorectal polyps and periampullary adenomas in these patients. Using a combination of loss of heterozygosity assays and direct DNA sequencing of the mutation cluster region in exon 15 of the *APC* gene, second-hit *APC* alterations were demonstrated in 51% of FAP-associated FGPs.¹⁰ In contrast, *APC* alterations are unusual in sporadic FGPs.¹⁰ Instead, most sporadic FGPs contain activating mutations on or near several phosphorylation sites in exon 3 of the β -*catenin* oncogene. β -*catenin* mutations have been found in 91%,¹¹ 76%,⁶ and 64%¹² of sporadic FGPs, but in none of the FAP-associated FGPs analyzed to date.^{6,11} Both types of mutations—inactivation of the *APC* tumor suppressor gene and activation of the β -*catenin* oncogene—result in stabilization of β -catenin protein and its abnormal accumulation in affected cells. In a study that specifically examined 8 non-FAP patients with fundic gland polyposis, Torbenson and colleagues showed that at least 2 FGPs from all patients contained independent β -*catenin* mutations; however, β -*catenin* mutations were never present in the nonpolypoid gastric mucosa of these patients nor were they present in the FGPs of a patient with clinical attenuated FAP.⁶ Overall, these results suggest an alternative means for excluding FAP in the setting of fundic gland polyposis: multiple FGPs are biopsied and analyzed for β -*catenin* mutations. If a majority contain β -*catenin* mutations, FAP/attenuated FAP is essentially excluded.

The presence of clonal *APC* or β -*catenin* mutations in FGPs indicates that they are neoplastic growths, albeit ones that have only very limited potential for malignant transformation. Low-grade dysplasia involving the foveolar epithelium is common in FAP-associated FGPs, with incidence rates of 25%,¹³ 41%,¹⁴ and 44%¹⁵ in three studies from the United States and Italy. Even in the

pediatric population, FAP-associated FGPs commonly show low-grade dysplasia. In one study that included 13 children with FAP, 31% of FGPs were dysplastic and 19% had epithelial atypia indefinite for dysplasia.⁵ High-grade dysplasia occasionally arises in FAP-associated FGPs,^{14,16,17} including one report of an 11-year-old child with high-grade dysplasia, fundic gland polyposis, and a family history of gastric cancer.¹⁸ The risk of gastric adenocarcinoma in FAP is markedly elevated in Japanese and Korean patients, but it has not been shown to be statistically increased in Western populations where the background rate of gastric cancer is low. Nevertheless, several well-documented cases of invasive adenocarcinoma arising from FGPs or fundic gland polyposis have been reported.¹⁹⁻²¹

In contrast, sporadic FGPs only rarely show neoplastic progression. Low-grade foveolar dysplasia is diagnosed in only approximately 1% of sporadic FGPs (3 of 270 in one study).¹³ To date, there is only a single case report of high-grade dysplasia arising in sporadic FGPs²² and no cases of adenocarcinoma arising in this setting. The patient discussed by Spiegel and colleagues—as with the two previously reported patients with giant sporadic FGPs—lacked evidence of even low-grade dysplasia despite the high number and large size of her polyps.³

The management of sporadic fundic gland polyposis, therefore, centers more on the concern for FAP and exclusion of colorectal neoplasia than on concern for neoplastic progression in the gastric mucosa. Several studies have claimed an association between sporadic FGPs and the presence of colonic adenomas or even adenocarcinomas,²³⁻²⁵ prompting the suggestion that every patient with a sporadic FGP should have surveillance for colorectal neoplasia.²⁶ However, in the most recent study of 25,687 adults who underwent both upper endoscopy and colonoscopy, there was only a slightly increased prevalence of colonic adenomas and no increased prevalence of colonic adenocarcinoma among patients with sporadic FGPs as compared to those without FGPs.¹ In women, the odds ratio for concomitant adenomas was 1.43, whereas in men it was only 1.15 (and not statistically significant). An interesting (but most likely not clinically significant) finding in that study was a slightly higher prevalence of colonic hyperplastic polyps in men with FGPs. Despite these associations, there was no difference in the rate of colonic adenocarcinomas in women with or without FGPs, and in men, the rate of colorectal cancer was statistically lower in those with FGPs.¹ Therefore, it is difficult to justify colonoscopic surveillance on the basis of sporadic FGPs alone.

There are little data on the best management—or indeed, whether any management is needed at all—for sporadic fundic gland polyposis and giant sporadic

FGPs, both of which were found in the patient treated by Spiegel and colleagues. The doctors elected to discontinue the patient's proton pump inhibitor therapy and recommended a surveillance upper endoscopy in 1 year's time.³ These decisions were entirely reasonable given the patient's polyp burden. Unfortunately, there is conflicting evidence regarding the role of acid suppression in the genesis of FGPs, and there is no empirical evidence regarding the role of gastric surveillance. Most studies suggest an association between proton pump inhibitor use and the increasing prevalence of FGPs in the general population.²⁷ However, this has been disputed by some researchers²⁸ and in some patients, the need for acid suppression may outweigh any concerns regarding gastric polyps. Given the overwhelmingly benign nature of sporadic FGPs, therapeutic decisions should be tailored to the clinical circumstances and the patient's wishes.

References

- Genta RM, Schuler CM, Robiou CI, Lash RH. No association between gastric fundic gland polyps and gastrointestinal neoplasia in a study of over 100,000 patients. *Clin Gastroenterol Hepatol*. 2009;7:849-854.
- Abraham SC, Singh VK, Yardley JH, Wu TT. Hyperplastic polyps of the stomach: associations with histologic patterns of gastritis and gastric atrophy. *Am J Surg Pathol*. 2001;25:500-507.
- Spiegel A, Stein P, Patel M, Patel R, Lebovics E. A report of gastric fundic gland polyps. *Gastroenterol Hepatol*. 2010;6:45-48.
- Sipponen P, Siurala M. Cystic "hamartomatous" epithelial polyps of the stomach. *Hepatogastroenterology*. 1978;25:380-383.
- Attard TM, Yardley JH, Cuffari C. Gastric polyps in pediatrics: an 18-year hospital-based analysis. *Am J Gastroenterol*. 2002;97:298-301.
- Torbenson M, Lee JH, Cruz-Correa M, Ravich W, Rastgar K, et al. Sporadic fundic gland polyposis: a clinical, histological, and molecular analysis. *Mod Pathol*. 2002;15:718-723.
- El Hajj II, Hawchar M, Soweid A, Maasri K, Tawil A, Barada KA. Giant sporadic fundic gland polyp: endoscopic and endosonographic features and management. *World J Gastroenterol*. 2008;14:6593-6595.
- Winkler A, Hinterleitner TA, Langner C. Giant fundic gland polyp mimicking a gastric malignancy. *Endoscopy*. 2007;39(suppl 1):E34.
- Carmack SW, Genta RM, Schuler CM, Saboorian MH. The current spectrum of gastric polyps: a 1-year national study of over 120,000 patients. *Am J Gastroenterol*. 2009;104:1524-1532.
- Abraham SC, Nobukawa B, Giardiello FM, Hamilton SR, Wu TT. Fundic gland polyps in familial adenomatous polyposis: neoplasms with frequent somatic APC gene alterations. *Am J Pathol*. 2000;157:747-754.
- Abraham SC, Nobukawa B, Giardiello FM, Hamilton SR, Wu TT. Sporadic fundic gland polyps: common gastric polyps arising through activating mutations in the β -catenin gene. *Am J Pathol*. 2001;158:1005-1010.
- Sekine S, Shibata T, Yamauchi Y, Nakanishi Y, Shimoda T, et al. β -catenin mutations in sporadic fundic gland polyps. *Virchows Arch*. 2002;440:381-386.
- Wu TT, Kornacki S, Rashid A, Yardley JH, Hamilton SR. Dysplasia and dysregulation of proliferation in foveolar and surface epithelia of fundic gland polyps from patients with familial adenomatous polyposis. *Am J Surg Pathol*. 1998;22:293-298.
- Bianchi L, Burke CA, Bennett AE, Lopez R, Hasson H, Church JM. Fundic gland polyp dysplasia is common in familial adenomatous polyposis. *Clin Gastroenterol Hepatol*. 2008;6:180-185.
- Bertoni G, Sassatelli R, Nigrisoli E, Pennazio M, Tansini P, et al. Dysplastic changes in gastric fundic gland polyps of patients with familial adenomatous polyposis. *Ital J Gastroenterol Hepatol*. 1999;31:192-197.
- Odze RD, Quinn PS, Terrault NA, Vivona AA, Ward MA, et al. Advanced gastroduodenal polyposis with ras mutations in a patient with familial adenomatous polyposis. *Hum Pathol*. 1993;24:442-448.

17. Sekine S, Shimoda T, Nimura S, Nakanishi Y, Akasu T, et al. High-grade dysplasia associated with fundic gland polyposis in a familial adenomatous polyposis patient, with special reference to APC mutation profiles. *Mod Pathol.* 2004;17:1421-1426.
18. Attard TM, Giardiello FM, Argani P, Cuffari C. Fundic gland polyposis with high-grade dysplasia in a child with attenuated familial adenomatous polyposis and familial gastric cancer. *J Pediatr Gastroenterol Nutr.* 2001;32:215-218.
19. Garrean S, Hering J, Saied A, Jani J, Espot NJ. Gastric adenocarcinoma arising from fundic gland polyps in a patient with familial adenomatous polyposis syndrome. *Am Surg.* 2008;74:79-83.
20. Hofgärtner WT, Thorp M, Ramus MW, Delorefice G, Chey WY, et al. Gastric adenocarcinoma associated with fundic gland polyps in a patient with attenuated familial adenomatous polyposis. *Am J Gastroenterol.* 1999;94:2275-2281.
21. Zwick A, Munir M, Ryan CK, Gian J, Burt RW, et al. Gastric adenocarcinoma and dysplasia in fundic gland polyps of a patient with attenuated adenomatous polyposis coli. *Gastroenterology.* 1997;113:659-663.
22. Jalving M, Koornstra JJ, Götz JM, van der Waaij LA, de Jong S, et al. High-grade dysplasia in sporadic fundic gland polyps: a case report and review of the literature. *Eur J Gastroenterol Hepatol.* 2003;15:1229-1233.
23. Jung A, Vieth M, Maier O, Stolte M. Fundic gland polyps (Elster's cysts) of the gastric mucosa. A marker for colorectal neoplasia? *Path Res Pract.* 2002;198:731-734.
24. Teichmann J, Weickert U, Riemann JF. Gastric fundic gland polyps and colonic polyps—is there a link, really? *Eur J Med Res.* 2008;13:192-195.
25. Eidt S, Stolte M. Gastric glandular cysts—investigations into their genesis and relationship to colorectal epithelial tumors. *Z Gastroenterol.* 1989;27:212-217.
26. Dechlich P, Tavani E, Ferrara A, Caruso S, Bellone S. Sporadic fundic gland polyps: clinico-pathologic features and associated diseases. *Pol J Pathol.* 2005;56:131-137.
27. Freeman HJ. Proton pump inhibitors and an emerging epidemic of gastric fundic gland polyposis. *World J Gastroenterol.* 2008;14:1318-1320.
28. Vieth M, Stolte M. Fundic gland polyps are not induced by proton pump inhibitor therapy. *Am J Clin Pathol.* 2001;116:716-720.