

# CASE STUDY IN GASTROENTEROLOGY & HEPATOLOGY

## Large Fundic Gland Polyps in the Stomach

Sonia Varghese, MD<sup>1</sup>  
Vu Le, MD<sup>2</sup>  
Tauseef Ali, MD<sup>2</sup>

<sup>1</sup>Department of Hematology and Oncology, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma; <sup>2</sup>Department of Gastroenterology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

A 42-year-old white man was referred to our center by his primary care physician for symptoms of chronic diarrhea associated with cramping, abdominal pain, and flatulence. The patient had chronic gastroesophageal reflux disease (GERD) and had been taking omeprazole 20 mg twice daily for the past 12 years.

A colonoscopy and esophagogastroduodenoscopy (EGD) were performed for symptom workup. The colonoscopy revealed no significant findings. The EGD showed approximately 30 large pedunculated polyps in the gastric body and fundus (Figure 1). The size of the largest polyp was approximately 2 cm. Biopsies of the polyps were obtained with cold forceps. Histologic examination of the specimens showed multiple fragments of fundic gland mucosa with occasional dilated glands. Based on the EGD and histology, the patient was diagnosed with fundic gland polyps (FGPs). The most likely etiology was thought to be the prolonged use of proton pump inhibitor (PPI) therapy. Therefore, omeprazole was discontinued, and ranitidine 150 mg bid was started. A repeat EGD performed 5 months later showed a significant decrease in the size of the polyps and no polyps were pedunculated (Figure 2). Pathology of the biopsy sample confirmed the presence of FGPs with no evidence of malignancy.

### Discussion

FGPs are the most commonly reported gastric polyps.<sup>1</sup> These polyps were originally described in patients with familial adenomatous polyposis (FAP). FGPs were thought to be an extracolonic manifestation of FAP<sup>2</sup> and were also called syndromic FGPs. They have also been seen in association with attenuated FAP, Zollinger-Ellison syndrome,<sup>3</sup> and Gardner syndrome.<sup>4</sup> FGPs that occur in the absence of such systemic diseases are called sporadic FGPs. FGPs are diagnosed based on clinical and histologic examinations.

Address correspondence to:

Dr Sonia Varghese, Department of Hematology and Oncology, Stephenson Cancer Center, University of Oklahoma Health Sciences Center, 800 NE 10th Street, Oklahoma City, OK 73104; Tel: 405-271-4022; E-mail: Sonia-Varghese@ouhsc.edu



**Figure 1.** An endoscopic image of fundic gland polyps while the patient was on omeprazole.

Sporadic FGPs are most commonly reported in patients in their 60s and have female predominance,<sup>5,6</sup> whereas syndromic FGPs are more frequently observed in patients in their 30s and 40s and have equal incidence in men and women.<sup>7,8</sup> FGPs occur in 12.5% to 84% of patients with FAP, while only 0.8% to 3.2% of sporadic FGPs have been reported in patients undergoing upper endoscopy.<sup>7,9</sup> Histologic examination reveals hamartomas with cystically dilated fundic glands lined with attenuated parietal, chief, and mucous neck cells.<sup>8</sup> Mutations in the beta-catenin gene may be the causative factor in the development of sporadic FGPs.<sup>10</sup> Sporadic FGPs are mainly found in patients who undergo EGD for symptoms such as persistent dyspepsia, GERD, and heartburn.<sup>8</sup> Declich and colleagues conducted a 9-year study in 70 patients with sporadic FGPs and found that 34% of these patients had esophageal complaints and most patients had GERD and a hiatal hernia.<sup>6</sup>

PPIs have been the most commonly prescribed drugs since they were introduced in 1988. There has been controversy regarding the role of PPIs in the formation of FGPs. In 1992, Graham was the first to describe the risk of gastric polyp formation due to PPI use.<sup>11</sup> Since then, many



**Figure 2.** An endoscopic image of fundic gland polyps after the discontinuation of omeprazole.

have supported this observation. Choudhry and colleagues reported that prolonged use of PPIs increased the risk of FGPs.<sup>12</sup> Jalving and colleagues reported a 4-fold increase in the risk of FGP formation due to prolonged use of PPIs.<sup>13</sup> This was supported by a study that examined 1780 patients who underwent EGD and found that 4.33% had FGPs; PPI use was thought to be the strongest risk factor.<sup>14</sup>

In contrast, in Declich and colleagues' 9-year study of 70 patients with sporadic FGPs, only 1 patient was on PPIs, and no association was found between PPI use and FGP formation.<sup>6</sup> Another study compared the incidence of FGPs in *Helicobacter pylori*-negative patients on PPIs, and no causal link was found between the use of PPIs and the incidence of FGPs.<sup>15</sup>

No clear mechanism has been found to explain the possible pathogenesis of FGPs due to PPI use. Hypergastrinemia due to PPI use was thought to be a probable cause of gastric mucosal hypertrophy and polyp formation. However, a study by Fossmark and colleagues found no relationship between FGP formation and serum gastrin levels due to PPI use.<sup>16</sup> Our patient had serum gastrin levels within normal limits.

There is no evidence that any PPI increases the incidence of FGPs. In most studies, the most common PPI was omeprazole, which could be because it was one of the earliest PPIs to be marketed and it is commonly prescribed.

However, the use of PPIs for more than 2 years may increase the risk of FGP formation.<sup>11,12</sup> Ally and colleagues demonstrated that PPI use of less than 1 year did not increase the development of gastric polyps, while PPI therapy for more than 2 years was an independent risk factor.<sup>17</sup> No dose-dependent association has been described in the literature. Our patient reported the use of PPIs for approximately 12 years.

No surveillance is required for FGPs because they are not premalignant lesions.<sup>18</sup> Genta and colleagues found no increase in gastric neoplasia in patients with FGPs.<sup>19</sup> There was an inverse correlation between the FGPs and gastric

neoplasia.<sup>19</sup> In our patient, we repeated the endoscopy within 6 months because of worsening GERD symptoms.

In conclusion, this case demonstrates a possible association between long-term PPI use and large FGPs. Because many patients take PPIs for GERD and other conditions, doctors should be aware of this potential adverse effect. The use of PPIs should be limited to patients who need them, and the duration of treatment should be monitored.

*The authors have no relevant conflicts of interest to disclose.*

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