

# Gastric Pyogenic Granuloma

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**P**yo-genic granuloma is a benign, lobular capillary hemangioma that most commonly occurs on the skin. It also has been occasionally found on the mucosal surfaces of the oral cavity and the upper respiratory tract. Only a handful of cases, most of which come from the Japanese literature, have been reported in the gastrointestinal tract, predominantly in the esophagus and intestine. We report here a rare case of gastric pyogenic granuloma associated with chronic bleeding and iron deficiency anemia and present its endoscopic and pathologic findings. We also report and discuss the use of endoscopic ultrasound in the evaluation of the endoscopic resectability of these lesions. Finally, we review the English, Japanese, and French literature on gastrointestinal pyogenic granulomas.

## Case Report

A 67-year-old woman presented to the emergency room with complaints of shortness of breath and chest pains suggestive of angina. Medical evaluation revealed microcytic hypochromic anemia (hematocrit of 24%) due to iron deficiency (serum iron of 19 µg/dL, transferrin of 485 µg/dL, transferrin saturation of 4%, and ferritin of 6.6 ng/mL). The patient received a transfusion of packed red blood cells, which led to the immediate resolution of her symptoms, and she was subsequently started on oral ferrous sulfate therapy. A recent screening colonoscopy had been reported to be unremarkable. The patient was therefore scheduled for an esophagogastroduodenoscopy (EGD).

EGD revealed a 10-mm sessile polypoid lesion with a short broad stalk in the gastric antrum. The surface of the lesion had a variegated appearance with yellow ulcerated areas overlying a reddish/erythematous background (Figure 1). The adjacent antral mucosa was mildly ery-

thematous but otherwise normal. No other potential sources of blood loss were evident in the upper gastrointestinal tract. Biopsies of the lesion obtained at EGD revealed nonspecific appearances, with acute inflammation, ulceration, and granulation tissue. Biopsies from the adjacent antral mucosa were unremarkable, with no evidence of gastritis or *Helicobacter pylori*.

An endoscopic ultrasound (EUS) was subsequently performed using Olympus radial and linear echoendoscopes. EUS confirmed that the lesion was confined to the mucosa. No large blood vessels or vascular spaces were noted within the lesion (Figure 2).

The polypoid mucosal lesion was then elevated with a submucosal injection of 12 mL of 1:100,000 epinephrine solution using a sclerotherapy needle. The lesion was then resected using a polypectomy snare and retrieved for pathology. No bleeding was noted following endoscopic resection of the lesion.

On pathologic analysis, the excised lesion was noted to be a discrete, exophytic, polypoid mass of granulation tissue with a lobular proliferation of capillary-sized vessels with intermixed acute and chronic inflammatory cells (Figure 3). Residual gastric glands formed collarettes along the sides of the vascular tissue proliferation. A Warthin-Starry stain for bacillary organisms tested negative. The histopathologic diagnosis was concluded to be pyogenic granuloma of the stomach.

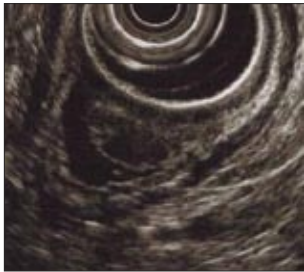
## Discussion

Pyogenic granuloma is a polypoid form of capillary hemangioma, reported most commonly on the skin and in the oral and nasal mucosa. Cutaneous forms of the lesion were initially described by Poncet and Dor in 1897,<sup>1</sup> although the term “pyogenic granuloma” was first applied by Hartzell in 1904.<sup>2</sup> The first clear reports of gastrointestinal pyogenic granulomas were attributed to Payson and associates in 1967.<sup>3</sup> A small number of additional gastrointestinal lesions have since been noted, predominantly in the colon, ileum, and esophagus. Our case report is the

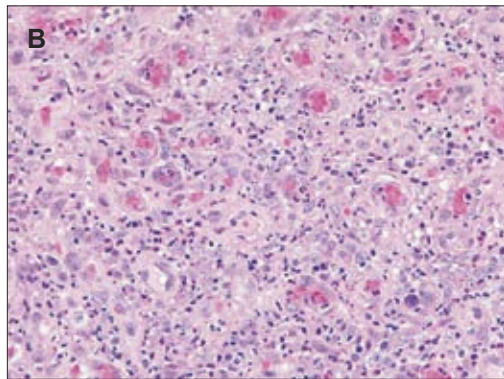
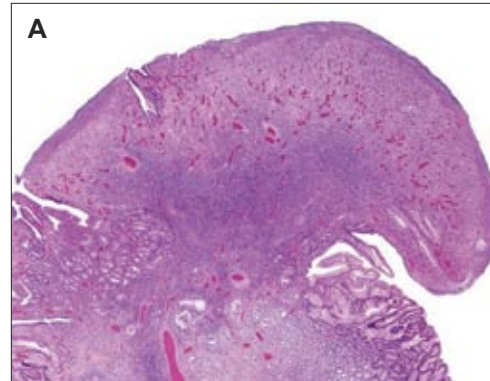
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**Figure 1.** Polypoid antral lesion.



**Figure 2.** Endoscopic ultrasound image of pyogenic granuloma.



**Figure 3.** Histology of pyogenic granuloma. Resection of the polyp at esophagogastroduodenoscopy revealed surface ulceration, acute inflammation, and lobular proliferation of capillary-sized vessels with a collarette of intact mucosa along the base. Figure 3B reveals details of the capillary structures, stromal edema, sparse lymphocytes, and marked neutrophilic infiltrate.

first description of a gastric pyogenic granuloma outside of Asia.

Gastrointestinal pyogenic granulomas in the adult literature have been reported in subjects ranging from 31 to 71 years of age (median age=56 years). Whereas cutaneous lesions occur equally in both sexes, among the small number of reported gastrointestinal cases, there appears to be a male preponderance, with a male-to-female ratio of approximately 2:1. The lesions typically appear as smooth, protruding, polypoid, reddish-colored nodules that may ulcerate. The reddish color is due to the vascular nature of the lesions. Esophageal lesions have been reported as having a superficial white coating of necrotic tissue.<sup>4</sup> On occasion, in patients presenting with significant gastrointestinal bleeding, the surface of these lesions has been noted to be necrotic and black.<sup>5</sup> Gastrointestinal lesions are typically pedunculated or semipedunculated and are less frequently sessile. The reported sizes of gastrointestinal lesions have ranged from 5 to 750 mm in diameter. Larger lesions are more likely to show surface ulceration.<sup>6</sup> Surface ulceration is therefore believed to be a secondary event, rather than the event inciting development of the lesion.<sup>5</sup> Areas of infarction have been described in large lesions.<sup>3</sup> The lesions typically involve the mucosa but may

extend to the submucosa<sup>7</sup> or, on occasion, involve the full thickness of the luminal wall, with protrusion into both luminal and serosal surfaces of the gut wall.<sup>5</sup>

Although gastrointestinal lesions are typically solitary, multiple (>10) gastrointestinal lesions have been reported in a single patient.<sup>8</sup> These lesions were detected in the sigmoid colon of a patient presenting with diarrhea and hemocult-positive stool. In another patient, presumed disseminated disease was reported.<sup>9</sup> This patient was a 73-year-old man with biopsy-confirmed cutaneous lesions of pyogenic granuloma. He subsequently developed symptoms of intermittent melena with associated anemia. <sup>99</sup>Tcm-labeled red blood cell scintigraphy revealed multiple areas of increased uptake in his skull, abdominal wall, intestine, scrotum, and right leg. The authors attributed the increased areas of intestinal uptake to

**Table 1.** Prior Reports of Gastrointestinal Pyogenic Granulomas

Reference	Sex, age	Location	Presentation	Lesion # (size)	Management
<b>English-language literature</b>					
Okada, et al. <sup>10</sup>	M, 56 y	Esophagus	Chest discomfort	1 (NA)	EMR
Craig, et al. <sup>11</sup>	M, 31 y	Esophagus	Dysphagia	1 (2.5 cm)	Snare polypectomy
Cho, et al. <sup>22</sup>	M, 60 y	Esophagus	Esophageal tumor	1 (0.5 cm)	Snare polypectomy
van Eeden, et al. <sup>7</sup>	• F, 55 y • F, 55 y	• Esophagus • Small bowel	• Hematemesis/ dysphagia • Anemia/melena	• 1 (0.9 cm) • 1 (1.1 cm)	• Polypectomy and laser photocoagulation • Surgical resection
Hirakawa, et al. <sup>6</sup>	M, 60 y	Duodenum	Anemia	1 (0.8 cm)	Heater probe: unsuccessful; then snare polypectomy
Meuwissen, et al. <sup>21</sup>	M, 37 y	Ileum (stoma)	Bleeding	NA	Surgical resection
Payson, et al. <sup>3</sup>	M, 45 y	Ileum	Intussusception	1 (7.5 cm)	Surgical resection
Yao, et al. <sup>5</sup>	• M, 56 y • F, 71 y • M, 55 y	• Jejunum • Ileum • Colon	• Anemia/melena • Anemia • Melena	1 (2.0–2.5 cm)	Surgical resection
Hocke, et al. <sup>17</sup>	F, 60 y	Hepatic flexure	Suspected colon cancer	1 (NA)	Hemicolectomy
Chen, et al. <sup>8</sup>	M, 36 y	Sigmoid	Diarrhea, guaiac-positive	Multiple, >10 (0.4–0.8 cm)	Snare polypectomy
Hizawa, et al. <sup>18</sup>	NA	NA	Peutz-Jeghers	1	Snare polypectomy
Gonzalez-Vela, et al. <sup>16</sup>	F, 62y	Sigmoid	Hematochezia	1 (2.0 cm)	Snare polypectomy
Kusakabe, et al. <sup>13</sup>	M, 82y	Stomach	Melena	1 (3.0 cm)	EMR
<b>Non-English-language literature</b>					
Yamane, et al. <sup>25</sup>	M, 64 y	Esophagus	NA	1 (NA)	NA
Imawari, et al. <sup>4</sup>	F, 70 y	Esophagus	Odynophagia	1 (0.4–0.5 cm)	Snare polypectomy
Manabe, et al. <sup>2</sup>	M, 45 y	Esophagus	Dysphagia	1 (1.5 cm)	Snare polypectomy
Okumura, et al. <sup>24</sup>	NA	Esophagus	NA	NA	Band ligation
Kogawa, et al. <sup>23</sup>	M, 50 y	Stomach	RUQ pain	1 (0.8 cm)	EMR
Viala, et al. <sup>14</sup>	M, 66 y	Duodenal bulb	UGI bleeding	1 (NA)	Laser ablation
Motohashi, et al. <sup>15</sup>	F, 58 y	Small intestine	UGI bleeding	1 (3.0 cm)	Surgical resection

EMR=endoscopic mucosal resection; RUQ=right upper quadrant; UGI=upper gastrointestinal.

intestinal pyogenic granulomas, to which they also attributed his symptoms of melena. However, the nature of the areas of increased intestinal uptake were not confirmed endoscopically or histologically. In addition, the patient had a past history of endoscopically confirmed duodenal ulceration, which might have explained his symptoms of intermittent melena.

Clinical presentation of the gastrointestinal lesions depends upon their site (Table 1). Esophageal lesions present with chest discomfort,<sup>10</sup> dysphagia,<sup>7,11,12</sup> odynophagia,<sup>4</sup> hematemesis,<sup>7</sup> or may be incidentally discovered.<sup>4</sup> A patient with a single gastric cardia lesion previously reported in the Japanese literature presented with upper abdominal discomfort, whereas a different patient with

gastric pyogenic granulomas presented with chronic melena.<sup>13</sup> Our gastric pyogenic granuloma patient presented with iron deficiency anemia, presumably due to intermittent bleeding from this vascular lesion. Duodenal lesions have presented with anemia unresponsive to iron therapy<sup>6</sup> or with overt upper gastrointestinal bleeding.<sup>14</sup> Small-bowel lesions have presented with melena, anemia,<sup>5,15</sup> and intussusception.<sup>3</sup> Colonic lesions have presented with melena,<sup>5</sup> hematochezia,<sup>16</sup> and diarrhea.<sup>8</sup> A single large circumferential stenosing colonic lesion mimicking colon cancer also has been reported.<sup>17</sup> A different single report notes a polyp-like intestinal lesion in a patient with Peutz-Jeghers syndrome. In this series of 75 polyps excised from seven patients with Peutz-Jeghers syndrome, a single "polyp" was determined to be a pyogenic granuloma.<sup>18</sup>

Pathologic examination of the lesions usually reveals a proliferation of dilated capillaries with a lobular arrangement. Endothelial cell swelling may also be seen. Stromal tissue is usually edematous, with an infiltration of inflammatory cells. Typically, the infiltrate is predominantly neutrophilic near the ulcerated surface of the lesion, although chronic inflammatory cells may be seen in deeper areas of the lesion. Surface ulceration and granulation tissue are frequently visible. Immunostaining for factor VIII-related antigen and CD34 has been used to identify endothelial cells in these lesions. Immunostaining with antibodies against human herpes virus 8 has been used to distinguish the lesions from gastrointestinal Kaposi sarcoma.<sup>7</sup>

Endoscopically obtained biopsies may not allow a firm diagnosis to be reached, as although they may show some combination of inflammation, granulation tissue, and ulceration, the lobular capillary arrangement may only be evident on pathology sections of the entirely excised specimen. Biopsies may also carry the theoretical risk of initiating bleeding from these vascular lesions. However, biopsy may allow other pathologic entities to be excluded.

The etiology of pyogenic granuloma is unclear. The lesions were initially thought to be infective in origin; however, no association with infection has been proven. It has been proposed that the lesions may be reactive and caused by minor trauma, with a subsequent overgrowth of granulation tissue. The occurrence of cutaneous lesions found predominantly on exposed skin surfaces, including the hands, face, and lips, has lent some support to this theory. However, a large retrospective study of pyogenic granulomas in children found clear evidence of trauma in only 5% of patients.<sup>19</sup> Hormonal influences may play a role, as dermal and oral lesions have been reported in up to 2% of pregnancies.<sup>20</sup> Similarly, a role has been proposed for angiogenic factors, as cutaneous pyogenic granuloma

has been reported to develop within preexisting vascular malformations such as hemangiomas, spider angiomas, and port wine stains.<sup>19</sup>

Several patients have undergone baseline endoscopic evaluation prior to the diagnosis of gastrointestinal pyogenic granuloma at a subsequent endoscopic evaluation. Review of these cases does suggest that gastrointestinal pyogenic granulomas may originate at sites of prior inflammation or ulceration. One patient developed an esophageal pyogenic granuloma at a site of documented esophagitis with stricturing and was treated over several years with proton pump inhibitor therapy and endoscopic dilation.<sup>11</sup> A duodenal pyogenic granuloma was reported in another patient with a duodenal ulcer that had been endoscopically documented 10 months prior.<sup>14</sup> Angiomatous proliferations with some features of pyogenic granuloma were reported at an ileal stoma in a patient who had documented *Campylobacter jejuni* gastroenteritis with ulceration at the stoma two months prior.<sup>21</sup>

Gastrointestinal lesions have been most commonly managed by excision using a polypectomy snare,<sup>4,6-8,11,12,16,18,22</sup> endoscopic mucosal resection,<sup>10,13,23</sup> or surgical resection.<sup>3,5,7,15,17,21</sup> Other modes of management have included heater probe coagulation,<sup>6</sup> laser photocoagulation,<sup>7,14</sup> intralesional injection of ethanol, band ligation,<sup>24</sup> and excision biopsy.

The optimal management of gastrointestinal lesions is by complete excision, preferably with snare resection or endoscopic mucosal resection. Management by other techniques such as heater probe coagulation and excision biopsy have been associated with persistence or recurrence of the lesion.<sup>6,24</sup> In addition, these incomplete therapies may trigger further bleeding. Hirakawa and colleagues initially treated an anemic patient with a duodenal lesion via heater probe.<sup>6</sup> Three months later, the patient was readmitted with worsening anemia. The patient's pyogenic granuloma, which had been nonulcerated at index endoscopy, was found to be actively oozing blood from its surface at repeat endoscopy. Surgical excision of gastrointestinal lesions has also been undertaken,<sup>5</sup> but with the currently available endoscopic resection techniques, this should be unnecessary for all but large, necrotic, or deep lesions. As these lesions may on occasion involve the full thickness of the luminal wall,<sup>5</sup> endoscopic ultrasound is an important tool in determining the depth of extension to determine the suitability of the lesion for endoscopic excision.

In conclusion, we have described for the first time outside of Asia, the clinical presentation of a gastric pyogenic granuloma, its endoscopic and pathologic features, and the utilization of endoscopic ultrasound for the evaluation of endoscopic resectability of these lesions.

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## Review

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Case reports are essential to the clinician's daily practice because they frequently cover unusual cases. After reading the case report by Quiros and colleagues,<sup>1</sup> it will be easier to confirm the diagnosis of granuloma pyogenicum in a patient.

Pyogenic granulomas represent the acquisition of vasodilative granulation tissue in the skin or mucosa. They are extremely rare in the alimentary tract, other than in the oral cavity. The vascular nature of gastrointestinal lesions leads to chronic blood loss, resulting in iron deficiency anemia, a well-known warning sign of gastrointestinal tumors. Due to their unusual appearance, gastrointestinal lesions can be easily misdiagnosed and mistreated, either as gastrointestinal cancer treated with extensive surgery or as hyperplastic polypoid lesions, which would indicate no further treatment. Therefore, an understanding of how to diagnose and treat this condition is important for gastroenterologists to know.

Quiros and colleagues report a rare case of pyogenic granuloma in the stomach of a 67-year-old woman with severe iron deficiency anemia.<sup>1</sup> The main difference between their case and the case of pyogenic granuloma that we reported<sup>2</sup> is the appearance of the lesion. The lesion described by Quiros and colleagues appeared to be polypoid, whereas we found a sessile form. Quite understandably, a polypoid lesion could easily be misdiagnosed as a hyperplastic polypoid, whereas our lesion would more likely be misdiagnosed as colonic cancer, if the biopsy result were inconclusive. Surgical intervention was obvious in our case regardless of the diagnosis reached; in the case reported by Quiros and colleagues, a crucial decision was taken to remove the polypoid lesion despite its harmless appearance. Before removing the polypoid lesion, an endosonographic investigation was conducted, which revealed no signs of infiltration of the stomach wall and which was followed by a complete mucosectomy. Although

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endosonographic investigation of polypoid lesions was fruitful in this case, it is not wholeheartedly recommended in the literature for several reasons: first, because a high-resolution endoscopy or examination for the lifting sign before snare polypectomy is equally accurate,<sup>3</sup> and second, because predicting postpolypectomy bleeding is difficult.<sup>4</sup> Nevertheless, endosonography is frequently used to predict the infiltrative nature of the lesion, as in a case of pyogenic granuloma in the esophagus reported by Hoekstra and coworkers.<sup>5</sup>

In almost all published case reports, a definitive diagnosis was made after resection of the lesion. It is very important to discuss the issue from the pathologic point of view, as Quiros and colleagues did, because of an often-misleading diagnosis based on endoscopic biopsy. The complete removal of the lesion—either by endoscopic snare resection when the lesion is small or by surgery where there is a large or infiltrative lesion—is the treatment of choice. The authors are correct to point out that the main factor in avoiding a recurrence of the lesion is complete resection.

The case report is well described by Quiros and colleagues, and their review of the current literature is nearly complete. However, in addition to the case report from Hoekstra and coworkers<sup>5</sup> discussed above, another interesting case report regarding two children with colonic pyogenic granulomas should be highlighted.<sup>6</sup> The unusual aspect of this case report is the treatment of the pyogenic granuloma in the case of an 18-month-old girl. This patient had undergone orthotopic liver transplantation for biliary atresia at the age of 7 months. Abdominal computed tomography scan revealed bowel wall thickening in the left mid-abdomen with localized fatty proliferation in the mesentery. Colonoscopy showed an area of circumferential black necrosis at the splenic

flexure. Histologic examination revealed a pyogenic granuloma. In this case, a combination of antibiotic and antifungal therapy was administered, and the lesion had almost disappeared after 2 weeks. This is especially unusual because all other published cases of pyogenic granulomas have involved removal by surgery or snare polypectomy. Two other case reports have been published regarding pyogenic granuloma in the non-English-language literature, one in the stomach<sup>7</sup> and one in the rectum.<sup>8</sup>

In summary, the article provides an easy-to-recall example of pyogenic granuloma, with good illustrations and details of the endoscopic and pathologic findings. The treatment options are also described concisely and accurately. Hopefully, after reading the case report, clinicians will be familiarized with this condition and avoid unnecessary diagnostic diversions.

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