Trakia Journal of Sciences, Vol. 8, No 4, pp 27-33, 2010
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Available online at:
http://www.uni-sz.bg

ISSN 1313-7050 (print)
ISSN 1313-3551 (online)

Original Contribution

CLINICAL CASE OF ACUTE BLEEDING FROM ADENOMATOUS GASTRIC POLYP AT THE TIME OF SINGLE INTAKE OF HIGH DOSE ASPIRIN

Iv. Sirakov*, M. Milashka, K. Katzarov

Clinic of Gastroenterology and Hepatology, Military Medical Academy, Sofia, Bulgaria

ABSTRACT

The gastric polyps are well-circumscribed luminal lesions prominent above the plane of the gastric mucosal surface. They are a comparatively common finding and their main significance is the malignant potential of a part of them. One of the complications occurring with gastric polyps is haemorrhage- an emergency requiring prompt diagnosis and treatment. Gastric polyp haemorrhage is relatively rare cause for bleeding in the upper gastrointestinal tract (GIT).

On the other hand, aspirin and the other non-steroidal anti-inflammatory drugs (NSAIDs) have been for a long time known cause of acute bleeding in GIT (particularly in the upper GIT). Complications (bleeding, perforation, obstruction) in the upper GIT occur in 1-1.5% of patients on NSAIDs and the relative risk of acute bleeding in the upper GIT at aspirin uptake is 1.5-2.5%.

We report the case of a female patient with bleeding caused by adenomatous gastric polyp at the time of single intake of high dose aspirin– 2.0 g, 12 hours prior the hospitalisation. The patient has been admitted to hospital in the condition of hemorrhagic shock. During the emergency esophagogastroduodenoscopy has been found massive bleeding from the surface of a large gastric polyp, managed by snare polypectomy (using coagulation electrode). In this case the polypectomy is a therapeutic method, being an alternative to surgery.

Key words: gasrtic polyp, polypectomy, acute bleeding, non-steroidal anti-inflammatory drugs (NSAIDs)

INTRODUCTION

The various subtypes of gastric polyps are generally divided into neoplastic and nonneoplastic.

I. Nonneoplastic Polyps Classification (1)

1. Hyperplastic Polyps

This is the second most common type of benign gastric polyp after fundic gland polyps. (2, 3)

They are pedunculated or sessile and composed of elongated and distorted pits lined by foveolar epithelium, with very few or no glands, and an inflamed, edematous lamina propria. (4)

1. 1. Clinical and Endoscopic Characteristics

They are most commonly found in adults and elderly (mean age, 65.5 – 70 years). A slight predisposition is noted in women, who represent between 58% and 70.5% of patients with hyperplastic polyps. Mean of 24 – 60% of these polyps are located in the antrum, 29 – 56.3% are in the body fundus, and only about 2.5% are in the cardia. (5,6)

Hyperplastic polyps are solitary in about 2/3 of cases. Most commonly they are 1 – 2 cm in size.

1. 2. Etiology and Pathogenesis

These polyps generally result from excessive regeneration following mucosal damage and commonly occur in chronic Helicobacter pylori-associated gastritis (25% of the cases), in pernicious anemia, adjacent to erosions and ulcers, or at gastroenterostomy sites. (6)

The majority develop in gastric mucosa, showing some degree of chronic atrophic gastritis and intestinal metaplasia.

1. 3. Histopathology

They are characterised by marked elongation of the pits with branching with a corkscrew appearance or cystic dilatation of foveolae, and

***Correspondence to:** *Ivan Sirakov, Clinic of Gastroenterology and Hepatology, Military Medical Academy – Sofia ; 3, "Georgi Sofiiski" street, e-mail address: ivansir@abv.bg*

extremely edematous lamina propria infiltrated by plasma cells and lymphocytes, eosinophils, mastocytes and macrophages, and variable numbers of neutrophils. The gastric glands do not normally participate in the formation of the gastric polyps.

1. 4. Clinical Significance and Treatment

Over time, hyperplastic polyps can increase in number and size or regress, either spontaneously or following Helicobacter pylori eradication. (7)

Malignant transformation, although rare, is possible and documented. In a small proportion (1.5%–3% of the cases), usually in polyps greater than 2 cm, dysplasia or intramucosal carcinoma is possible.

2. Inflammatory Fibroid Polyp (Eosinophilic Granuloma,Vanek's Tumor)

It is characterised by the proliferation of spindle cells, small blood vessels, and inflammatory cells, dominated by eosinophils.

2. 1. Clinical and Endoscopic Characteristics

Uncommon polyps of unknown etiology; they may be found throughout the gastrointestinal tract, but are most common in the antrum and pylor (80% of the cases). They are diagnosed in male and female adults of all ages and are associated in some cases with hypochlorhydria or achlorhydria. (8, 9)

They may be found incidentally during endoscopy or evaluation of gastric haemorrhage, anemia, or symptoms of gastric outlet obstruction. Inflammatory fibroid polyps are well-circumscribed, solitary, sessile or pedunculated, can be ulcerated.

2. 2. Histopathology

Inflammatory fibroid polyps are usually located on the submucosa, although sometimes mucosal lesions have been also described. They are composed of small, thin-walled blood vessels surrounded by short spindle cells that may be arranged in an “onion-skin” pattern around larger vessels. A chronic inflammatory cell infiltrate is common, dominated by eosinophils.

2. 3. Clinical Significance and Treatment

Most patients are asymptomatic and these polyps are incidentally diagnosed; furthermore, they usually do not recur after resection. Local excision (polypectomy) is an adequate treatment.

3. Xanthoma/Xanthelasma

These clinically insignificant lesions are more commonly found in patients with increasing age. In males they are more common than in females, and are often associated with chronic gastritis and intestinal metaplasia, and bile reflux gastropathy. They are not related to hypercholesterolemia and may be found in association with hyperplastic polyps. They are single or multiple, 1 to 2 mm in diameter, round or oval, well circumscribed, yellow, macular, or nodular lesions.

Histologically, they consist of mature lipid-laden macrophages occupying the lamina propria and containing cholesterol and neutral lipids.

4. Hamartomatous Polyp of the Peutz-Jeghers Type

The gastric mucosa may be involved in Peutz-Jeghers polyposis, although less frequently than the small intestine or colon. (4, 24)

Gastric hamartomatous polyps are composed of hyperplastic glands lined by foveolar-type epithelium and separated by cores of smooth muscle, with atrophy of the deep glandular components. (12,13)

5. Juvenile Polyp

Gastric juvenile polyps are rarely observed and within the context of juvenile polyposis, either of the stomach alone or of the entire gastrointestinal tract (with or without a family history).

They may present at any age, usually with anemia or hypoproteinemia, and are most commonly located in the antrum. They are composed of edematous and inflamed mucosa with marked elongation and cystic dilatation of the foveolar zones. Juvenile polyposis is associated with an increased risk of carcinoma, particularly in the colon, but the stomach also may be at increased risk.

6. Gastric Polyps in Cowden Disease

In this disease the polyps consist of elongated foveolar glands along with more basal, cystically dilated glands that contain papillary infoldings. Smooth muscle fibers are intermingled within mucosal components, and the cystic structures extend into the submucosa.

7. Gastric Polyps in Cronkhite-Canada Syndrome

These polyps are found usually in conjunction with lesions in other parts of the gastrointestinal tract. They are

indistinguishable from juvenile and hyperplastic polyps and can be diagnosed only in the presence of clinical manifestations of alopecia, nail atrophy, or hyperpigmentation. (14,15)

II. Neoplastic Polyps Classification (1)

1. Fundic Gland Polyps (FGPs)

They are small sessile lesions located uniquely in the fundus and proximal body of the stomach. Their morphology is characterised with cystic transformation of the gland lined by parietal cell and chief cells. (4)

1. 1. Clinical and Endoscopic Characteristics

Fundic gland polyps occur rarely, sporadically, in patients with familial adenomatous polyposis, or as a familial condition of the stomach and not involving the colon.

Endoscopically, they appear as smooth, sessile polyps, less than 1 cm in diameter. They are usually multiple and are found in men and women of any age. Their association with prolonged proton pump inhibitor therapy is debated, in part because of the inhibiting role of Helicobacter pylori, which may inhibit their formation and has not been controlled in various studies

1. 2. Etiology and Pathogenesis

Although traditionally thought to be hamartomatous in origin, the frequent finding of genetic alteration in familial adenomatous polyposis and also in sporadic cases strongly suggests that these lesions are actually neoplastic. Activating somatic mutations (of the β-catenin gene) have been detected in the foveolar and glandular epithelium of most patients with fundic gland polyps, but also in such polyps in patients with long-term proton pump inhibitors administration. These polyps in syndromic patients, instead of β-catenin gene mutations, harbor APC gene mutations and subsequent somatic mutation. (16, 17)

1. 3. Histopathology

Fundic gland polyps are composed of cystically dilated glands lined by fundic epithelium, including chief cells and parietal cells, admixed with normal glands. In patients with long-term proton pump inhibitors administration, there is associated hypertrophy and hyperplasia of parietal cells that protrude into the lumen of the pits, producing a serrated profile.

1. 4. Clinical Significance and Treatment

Cases of spontaneous regression have been found and documented. (17)

The finding of fundic gland polyps in young patients requires excluding underlying familial adenomatous polyposis. At the presence of familial adenomatous polyposis, fundic gland polyps can be seen in up to 40% of the patients. (18)

2. Gastric Adenoma

Gastric adenomas according to the World Health Organization are circumscribed, polypoid lesions composed of either tubular and/or villous structures lined by dysplastic epithelium. (19)

As in any segment of the gastrointestinal tract, gastric epithelial dysplasia is defined as a neoplastic epithelial alteration representing both a precursor lesion of adenocarcinoma and also a marker of high risk.

2. 1. Clinical and Endoscopic Characteristics

The incidence of gastric adenoma ranges from 0.5% to 3.75% in countries in the Western Hemisphere, up to 9% – 20% in nations where high frequency of gastric cancer is found. (20)

They usually arise in the context of atrophic gastritis with intestinal metaplasia. The majority of gastric adenomas are located in the antrum, often just in the gastric angulus or in the fundus. (21)

Most are solitary, exophytic sessile or pedunculated lesions and usually are 3 to 4 cm in size. More rarely, lesions are “flat” or even depressed below the contour of the surrounding mucosa (“concave”), suggesting that adenomas and dysplasia should be considered a single group.

Gastric adenomas have “velvet” fine lobulated surface contrasting with the smooth and atrophic adjacent mucosa. They are usually asymptomatic, unless they ulcerate and bleed.

2. 2. Etiology and Pathogenesis

Most gastric adenomas arise in the context of atrophic gastritis with intestinal metaplasia. Their incidence increases with age and may be combined with familial adenomatous polyposis.(22)

2. 3. Histopathology

Most adenomas are composed of tubules or villi of dysplastic epithelium, which usually show some degree of intestinal-type differentiation toward absorptive cells, goblet

cells, endocrine cells, or even Paneth cells. (19, 18)

A minority of gastric adenomas show morphologic and histochemical characteristics of mucin as gastric foveolar or pyloric gland–type epithelium. Others have combined gastric and intestinal-type features.

Pyloric adenomas are characterised by short columnar epithelium with basal nuclei and pale eosinophilic cytoplasm. They are more common in older patients and are more common in women compared to men. About 26% of pyloric gland adenomas showed evidence of malignant transformation. (25)

Other rare variants, the so called Paneth cell adenomas are predominantly composed of Paneth cells. The malignancy in gastric adenomas depends on the size, degree of dysplasia, and villosity.

Larger adenomas are most frequently villous with high-grade dysplasia, and have high proportion carcinomatous transformation – 40% to 50% of lesions larger than 2 cm. Caution is necessary, since an adenocarcinoma can develop in small lesions also. The diagnosis of adenocarcinoma includes the presence of invasion of the neoplastic epithelium into the lamina propria.

2. 4. Clinical Significance and Treatment

Since it has been found that gastric adenomas are premalignant lesions with high malignant potential their total resection is absolutely obligatory. It is achieved by endoscopic polypectomy or endoscopic mucosal resection. Since, it has been found that gastric adenomas may be accompanied by coexistent carcinoma elsewhere in the stomach, when adenoma is found the thorough endoscopic evaluation of the complete stomach should be extremely precise. (26)

3. Gastric Carcinoid

Gastric carcinoid tumors are defined as well-differentiated endocrine neoplasms composed of nonfunctioning enterochromaffin-like cells arising in the mucosa of the corpus or fundus. (27)

3. 1. Clinical and Endoscopic Characteristics

There are 3 types of gastric carcinoids:

- type 1- they are associated with atrophic gastritis and almost half of the patients have pernicious anemia.
- type 2- they are associated with Zollinger-Ellison syndrome and multiple endocrine neoplasia (MEN -1) syndrome. Almost 10-20% of the patients with carcinoid tumors have synchronous adenocarcinomas of the gastrointestinal tract most frequently of the colon.
- type 3– sporadic gastric carcinoids, which are rare and could not be associated with any of the known diseases. (28)

In the first two types, the polyps commonly are multiple yellowish, broad-based, usually less than 2 cm in size and overlined by an unchanged mucosa. In the sporadic carcinoids, the tumors are larger, solitary and can present with features similar to those of a carcinoma (i.e., gastrointestinal haemorrhage, obstruction, or metastases). (29, 30)

3. 2. Etiology and Pathogenesis

In the two types of gastric carcinoids are associated with precursor lesions composed of various degrees of enterochromaffin-like cell proliferation, classified in four groups as hyperplasia, adenomatoid hyperplasia, dysplasia, and neoplasia. Eventually, intramucosal lesions greater than 0.5 mm in diameter will constitute an intramucosal carcinoid tumor, whereas extension beyond the muscularis mucosa will qualify for invasive carcinoid tumor.

3. 3. Histopathology

Gastric carcinoids exhibit ribbons or trabecular patterns with occasional rosetting. The nuclei are usually centrally located and demonstrate a finely granulated chromatin.

3. 4. Clinical Significance and Treatment

Large carcinoid tumors can metastasise to lymph nodes and the liver as well as to more distant organs. However, their growth is usually slow, and the survival is most commonly compatible with distant metastases. Size and invasiveness correlate with the probability of metastases. Carcinoids less than 2 cm in size, and multiples, have a very low risk of metastases, whereas tumors less than 1 cm in diameter may remain stable and with no growth for many years. It is recommended that tumors larger than 2 cm in diameter be resected due to the risk for lymphatic invasion and metastases. The prognosis is variable depending on multiple factors (i.e., size, invasiveness, and histological finding).

Therapeutic strategy depends on the clinical manifestations. Large, solitary carcinoids should be resected like other epithelial gastric

tumors. The management of multiple, small, superficial carcinoids is much more problematic. Successful endoscopic removal of small carcinoids has been reported by some colleagues, whereas others prefer an antrectomy as it causes regression of the carcinoids as well as hyperplastic lesions.
In conclusion, the existence of different types of gastric polyps, all with different risks of malignant transformation, makes their histological analysis mandatory. Based on the histological results, the diagnostic criteria and the clinical manifestations, the most appropriate therapeutic strategy is determined.

Case report

We report a case of a 51 years old female patient T.K.V, admitted to the Emergency Department of Military Medical Academy, Sofia, in impaired general condition diagnosed by the reanimation team as haemorrhagic shock. On the occasion of malaise and subfebrility for 2 – 3 days, 12 hours prior the hospitalisation she took single dose of 2.0 g Upsarin (aspirin).

Physical examination:

- hypotension 80/50 mm Hg; tachycardia -120 bt/min with filiform pulse;
- adequate reactions, sociable, severely weak, pale moist skin;
- clear arterial blood from the nasogastric tube inserted;
- melaenic faeces at digital palpation of the rectum.

Laboratory tests:

- severe anaemic syndrome – Hb-54 g/l; Htc-0,16; Leuc-12,2; Thr-199; ESR - 32 mm;
- the rest laboratory tests - within normal limits;
- Serological Helicobacter pylori test - negative.

Instrumental investigations:

- UST– abdomen– evidence of haemangioma 15 mm in diameter in the right liver lobe; other organs– normal;
- Videogastroscopy – the stomach was filled with arterial blood and "fresh" coagulums to 2/3 of its volume; in the corpus along the line of the big curve a polyp 30 mm in diameter with rough surface dripping artherial blood was observed; long pedunculus of the polyp. Snare polypectomy with coagulation electrode was performed and the polyp was sent for histological evaluation, and its base was infiltrated by 10 ml adrenalin solution 1:10 000; bleeding was stopped.

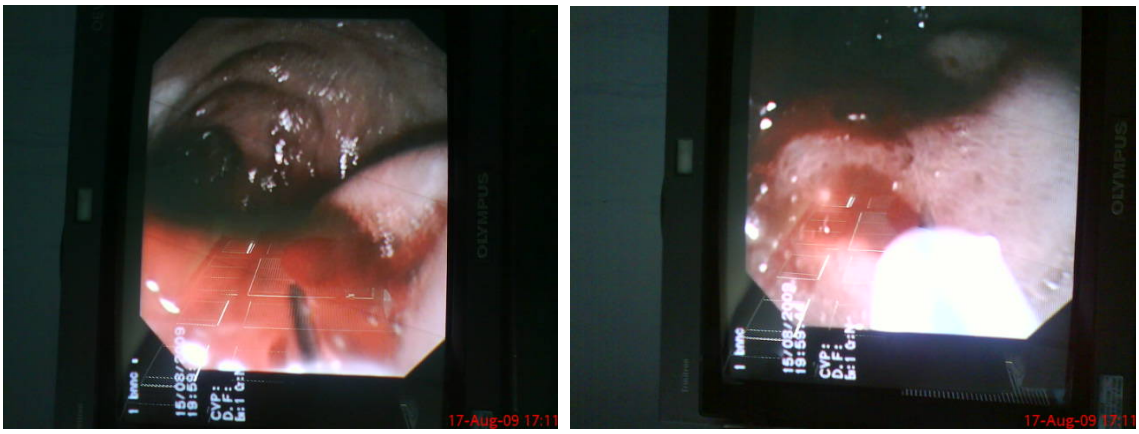

Fig. 1. Infiltration with adrenalin solution of the mucous defect after polypectomy.

After the procedure performed the patient was accommodated in Reanimation and Intensive Care Clinic of MMA and subjected to 72 h intensive treatment with Nexium 3 x 80 mg/24h; Terlipressin 4 x 1 mg/24h; Somatostatin 6 mg/24h via perfusor; saline solutions infusions - 2,0 l/24h; 3 transfusions of erythrocyte concentrate.
On day 4, with control Hb 105 g/l, Htc 0,29; Leuc 8,4; Thr 236, the patient was transferred to Gastroenterology Clinic where the treatment was continued with oral proton pump inhibitor (Nexium) and infusions of ferro preparation (Venofer 1 fl i.v./24h) for 6 days.

Control videogastroscopy (on hour 72) – in the corpus along the line of the big curve mucosal lesion 15 mm in diameter was observed covered by thick fibrin coating (the site of the polypectomy performed during the previous

gastroscopy); without evidence of bleeding. One biopsy for Helicobacter pylori was taken from antrum, and 3 biopsies from the polypectomy site.

On day 10, in good condition, with compensated posthaemorhagic ferrodeficiency anaemia the patient was discharged and continued her treatment ambulatory.

Histological result – evidence of adenomatous gastric polyp with moderate dysplasia without pedunculus infiltration. Moderate gastritis, Helicobacter pylori negative.
Control videogastroscopy on day 30 – normal endoscopic image of oesophagus, stomach and duodenum.

DISCUSSION

The reported case describes diagnostic-therapeutic algorithm in acute bleeding from large adenomatous gastric polyp at the background of use of NSAIDs (aspirin), a proven risk factor for GIT bleeding. Timely polypectomy is an alternative to surgery in the described condition, while the multidisciplinary team work of gastroenterologist, surgeon and anesthesiologist is the only decision for the emergency management and cure of the patient.

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