

Clinicomorphological Profile of Gastric Polyps in Anatomical Pathology Department, Faculty of Medicine, Universitas Indonesia-Cipto Mangunkusumo Hospital: A Retrospective Study in Correlation of Long-Term Use of Proton-Pump Inhibitors

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ABSTRACT

Background: Gastric polyps are mucosal elevation into the lumen, found incidentally during endoscopic examination and generally brings no specific symptoms. Long-term use of proton-pump inhibitors (PPIs) is related to the development of the fundic gland polyp (FGP). This retrospective study was conducted to determine the distribution of gastric polyps in CiptoMangunkusumo Hospital along with histomorphological features and their relation with long-term PPI use.

Method: This retrospective review is a descriptive analytic study. Gastric polyp cases were taken consecutively from the archive of the Anatomical Pathology Department, Faculty of Medicine Universitas Indonesia/ CiptoMangunkusumo Hospital the period of 2016-2017. Clinical data obtained from patient's medical records. Statistical analysis was carried out with the IBM ® SPSS version 23 program.

Results: Among 83 cases of gastric polyps, there were 66 cases of FGP, 11 cases of inflammatory polyps, 5 cases of hyperplastic polyps, and 1 case of Peutz-Jegher polyp. Long term PPI was used in 40 cases and was related with parietal cell hyperplasia.

Conclusion: FGP is the most common type of gastric polyp in the Department of Anatomical Pathology Cipto Mangunkusumo Hospital. Long term PPI use was found in half of gastric polyps and was related to parietal cell hyperplasia morphology.

Keywords: gastric polyps, fundic gland polyp (FGP), proton-pump inhibitor (PPI)

ABSTRAK

Latar belakang: Polip gaster adalah lesi elevasi mukosa ke arah lumen, ditemukan secara insidental saat pemeriksaan endoskopi dan umumnya tanpa gejala klinik. Penggunaan PPI jangka lama dikatakan berkaitan dengan perkembangan fundic gland polyp (FGP). Telaah retrospektif ini dilakukan untuk mengetahui sebaran jenis polip gaster yang ada di RSCM disertai gambaran histomorfologi dan kaitannya dengan penggunaan PPI

jangka panjang.

Metode: Telaah retrospektif ini merupakan penelitian deskriptif analitik. Kasus polip gaster diambil secara consecutive sampling dari arsip Departemen Patologi Anatomi Fakultas Kedokteran Universitas Indonesia/ Rumah Sakit Cipto Mangunkusumo pada kurun waktu tahun 2016-2017. Data klinis didapatkan dari rekam medis. Analisis statistik dilakukan dengan program IBM® SPSS versi 23.

Hasil: Telaah demografik pada 83 kasus polip gaster menunjukkan 66 kasus FGP, 11 kasus polip inflamasi, 5 kasus polip hiperplastik, 1 polip Peutz-Jegher. Terdapat kaitan antara 40 kasus dengan riwayat penggunaan PPI jangka lama dan hiperplasia sel parietal.

Simpulan: Fundic gland polyp (FGP) merupakan polip yang terbanyak ditemukan di Departemen Patologi Anatomi, Fakultas Kedokteran Universitas Indonesia (FKUI)/RS Cipto Mangunkusumo. Penggunaan PPI jangka panjang pada kasus berkaitan dengan gambaran hiperplasia sel parietal.

Kata kunci: polip gaster, fundic gland polyp (FGP), proton-pump inhibitor

INTRODUCTION

Dyspepsia and gastroesophageal reflux disease (GERD) are clinical complaints that are often encountered in daily clinical practice. Dyspepsia consists of various symptoms in the upper abdomen that can be caused by various diseases (referred to as organic dyspepsia), or without the underlying organic disease (referred to as functional dyspepsia). Esophagogastroduodenoscopy (EGD)/endoscopy of the upper gastrointestinal tract plays a role in determining type of dyspepsia.^{1,2}

Gastric polyps were found in about 3-5% of total dyspepsia cases endoscopically. Polyp itself is loosely defined as a prominent luminal lesion in the form of elevated gastric mucosa. It can be divided as hyperplastic polyps originating from epithelial cell, polyps with inflammation, hamartoma, or neoplastic polyps. Prevalence and type of gastric polyps were reported to be different in several regions.^{3,4} Information regarding anatomic location, endoscopic features, number of lesions and presence of pathological conditions around the gastric mucosa were thought to be important in diagnosing gastric polyps.^{5,6} Large polyps can manifest in severe symptoms like abdominal pain, gastrointestinal bleeding, anemia and obstruction.^{7,8} Histopathological examination will show type of polyps and assess risk factors to develop malignancy such as presence of dysplasia.⁸

At present, there is substance known to have impact that can cause pathological change in gastric mucosa, namely proton-pump inhibitors (PPI). The use of long-term PPI (more than 12 months) is said to be related to the development of FGP.^{3,4,8-10} To best of our knowledge, this is the first published Indonesian data describing both histopathological and clinical profile of gastric polyp cases on its relation with PPI use.

METHOD

This retrospective study was a descriptive analytical study that conducted in the Department of Anatomical Pathology Faculty of Medicine, Universitas Indonesia/ Cipto Mangunkusumo Hospital with a cross sectional study design. Samples were taken consecutively, includes all cases diagnosed as gastric polyps in the Department of Anatomical Pathology in from January 2016 to December 2017. Exclusion criteria were of cases with slides/clinical data that could not be retrieved from archive/medical records.

We used secondary data from tissue slides and histopathology examination records of all gastric polyp cases from January 2016 to December 2017 archived at Department of Anatomical Pathology Faculty of Medicine, Universitas Indonesia/Cipto Mangunkusumo Hospital. Cases were retrieved using ICD.0 morphological codes of H 211.1, H 759.6, H 211.4, M8210/0, M8140/0. Clinical history including endoscopy reports were taken from medical records. Only cases with complete slides and clinical data were submitted as samples for this study. There were 48 cases of gastric polyps in the year of 2016 and 78 cases in 2017. Forty three of them had incomplete medical history, leaving 83 cases were eligible for this study.

The original copy of histopathology reports and hematoxylin-eosin (HE) stained slides were collected and reviewed by two assessors (FS and NR). Clinical and histomorphological criteria were assessed based on criteria as in Table 1. Statistical analysis was carried out by IBM® SPSS version 23 for bi-and multivariate tests. In bivariate analysis the authors classify the types of pathological diagnosis into two groups, FGP and non FGP. Bivariate analysis between numerical variables using unpaired T-test. Bivariate analysis between nominal variables uses a Chi-square test with an alternative Fisher test if the preconditions of the

Chi-square test are not fulfilled. Furthermore, bivariate analysis is performed to see the relationship between histopathological variables and the pattern of PPI use. All bivariate analysis uses the Chi-square test. P values of < 0,05 were considered significant with confidential interval 95%.

RESULTS

Among the 83 polyp cases studied, majority (79.5%) were fundic gland polyp, some portion (13.3%) were inflammatory polyps, and the rest were hyperplastic polyps (6%) and Peutz-Jegher polyps (1.2%) (Table 2). Authors made grouping of diagnosis for analytical purposes into fundic gland polyp (FGP) and non-FGP (which include inflammatory polyps, hyperplastic polyps and Peutz-Jegher polyps). Table 2 shows relatively similar characteristic between FGP in general and non-FGP group. In comparison of histomorphological criteria with polyp types, there were significant differences in gland proliferation, parietal hyperplasia, and diameter lumen of gland between FGP and non-FGP groups. Histomorphological appearances of FGP were shown in Figure 1.

Table 3 shows histomorphological appearance in relation with the use of PPI. Almost all criteria shows comparable result between the long-term and short-term use of PPI-groups, except for the parietal cell hyperplasia that give significant different ($p = 0.023$).

DISCUSSION

Gastric polyps known to be found incidentally during EGD. Type of polyps vary depending on the study population. In this study FGP was the highest type of all 83 cases. This is in line with the research of Islam et al which reported that FGP was the highest number of cases by 47%.¹² A study by Olmez et al in Germany also shows that almost half of gastric polyp among 5,000 cases were FGP, followed by hyperplastic type. Mean while in Greece, one third of cases were shown to be hyperplastic polyps.^{7,8}

Fundic gland polyps are characterized by oxyntic gland proliferation/hyperplasia nearing the surface, causing foveolar to shorten and even disappear. The gland is cystic and irregular, lined with parietal, chief cells and mucous neck cells.^{3,6,11-13} FGPs fall into two categories based on the clinical circumstances: sporadic cases and syndromic cases that develop in the context of familial adenomatous polyposis (FAP).^{14,15} In the study of Lee PL et al, the mean age of FGP cases was 57.07 years.¹⁶ Male and female ratio 1:3. Similar to this study, the mean age was 58.1 years with a male and female ratio of 1:2.88. Number of polyps found in single or multiple, multiple polyps, especially in FGP related to FAP.^{3,6,13-14}

Hyperplastic polyps are characterized by dilated, elongated, branched foveolar epithelium, foveolar is dilated to varying sizes and even forms cysts. Generally occurring at the age of 65-75 years, the

Table 1. Clinical and histomorphological criteria assessed in every cases

Variable	Definition
Clinical criteria	
Long-term use of proton pump inhibitor (PPI)	On medical record, there were data that patients received PPI prescriptions for more than 12 months period before the esophagogastroduodenoscopy (EGD)
Short-term use of PPI	On medical records, there were data that patients received PPI prescriptions for less than 12 months period before the EGD
No information on the use of PPI	On medical records, there were no data that patients received PPI prescriptions before EGD
Anemia	Laboratory and physical examination showed data that support anemia. (Hb for male < 13gr/dL and Hb for female < 12 gr/dL)
Histomorphological criteria	
Dysplasia in the surface epithelium	Nuclear enlargement, hyperchromasia, pseudostratification on surface epithelial ¹¹
Intestinal metaplasia in the surface epithelium	Normal gastric surface epithelium is replaced by intestinal type epithelium with goblet cells ¹¹
Foveolar hyperplasia	Increasing the amount of foveola to reach the bottom of the mucosa ¹¹
Mild chronic inflammation	Mild increase in density of mononuclear cells
Moderate chronic inflammation	Moderate increase in density of mononuclear cells
Severe chronic inflammation	Severe increase in density of mononuclear cells
Gland proliferation	The number of glands increases to reach the foveolar region/near the surface epithelium ¹¹
Hyperplasia of parietal cells	The presence of swelling parietal cells, protruding towards the lumen of the gland ¹¹
Dysplasia of the gland	Nuclear enlargement, hyperchromasia, pseudostratification on surface epithelial.
Cystic lumen of the gland with a luminous diameter	Lumen of the gland dilates with a width > 3x of gland diameter (low power field)
Cystic lumen of the gland with lumen diameter slightly dilated	The gland lumen is dilated with a width of 2x diameter of surrounding normal gland (low power field)
There is no cystic lumen in the gland	There are no glands that dilate (low power field)
The presence of H.pylori	<i>H. pylori</i> presence in Giemsa staining (high power field)
Branching bundles of smooth muscles	Branching bundles of smooth muscles emerging from the muscularis mucosae ¹¹

Table 2. Correlation between clinical and histomorphological criteria of polyps

Variable	Type of polyps		p
	Fundic gland polyp (FGP), n = 66 n (%)	Non-fundic gland polyp (non-FGP), n = 17 n (%)	
Clinical criteria			
Age in year (mean)	58.1	55.6	0.548
Gender ^a			
Male	17 (73.9)	6 (26.1)	0.433
Female	49 (81.7)	11 (18.3)	
Indication of EGD ^b			
Dyspepsia	37 (78.7)	10 (21.3)	0.838
GERD	19 (86.4)	3 (13.6)	0.353
Hematemesis and melena	11 (68.8)	5 (31.2)	0.235
Anemia	16 (69.6)	7 (30.4)	0.164
Abdominal pain	3 (100)	0 (00.0)	N/A
Others	9 (81.8)	2 (18.2)	0.839
Location			
Cardia ^c	0 (80.3)	2 (100)	0.040
Fundus ^b	30 (81.1)	7 (18.9)	0.752
Corpus ^b	40 (83.3)	8 (16.7)	0.313
Antrum ^c	0 (80.3)	1 (100)	0.205
Polyp number ^b			
1-2 polyp	36 (81.8)	8 (18.2)	0.177
Multiple	27 (81.8)	6 (18.2)	
Others	3 (50.0)	3 (50.0)	
Use of PPI ^b			
Long term	35 (87.5)	5 (12.5)	0.220
Short term	8 (72.7)	3 (27.3)	
No information	23 (71.9)	9 (28.1)	
Histomorphology criteria			
Histopathology diagnosis			
FGP inflammation polyp	66 (79.5)	11 (13.3)	
Hyperplastic polyp		5 (6.0)	
Peutz-Jegher polyp		1 (.2)	
Dysplasia in the surface	N/A		
Intestinal metaplasia in the surface ^c	1 (33.3)	2 (66.7)	0.105
Gland proliferation ^b	66 (100)	0 (00.0)	< 0.001*
Hyperplasia of parietal cells ^b	33 (100)	0 (00.0)	< 0.001*
Dysplasia of the gland	N/A		
Cystic lumen ^b	32 (100)		
Cystic lumen in the gland with a luminous diameter		0 (00.0)	<0.001*
Cystic lumen in the gland with lumen diameter slightly dilated	13 (100)	0 (00.0)	
Chronic inflammation ^b			
Mild	46 (85.2)		
Moderate	16 (69.6)	8 (14.8)	0.215
Severe	4 (66.7)	7 (30.4)	
Foveolar hyperplasia ^c	0 (00.0)	2 (33.3)	
Branching bundles of smooth muscles ^c	0 (00.0)	5 (100)	< 0.001*
<i>Helicobacter pylori</i>	N/A	1 (100)	0.205

^aUnpaired T-test; ^bChi-square test; ^cFisher test

EGD: esophagogastroduodenoscopy; GERD: gastroesophageal reflux disease; PPI: proton pump inhibitor

Table 3. Relationship between histomorphological criteria and the use of proton pump inhibitor (PPI)

Histomorphology criteria	Use of proton pump inhibitor (PPI)		n (%)	p
	Yes, Long term (%)	Yes, Short term (%)		
Dysplasia in the surface	N/A			
Intestinal metaplasia in the surface	0 (00,0)	1 (33,3)	2 (66,7)	0,214
Gland proliferation ^b	35 (53,0)	8 (12,1)	23 (34,8)	0,220
Hyperplasia of parietal cells	22 (66,7)	3 (09,1)	8 (24,2)	0,023*
Dysplasia of the gland	N/A			
Cystic lumen	26 (57,8)	06 (13,3)	13 (28,9)	0,119
Chronic inflammation				
Mild-moderate	39 (50,6)	10 (13,0)	28 (36,4)	0,257
Severe	1 (16,7)	1 (16,7)	4 (66,7)	
Foveolar hyperplasia	2 (40,0)	1 (20,0)	2 (40,0)	0,878
Branching bundles of smooth muscles	0 (00,0)	0 (00,0)	1 (100)	0,446
<i>Helicobacter pylori</i>	N/A			

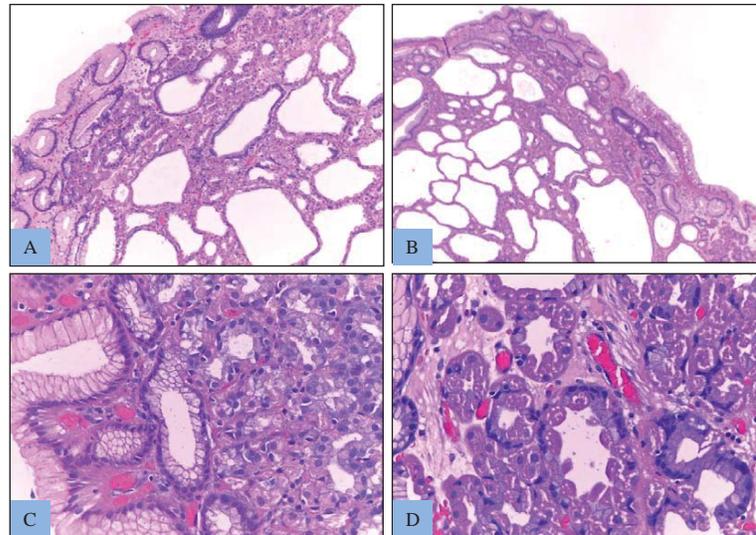


Figure 1. A and B. FGP is characterized by cystic proliferation and dilatation of the oxyntic gland (low power field). C. The gland is lined by parietal cells and chief cells (100x). D. Parietal cell hyperplasia is characterized by parietal cells that swell and protrude towards lumen (snouts) (high power field). (A-D in HE)

location of most lesions is antrum.^{13,17} Inflammatory polyps are characterized by lamina propria edema and accompanied by inflammatory cells.⁴ Polyp peutz-Jegher associated with autosomal dominant abnormalities. The lesion is characterised by thin dissecting bands of smooth muscle covered by disorganized foveolae with no cystic changes.¹³

The most common indication of EGD was dyspepsia at 47 (56.6%). In line with the research of Olmez S et al, dyspepsia were the highest complaint of 31.3%.⁸ Several other studies indicate that the most EGD is GERD.^{4,10} A few years ago, the location of gastric polyps in antrum was twice as much as in the corpus. This tendency later were switch to corpus in the last 10 years, as in this present study.¹⁷

Several studies showed that the increased use of PPI has an impact on the pathogenesis of FGP.^{3,6,13-20} Long term use of PPI can cause substantial changes in gastric structure and function, including increasing the risk of FGP, increased parietal cells, hypergastrinemia, and enterochromaffin-like cells hyperplasia. FGP is found 2-4 times more in patients who use long-term PPI. A systematic review with a meta-analysis concluded that the use of PPI at least 12 months affected the pathogenesis of FGP.¹⁸ This current study failed to showed the same profile due to high number of cases with incomplete data of PPI use. There were 32 cases with no available information about the use of PPI that might affect the statistical result. However the appearance of hyperplastic parietal cells as it is found in FGP was successfully correlated with the long term use of PPI.

This present research showed that FGP should be the first on diagnosis list in terms of polyps found in stomach during EGD, and administration of PPI to patient could lead to the development of FGP. Thus should be considered on routine practice of clinician.

CONCLUSION

Gastric polyps are one of the cases found on EGD, predominantly diagnosed as FGP, and one of its characteristics (parietal cell hyperplasia) was associated with the long term of use of PPI. Information from clinician regarding history of previous medications which were administered to the patient is important to be documented and shared to pathologist upon admission of EGD samples.

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