Extra-ampullary duodenal adenoma: a clinicopathological study

Running title: Extra-ampullary duodenal adenoma

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Conflict of interest

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ABSTRACT

Aim: Extra-ampullary duodenal adenoma (EADA) is a rare condition with poorly described clinicopathological details. In this study, we aimed to clinicopathologically characterize EADA.

Methods and results: We performed a retrospective review of 44 serial cases of EADA. Each EADA was categorized as either gastric-type (n=5) or intestinal-type (n=39). All gastric-type adenomas were located in the first portion of the duodenum and exhibited a pedunculated shape. Gastric-type adenomas were classified into two subtypes: a pyloric gland type and a foveolar type. The former consisted of MUC6-positive glands covered with MUC5AC-positive cells, whereas nearly all of the latter consisted of MUC5AC-positive cells. When EADAs were categorized into high and low grades, approximately 40% (16/44) were high grade. The high-grade adenomas were significantly larger than the low-grade adenomas (19.4±8.6 mm vs. 11.8±5.1 mm, p=0.021), and all adenomas over 20 mm in largest diameter were categorized as high-grade adenomas. Among 16 individuals who underwent total colonoscopy before or after duodenal mucosal resection, nine **had a** colorectal neoplasm, and all 9 duodenal lesions were of the intestinal phenotype.

Conclusions: We clarified the clinicopathological characteristics of gastric- and intestinal-type EADAs. EADAs over 20 mm at the largest diameter were consistently high grade and are thought to have the potential to progress to adenocarcinoma. These findings should be helpful for the clinical management of EADA.

Keywords: duodenum, adenoma, extra-ampullary, clinical-pathology, mucin phenotype

INTRODUCTION

Adenocarcinomas that arise from the duodenum account for only 0.3%-0.5% of all alimentary tract malignancies.[1,2] The incidence of extra-ampullary tumors is considered to be extremely low, and few studies have examined this tumor type. Although several recent studies have examined the pathological characteristics of extra-ampullary duodenal adenocarcinomas,[3] extra-ampullary duodenal adenoma (EADA), which is regarded as a precursor lesion of invasive adenocarcinoma, has not been examined in detail either histopathologically or clinicopathologically. Pyloric gland adenoma (PGA), a subtype of gastric-phenotype tumors, arises from the duodenum, is mainly located in the duodenal bulb and may have malignant potential.[4,5] The relative proportion of PGA to other types of adenoma remains unclear. Intestinal-type adenomas of the duodenum have not been well analyzed histopathologically, and almost all previous reports of EADA were written from a clinical perspective. To the best of our knowledge, there is no English-language literature describing a clinicopathological study of EADA analyzing case series. In the present study, we analyzed serial cases of extra-ampullary adenomas that were endoscopically resected at a single institute in Japan to clarify the clinicopathological characteristics of EADA and to extract useful findings to guide clinical management.

MATERIALS AND METHODS

Patients

All endoscopically resected cases of adenoma/dysplasia/non-invasive epithelial neoplasm from the extra-ampullary duodenum were extracted from the continuous pathology archive of Toho University Omori Medical Center, Tokyo, Japan, between January 2002 and December 2015. We excluded cases with polyposis syndrome, such as familial adenomatous polyposis.

We retrospectively extracted clinical information, such as tumor location, macroscopic appearance and comorbidity of colorectal epithelial neoplasms, from medical records.

Tumor location

Tumor location was classified into 5 parts as follows[6]: a) first portion: the duodenal bulb; b) proximal second portion: the **proximal** side of the major duodenal papilla of the descending part; c) distal second portion: the **distal** side of the major duodenal papilla of the descending part; d) third portion: horizontal part; and e) fourth portion: ascending part.

Macroscopic appearance and size of tumors

All tumors were classified by reviewing endoscopic images. Lesion shape was classified according to the Paris endoscopic classification (Ip/Isp/IIa/IIc). Tumors were classified into two groups by color: erythematous or whitish. Tumor size was determined by measuring the largest diameter of each fixed specimen. In some cases, when the fixed materials were fragmented, the size was estimated by reviewing the endoscopic images.

Histomorphological examinations

All specimens were fixed with 10% buffered formalin and embedded in paraffin using a standard procedure. For each lesion, 3-μm-thick sections of a representative section with maximum diameter of the lesion were prepared and used for hematoxylin and eosin (HE) and immunohistochemical staining.

All tumors were histologically classified as intraepithelial neoplasms and were identified as premalignant lesions according to the criteria of the World Health Organization classification of tumors of the gastric adenoma.[7]

The tumors were classified into two groups, “intestinal-type adenoma” and “gastric-type adenoma,” using HE-stained slides and according to the classification of the WHO 2010 criteria for gastric adenoma. Intestinal-type adenomas resemble colonic adenomas with crowded tubular glands lined by atypical columnar cells with overlapping, pencillate, hyperchromatic and/or pleomorphic nuclei, with

pseudostratification and inconspicuous nucleoli, mucin depletion and lack of surface maturation. Gastric-type (foveolar or pyloric phenotype) adenomas resemble gastric foveolar epithelium or pyloric gland epithelium, in which the cells are cuboidal or columnar with clear or eosinophilic cytoplasm and round to oval nuclei. Tumors were also classified as low- or high-grade according to the WHO 2010 criteria.

Immunohistochemistry

Immunohistochemical staining of 3-μm sections was performed using a BenchMark XT auto-stainer (Ventana Medical Systems, Tucson, AZ, USA) according to the manufacturer's instructions. The primary antibodies and their working dilutions are shown in Table 1. Staining for CD10, MUC2, MUC5AC and MUC6 was semiquantitatively graded. The percentage of positive cells was divided into four grades: −, +, ++ and +++ (0%, 1%-9%, 10%-29%, and ~30%, respectively). Diffuse and strong nuclear expression was regarded as positive staining for p53. Histological and immunohistochemical evaluations were determined based on the consensus of at least two reviewing study pathologists at multi-headed microscopes without knowledge of clinical information.

Statistical analysis

Statistical analyses were performed using the Mann–Whitney *U* test and Fisher's exact

test. All tests were two-sided, and statistical significance was set at $p<0.05$.

Ethics

The use of human materials in this study was approved by the Ethics Committee of the Toho University Omori Medical Center, Tokyo, Japan (approval number: 27-179, M16134).

RESULTS

We identified 44 cases with EADA endoscopic resection materials from the pathology archive. The anatomic distribution of the tumors was as follows: first portion, 12 cases (27.3%); proximal second portion, 15 cases (34.1%); and distal second portion, 17 cases (38.6%). No cases were found in the third or fourth portion in our archive because endoscopic observation and endoscopic therapy for those portions are not generally performed. The macroscopic appearance of the lesions was as follows: Ip, 3 cases (6.8%); Isp, 9 cases (20.5%); IIa, 31 cases; and IIc, 1 case (2.3%). In 13 cases (29.5%), the tumors exhibited an erythematous color, and in 31 cases (70.5%), they exhibited a whitish color. Tumor size ranged from 3 to 35 mm with a mean of 14.6±7.5 mm and a median of 12.5 mm. There were 28 cases (63.6%) of low-grade adenoma (LGA) and 16 cases (36.4%) of high-grade adenoma (HGA).

Histological tumor phenotypes

There were 5 cases (11.4%) of gastric-type adenoma and 39 cases (88.6%) of intestinal-type adenoma when we categorized the lesions into two groups according to the WHO 2010 criteria on the basis of the predominant HE-staining morphotypes. When gastric-type adenomas were subclassified into two subtypes, we found 3 foveolar-type and 2 pyloric gland-type adenomas. All gastric-type adenomas were located in the first portion, whereas the intestinal-type adenomas were found in the first portion in 7 cases (17.9%), in the proximal second portion in 15 cases (38.5%) and in the distal second portion in 17 cases (43.6%). Gastric-type adenomas had a greater tendency to arise in the first portion than intestinal-type adenomas (p=0.0007). In addition, all gastric-type adenomas exhibited a pedunculated shape (Ip; 1/ Isp; 4), whereas 32 of 39 (82.1%) cases of intestinal-type adenomas were non-pedunculated (Ip; 2/Isp; 5/IIa; 31/IIc; 1) (p=0.0007). However, there was no significant trend in color between the gastric and intestinal phenotypes. In the gastric adenomas, all 3 lesions of the foveolar subtype exhibited an erythematous color, whereas both pyloric gland-type lesions were whitish. The clinicopathological characteristics of each tumor type are summarized in Table 2, and the macroscopic appearance, morphological phenotype and location of the tumors are illustrated in Figure 1. When comparing the clinicopathological findings of the intestinal-type adenomas by location (i.e., proximal and distal of the ampulla), there was

no significant difference between these two embryologically distinct locations.

Histological grade and clinicopathological factors

The clinicopathological characteristics of every LGA and HGA are summarized in Table 3. The mean size of the HGAs was significantly greater than that of the LGAs (19.4±8.6 mm vs. 11.8±5.1 mm, p=0.021). In addition, all adenomas over 20 mm in diameter were classified as HGAs.

Four of 12 HGAs were erythematous, whereas 9 of 19 LGAs were erythematous. There was no significant trend in color for either the HGAs or LGAs.

Immunohistological characteristics

The immunohistochemical findings of EADA are summarized in Table 4. All gastric-type adenomas (5/5), which were diagnosed using HE-stained slides, were covered with MUC5AC-positive cells, which comprised 30% or more of each lesion. All gastric-type adenomas had variable amounts of a MUC6-positive component beneath a covering of MUC5AC-positive cells. Pyloric gland-type adenomas mostly consisted of a MUC6-positive component. Foveolar-type adenomas consisted of MUC5AC-positive cells as the major component (Figure 2). Two cases of foveolar-type adenoma showed scattered MUC2-positive cells. All gastric-type adenomas were negative or less than 10% positive for CD10. All gastric-type adenomas were negative

for p53.

Thirty-seven out of 39 (94.9%) cases of intestinal-type adenomas showed enteric characteristics with CD10 expression on the apical surface. Thirty-four cases (87.2%) of intestinal-type adenoma sporadically expressed MUC2. Thirty-one cases (79.5%) of intestinal-type adenoma expressed MUC6, and 16 cases (41.0%) had 10% or greater staining. Twenty-three of 39 (59.0%) cases of intestinal-type adenoma had a small number (1%-9%) of MUC5AC-positive cells (Figure 3). All intestinal-type adenomas were negative for p53.

EADA and comorbid colorectal neoplasms

We reviewed the medical records of 44 EADA cases and determined that 16 had undergone a total colonoscopy. The day of colonic evaluation ranged between 4 years prior to and 2 years after duodenal endoscopic mucosal resection. In seven cases, no lesions were found endoscopically, whereas neoplasms were detected and confirmed histologically in 9 patients, including 6 cases of adenoma and 3 cases of adenocarcinoma.

The duodenal lesions of all nine patients with colorectal neoplasm were intestinal-type adenomas without exception. However, there was no statistically significant relationship between the histological type of duodenal adenoma and the

presence of colorectal lesions (p=0.175).

DISCUSSION

To the best of our knowledge, no English-language literature features a clinicopathological study analyzing a large EADA case series. Although EADA has been empirically classified into gastric and intestinal types, a full classification of EADA was not described in the WHO 2010 criteria.

In the present study, by histologically analyzing 44 serial cases of EADA, we clearly showed that there are two distinct types of adenoma: a gastric type and an intestinal type. Although our series was not large, the analyzed cases constitute a continuous series, and the cases were not artificially extracted. In this study, the proportions of gastric and intestinal EADA were approximately 10% and 90%, respectively.

All gastric-type adenomas classified with HE staining showed an intense MUC5AC-positive gastric foveolar-like cell component. In addition, MUC6 immunostaining was useful for subclassifying gastric-type adenomas into a pyloric gland type and a foveolar type.

In the stomach, pyloric gland-type adenomas tend to show a nodular or

dome-like shape,[8] whereas the shape of foveolar-type adenoma is depressed or flat.[9] In the present study of the extra-ampullary duodenum, all 5 gastric-type adenomas, including both pyloric gland and foveolar types, exhibited pedunculated features. This may be one of the morphologic characteristics of gastric-type duodenal adenomas. Our two pyloric gland-type adenomas also exhibited a whitish color. In a prior study by Kushima, only 5 out of 19 pyloric gland-type adenomas in the stomach exhibited a reddish color.[10] A whitish color is considered to be a characteristic of pyloric gland-type tumors.

Ushiku *et al*. reported that 20 out of 38 (51.6%) duodenal adenocarcinoma cases had a dysplasia component around the carcinoma component.[3] Okada *et al*. attempted an endoscopic follow-up study of histologically confirmed low-grade duodenal adenoma and revealed that 9 of 43 cases (20.9%) showed progression to high-grade dysplasia, including two non-invasive carcinomas.[11] These reports suggest that some duodenal adenomas have the potential to progress to adenocarcinoma with an adenoma–carcinoma sequence similar to that recognized in colon cancer. Okada *et al*. reported that one of the factors that predicts progression to adenocarcinoma is histological high-grade dysplasia (HGD) based on multivariate analysis.[11] Therefore, endoscopic resection of lesions with HGD is a clinical objective. In our study, HGAs were

significantly greater in size than LGAs. Furthermore, all adenomas over 20 mm at the largest diameter were classified as HGAs. When we set a cut-off value of 20 mm to distinguish HGAs and LGAs, the sensitivity and specificity were 0.74 and 1.00, respectively. This should serve as a clinically useful landmark. Our findings are consistent with a study by Okada that concluded that duodenal adenomas 20 mm or larger in diameter are at high risk of progression to adenocarcinoma based on multivariate analysis.[11] In contrast, some cases of HGA were smaller than 10 mm at the largest diameter. There is a report that HGD lesions frequently exhibit erythematous color.[11] However, we observed no relationship between color and histological grade in the present study. It is difficult to estimate histological grade based only on an endoscopic observation of color. Histological evaluation by forceps biopsy is necessary even for small EADAs.

In this study, all gastric-type adenomas were located in the first portion. This seems to be characteristic of gastric-type EADA. Vieth *et al*. described 7 of 8 cases (87.5%) of duodenal PGA that were located in the first portion of the duodenum,[5] which agrees with our results. In contrast, Ushiku *et al*. found that 19 of 38 (50.0%) extra-ampullary duodenal adenocarcinoma cases showed the gastric phenotype as the major component, and gastric-type adenocarcinomas were distributed in the first and

second portion as well as in the third and fourth portions.[3] Extra-ampullary gastric-type adenocarcinomas appeared to make up a larger proportion and had a wider distribution than gastric-type adenomas in our study.

Several possibilities should be considered to explain the above discrepancies. The first is that progression of the gastric-type component included intestinal-type adenomas. The second is that cancerization of pluripotent cells occurred in the intestinal adenomas, which can differentiate into both gastric- and intestinal-type neoplasms. Finally, gastric-type adenomas have a higher potential for malignant transformation than intestinal-type adenomas. We confirmed that most intestinal-type adenomas had, to a variable degree, a gastric component that expressed MUC5AC and/or MUC6. This may explain the distribution observed for duodenal gastric-type carcinoma. However, considering the proportion of gastric and intestinal cells in all EADAs, the gastric component is apparently minor. Vieth *et al*. showed that 30% of PGAs in the stomach continuously transformed into well-differentiated adenocarcinomas, and they suggested PGA as a subtype with high-frequency cancerization.[5] Additionally, in the present study, 60% of gastric-type adenomas were classified as HGA, and the frequency of HGA was higher than intestinal-type adenoma (33.3%). Therefore, the third hypothesis warrants further study.

It is known that patients with sporadic duodenal adenoma are typically comorbid with colorectal neoplasia.[12] Maruoka *et al*. reported that patients with sporadic non-ampullary duodenal adenoma/carcinoma located on the distal side of the major papilla showed comorbidity with colon adenoma/carcinoma.[13] However, in the present work, we did not find any significant differences between the location and comorbidity of colorectal neoplasms (data not shown). We therefore presumed that differences in the proximal or distal side of the major papilla reflect differences in gastric and intestinal phenotypes because all gastric-type adenomas were located in the first portion. Although all duodenal adenomas that were comorbid with colorectal neoplasms were the intestinal type, we could not find any statistically significant differences between the comorbidity of colorectal neoplasm and histological phenotype. As we analyzed only a small colonoscopy series of 16 cases, including only two gastric subtype cases, further studies using large case series are needed to clarify this issue.

Conclusion

In the present study, we clarified the clinicopathological characteristics of EADA. The proportion of gastric-type adenomas was approximately 10% of all EADAs. All gastric-type adenomas were located in the first portion and showed pedunculated features. Approximately 40% of EADAs showed HGD, and their size was significantly

greater than LGAs. Endoscopic resection should be considered for EADAs over 20 mm at the largest diameter because such lesions were classified as HGAs, which are thought to have the potential to progress to adenocarcinoma.

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Author contributions

K. Hijikata: substantial contributions to conception and design; acquisition of data; analysis and interpretation of data; and drafting of the manuscript. T. Nemoto: substantial contributions to conception and design; analysis and interpretation of data; and drafting of the manuscript; revising it critically for important intellectual content. Y. Igarashi, K. Shibuya: revising it critically for important intellectual content; final approval of the version to be published.

REFERENCES

1. Alwmark A, Andersson A, Lasson A. Primary carcinoma of the duodenum. Ann. Surg. 1980; 191; 13-18.

2. Spira IA, Ghazi A, Wolff WI. Primary adenocarcinoma of the duodenum. Cancer 1977; 39; 1721-1726.

3. Ushiku T, Arnason T, Fukayama M, Lauwers GY. Extra-ampullary duodenal adenocarcinoma. Am. J. Surg. Pathol. 2014; 38; 1484-1493.

4. Vieth M, Kushima R, Mukaisho K, Sakai R, Kasami T, Hattori T. Immunohistochemical analysis of pyloric gland adenomas using a series of mucin 2, mucin 5ac, mucin 6, cd10, ki67 and p53. Virchows Arch. 2010; 457; 529-536.

5. Vieth M, Kushima R, Borchard F, Stolte M. Pyloric gland adenoma: A clinico-pathological analysis of 90 cases. Virchows Arch. 2003; 442; 317-321.

6. Williams PL, Warwick R, Dyson M, Bannister LH. Gray's anatomy, 37th edn. New York: Churchill Livingstone, 1989.

7. Lauwers GY, Carneiro F, Graham DY *et al*. Gastric carcinoma. In Bosman FT, Carneiro F, Hruban RH, Theise ND eds. WHO classification of tumours of the digestive system, 4th edn. Lyon, France: IARC, 2010; 48-58.

8. Kushima R, Vieth M, Borchard F, Stolte M, Mukaisho K, Hattori T. Gastric-type well-differentiated adenocarcinoma and pyloric gland adenoma of the stomach. Gastric Cancer 2006; 9; 177-184.

9. Park DY, Srivastava A, Kim GH *et al*. Adenomatous and foveolar gastric dysplasia: Distinct patterns of mucin expression and background intestinal metaplasia. Am. J. Surg. Pathol. 2008; 32; 524-533.

10. Ryoji K, Akiko M, Shigetaka Y *et al*. Clinicopathological Characteristics of Gastric-Type Adenoma（Pyloric Gland Adenoma）:Endoscopic Findings, Histogenesis, Gene Mutations, and Malignant Transformation. Stomach and Intestine (Tokyo) 2014; 49; 1838-1849.

11. Okada K, Fujisaki J, Kasuga A *et al*. Sporadic nonampullary duodenal adenoma in the natural history of duodenal cancer: A study of follow-up surveillance. Am. J. Gastroenterol. 2011; 106; 357-364.

12. Murray MA, Zimmerman MJ, Ee HC. Sporadic duodenal adenoma is associated with colorectal neoplasia. Gut 2004; 53; 261-265.

13. Maruoka D, Arai M, Ishigami H *et al*. Sporadic nonampullary duodenal adenoma/carcinoma is associated with not only colon adenoma/carcinoma but also gastric cancer: Association of location of duodenal lesions with comorbid

diseases. Scand. J. Gastroenterol. 2015; 50; 333-340.

TABLES

Table 1. Immunohistochemical antibodies used

Antibodies	Clone	Dilution	Source
CD10	56C6	1:80	Leica Microsystems, Newcastle upon Tyne, UK
MUC2	Ccp58	1:100	Leica Microsystems
MUC5AC	CLH2	1:100	Leica Microsystems
MUC6	CLH5	1:100	Leica Microsystems
Ki-67	MIB-1	1:200	DAKO Cytomation, Copenhagen, Denmark
p53	DO-7	1:200	DAKO Cytomation

Table 2. Characteristics of each gastric- and intestinal-type extra-ampullary duodenal adenoma

Factors	**All patients**	**Gastric (n=5)**	**Intestinal (n=39)**	**p-Values**
Age (mean±SD)(years old)	64.1±10.1	71.0±9.2	63.2±10.6	N.S.
Sex (male/female)	31/13	3/2	28/11	N.S.
Mean size (mean±SD)(mm)	14.6±7.5	13.0±4.0	14.8±7.8	N.S.
Location of the lesion (first portion/second portion)	12/32	5/0	7/32	<0.01
Macroscopic appearance (pedunculated/non-pedunculated)	12/32	5/0	7/32	<0.01
Color (erythematous/whitish)	13/31	3/2	10/29	N.S.
Histopathological phenotypes (duodenal LGA/HGA)	28/16	2/3	26/13	N.S.

Abbreviations: LGA=low-grade adenoma; HGA=high-grade adenoma

Table 3. Characteristics of each low- and high-grade extra-ampullary duodenal adenoma

Factors	**LGA (n=28)**	**HGA (n=16)**	**p-Values**
Age (mean±SD)(years old)	61.8±11.2	68.2±8.4	N.S.
Sex (male/female)	19/9	12/4	N.S.
Mean lesion size (mean±SD)(mm)	11.8±5.1	19.4±8.6	0.021
Lesion ≦20mm/>20mm	28/0	10/6	<0.01
Location of the lesion(first portion/proximal second portion/distal second portion)	8/8/12	4/7/5	N.S.
Macroscopic appearance (Ip/Isp/IIa/Ilc)	1/4/22/1	2/5/9/0	N.S.
Color (erythematous/whitish)	9/19	4/12	N.S.
Histopathological phenotypes (Gastric/Intestinal type adenoma)	2/26	3/13	N.S.

Abbreviations: LGA=low-grade adenoma; HGA=high-grade adenoma

Table 4. Immunohistochemical findings of extra-ampullary duodenal adenoma

Mucin phenotype Histological subtype	**CD10** -/+/++/+++	**MUC2** -/+/++/+++	**MUC5AC** -/+/++/+++	**MUC6** -/+/++/+++
Gastric (n=5)	2/3/0/0	2/2/0/1	0/0/0/5	0/1/3/1
foveolar (n=3)	1/2/0/0	1/1/0/1	0/0/0/3	0/1/2/0
pyloric (n=2)	1/1/0/0	1/1/0/0	0/0/0/2	0/0/1/1
Intestinal (n=39)	2/4/21/12	5/21/11/2	16/23/0/0	8/15/15/1

Percentage of positive cells: -: 0%; +: 1%-9%; ++: 10%-29%; +++: ~30%

FIGURE LEGENDS

Figure 1. Macroscopic appearance, morphological phenotype and distribution of extra-ampullary duodenal adenomas. Closed circles represent gastric-type adenomas, and open circles represent intestinal-type adenomas. Circles with a protruding element represent pedunculated lesions. All gastric-type adenomas were located in the first portion and showed pedunculated features. Intestinal-type adenomas tended to be located in the second portion and showed non-pedunculated features.

Figure 2. Photomicrographs of gastric-type adenomas (foveolar type A, B and C; pyloric gland type D, E and F). Foveolar-type adenomas consisted of epithelial cells resembling gastric foveolar epithelium (HE). A, Strong expression of MUC5AC in the majority or entirety. B, MUC6 was negative or positive in the small portion. C, Pyloric gland adenomas exhibited closely packed pyloric-type glands. D, MUC6-positive component located beneath the covering of MUC5AC-positive cells. E, F.

Figure 3. Photomicrographs of intestinal-type adenomas. Intestinal-type adenomas are composed of intestinal-type epithelium. A, CD10 expressed on the apical surface of epithelial cells. B, MUC5AC was negative or positive as a minor component. C

Figure 1

Illustration of macroscopic appearance, morphological phenotype and location of tumor

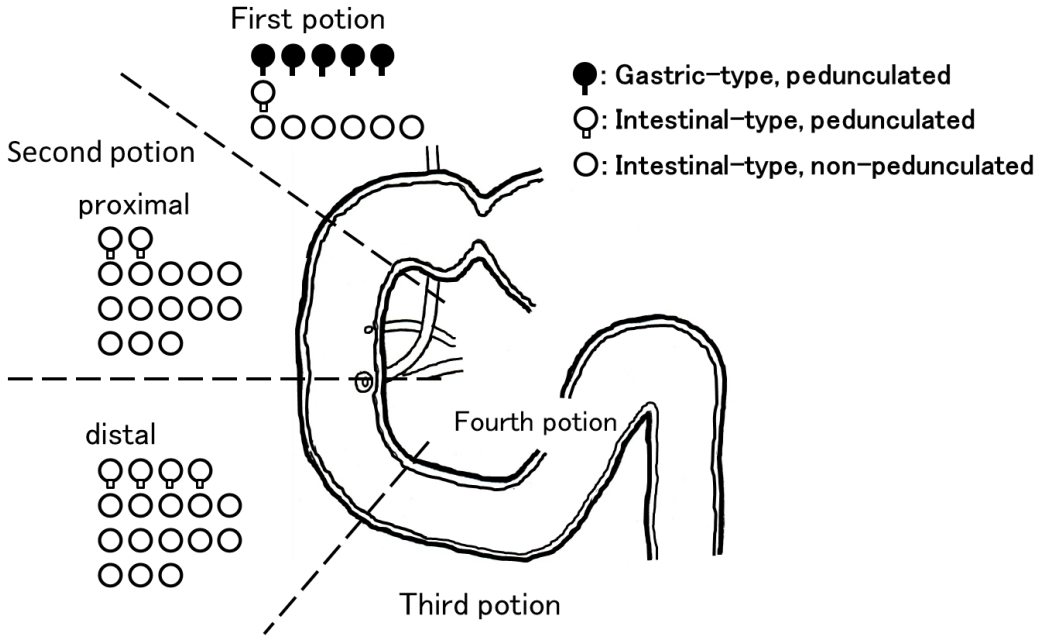

Figure 2
Gastric type adenomas (foveolar-type and pyloric gland type)

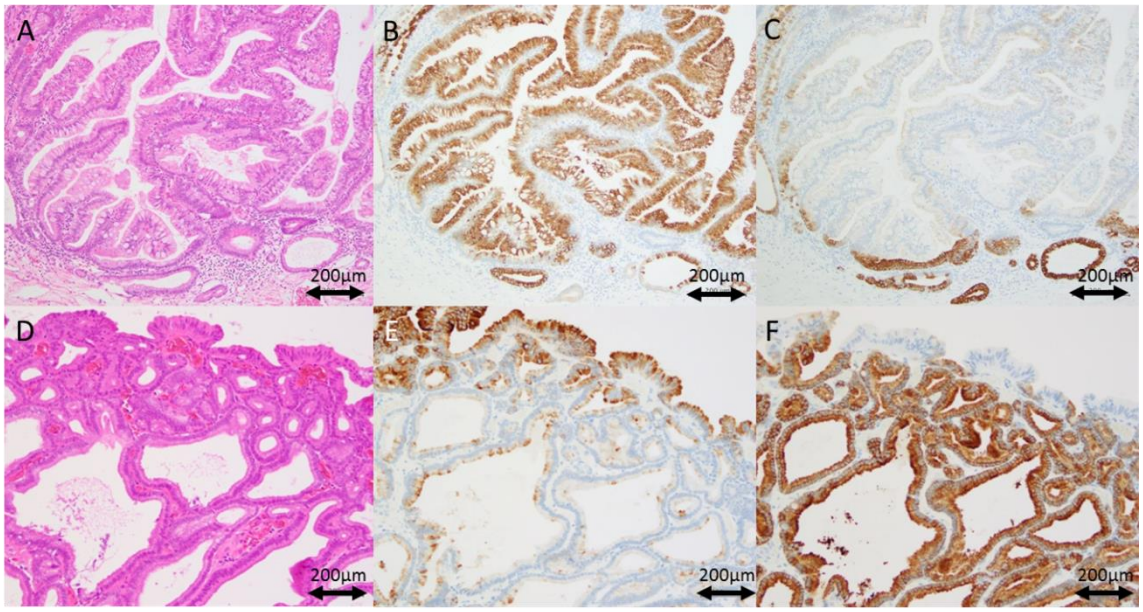

Figure 3
Intestinal-type adenoma