Neoplastic Lesions of Gastric Adenocarcinoma and Proximal Polyposis Syndrome (GAPPS) Are Gastric Phenotype

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de Boer WB, et.al. Am J Surg Pathol. 2018;42(1):1-8.

BACKGROUND

1. A new autosomal dominant gastric polyposis syndrome.

2. Gastric body and fundus, usually >100,“carpet-like”, predominantly <10 mm.

3. No duodenal or colorectal polyposis.

4. Initially thought not to be associated with other heritable gastrointestinal (GI) cancer syndromes.

BACKGROUND

histopathology:

1. fundic gland polyposis (FGP) +/- areas of dysplasia.

2. occasional hyperplastic and pure adenomatous polyps.

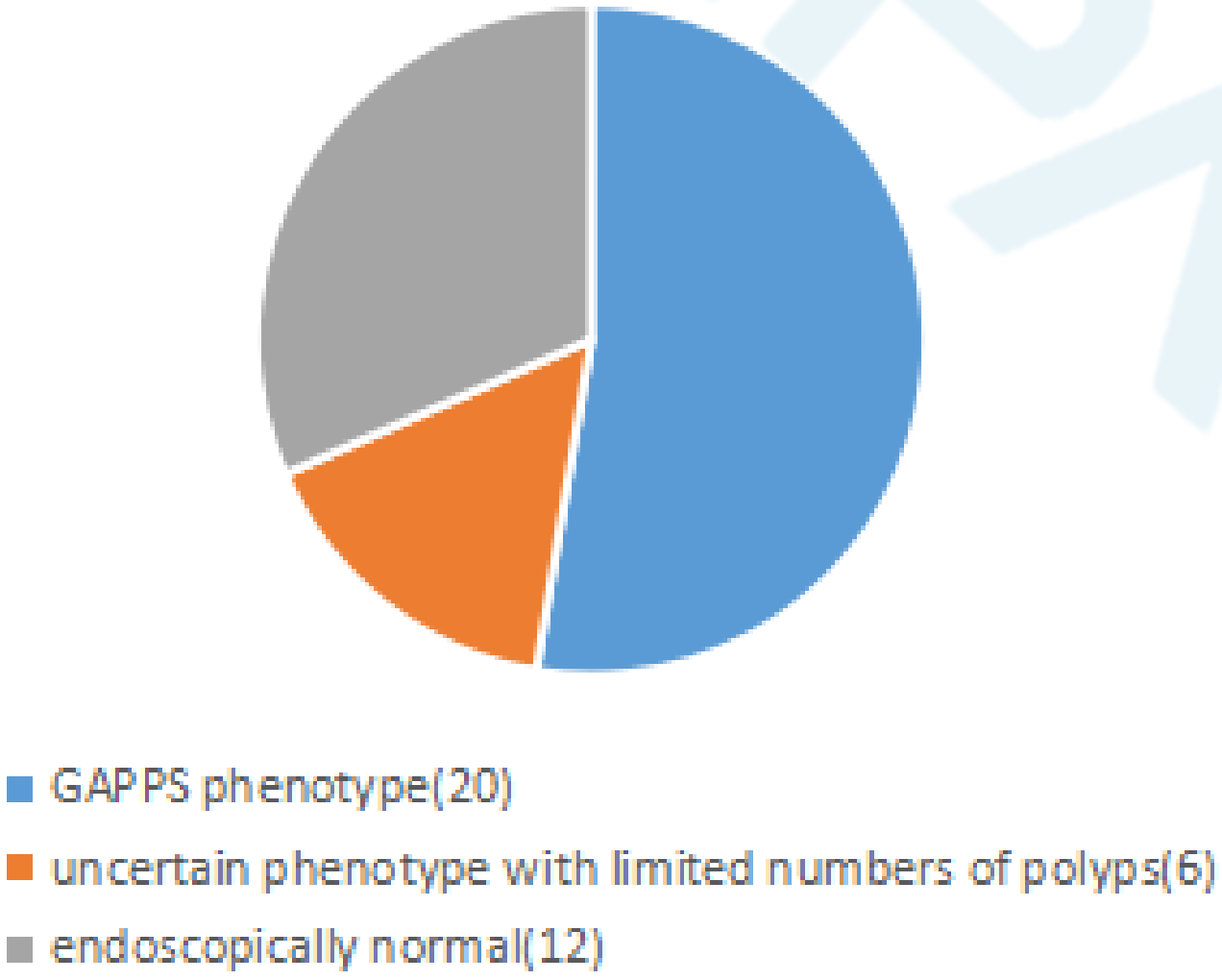
3. mixed FGP-like,adenomatous,and hyperplastic polyps.

4. adenocarcinoma of intestinal type.

The morphology of these polyps and malignancies have not been reported in detail.

BACKGROUND

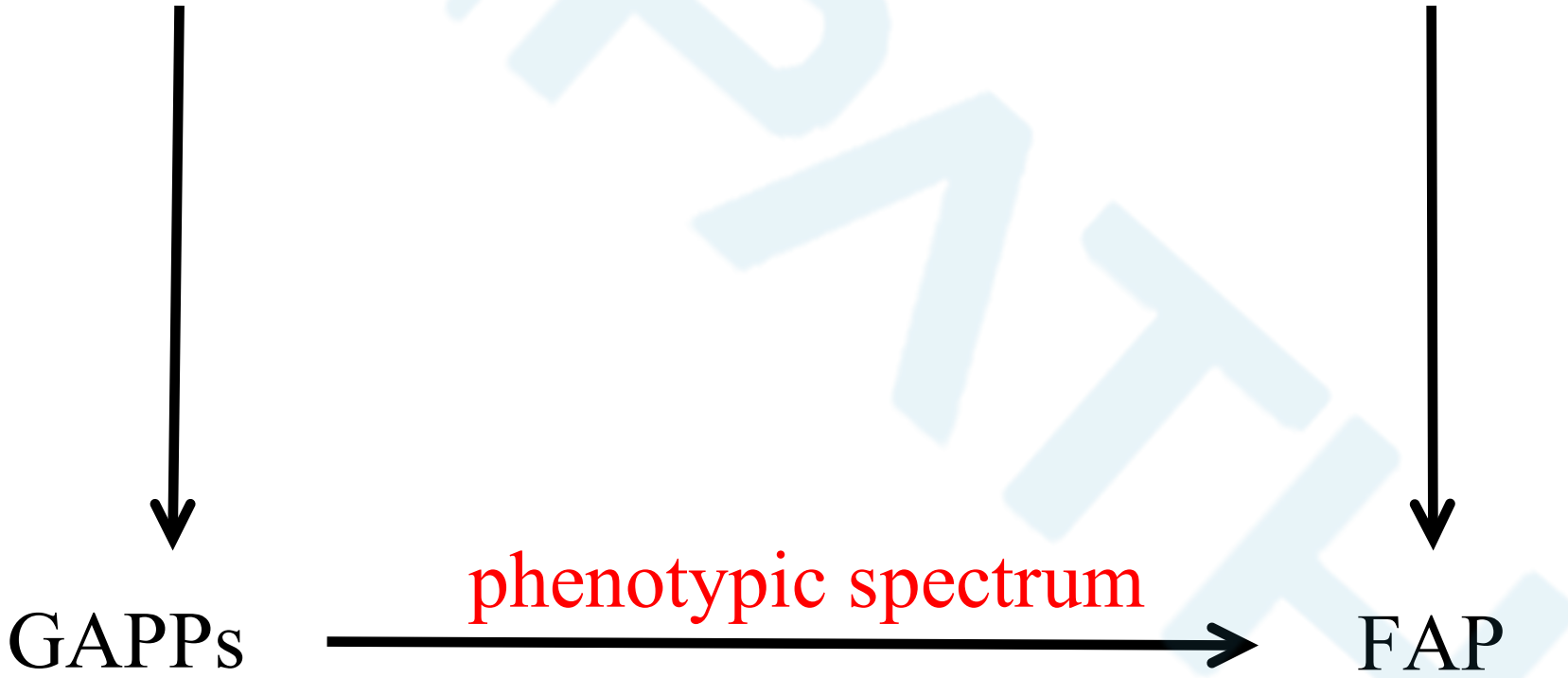
Variable (incomplete) penetrance



2 developed gastric cancer.

BACKGROUND

a point mutation in the promoter 1B of the APC gene



BACKGROUND

Diagnostic criteria :

1. Gastric polyps restricted to gastric body and fundus with no duodenal or colorectal polyposis.

2. Index case: >100 polyps carpeting the proximal stomach. First degree relative of another case: > 30 polyps.

3. Predominantly FGPs, some with regions of dysplasia .

4. Autosomal pattern of inheritance.

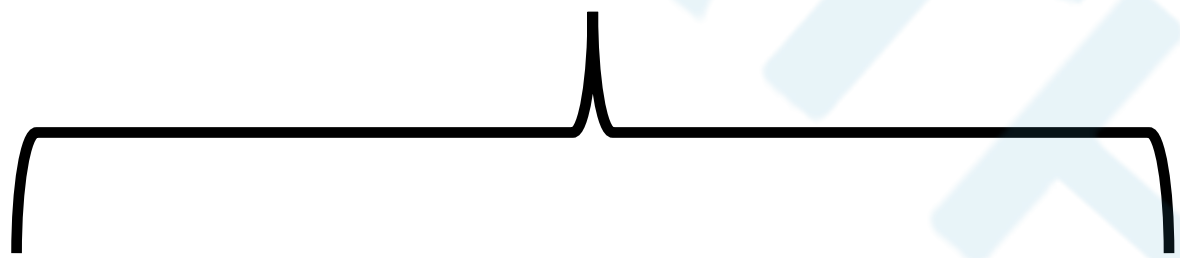
5. Exclusion of other gastric polyposis syndromes and the use of proton pump inhibitors (PPIs).

Study aim

Clinical and endoscopic findings

Detailed morphologic description

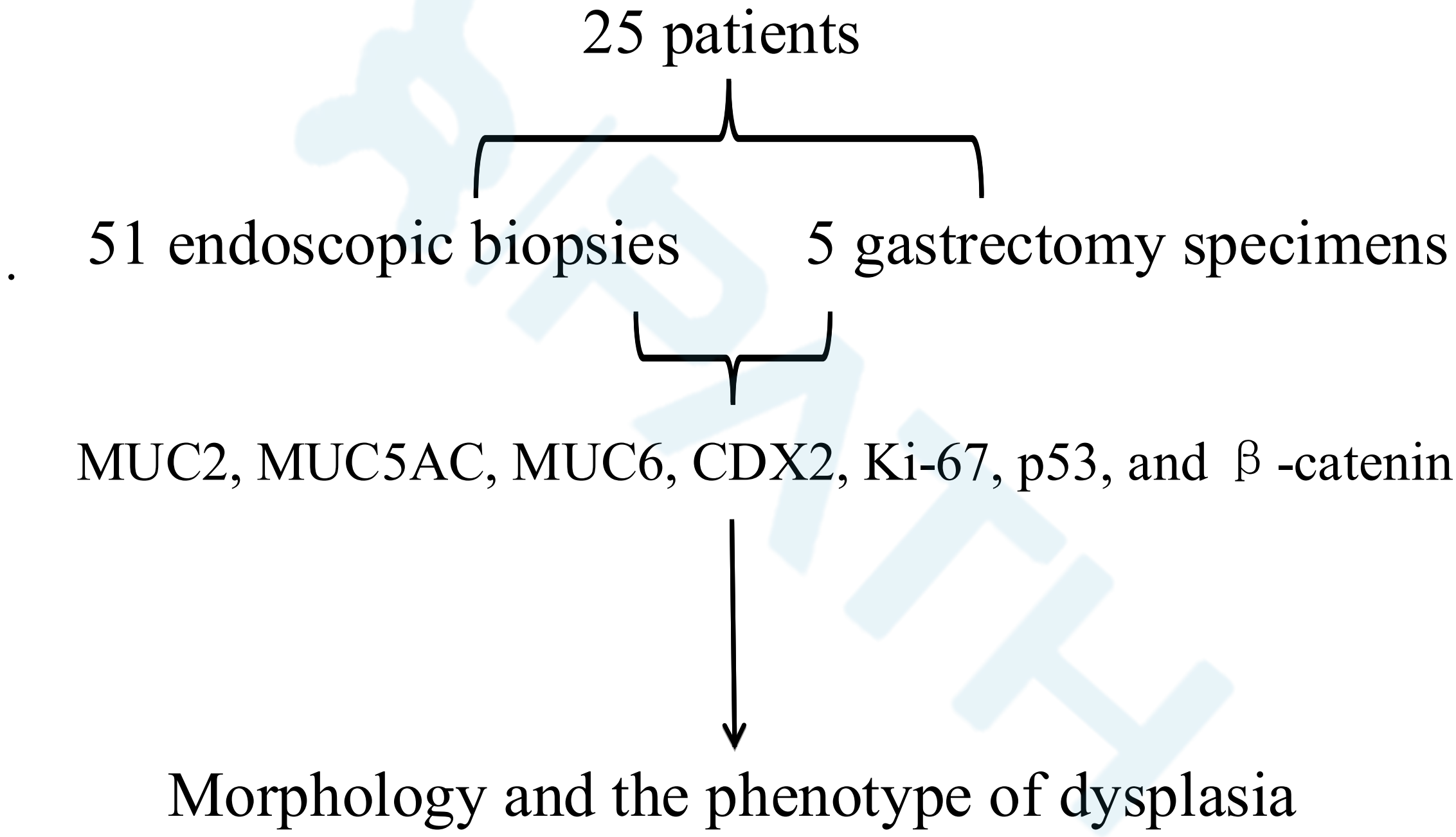
systematic description of lesions in a cohort of GAPPS family members



Diagnostic clues

Possible path of progression

MATERIALS AND METHODS:

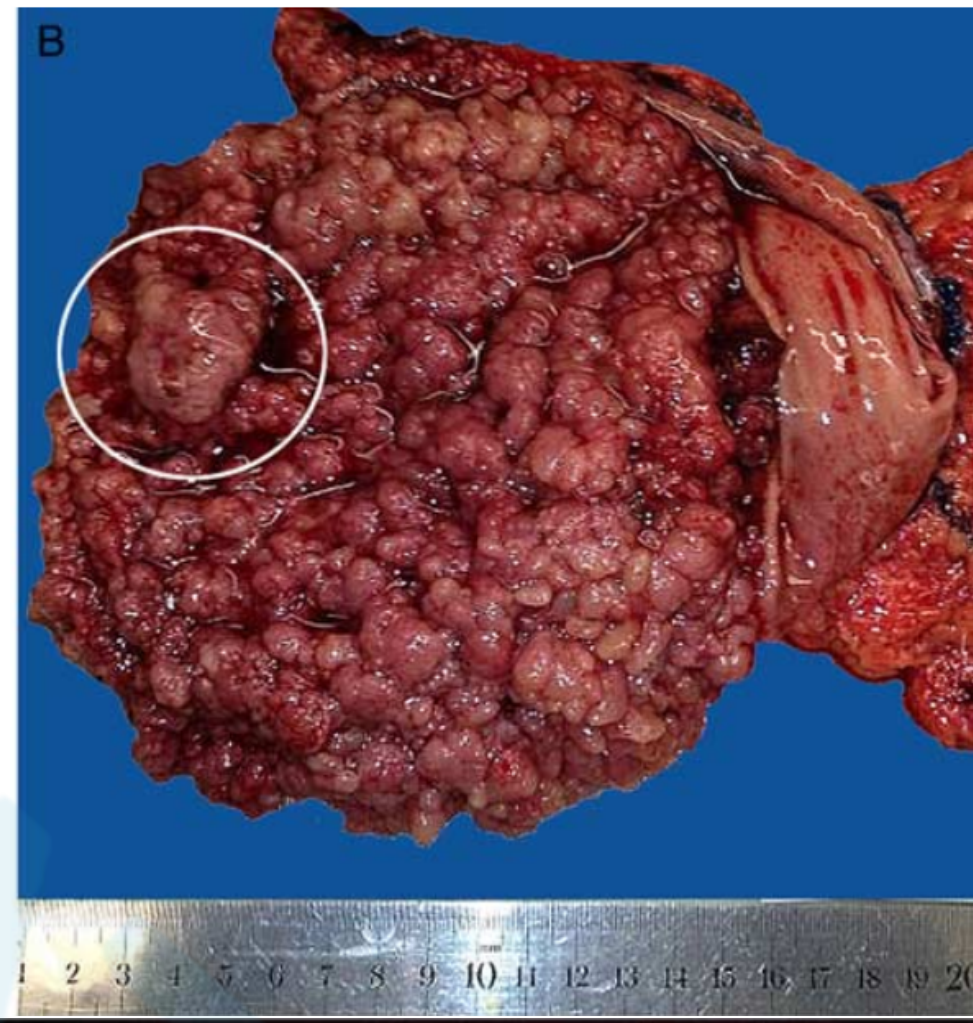


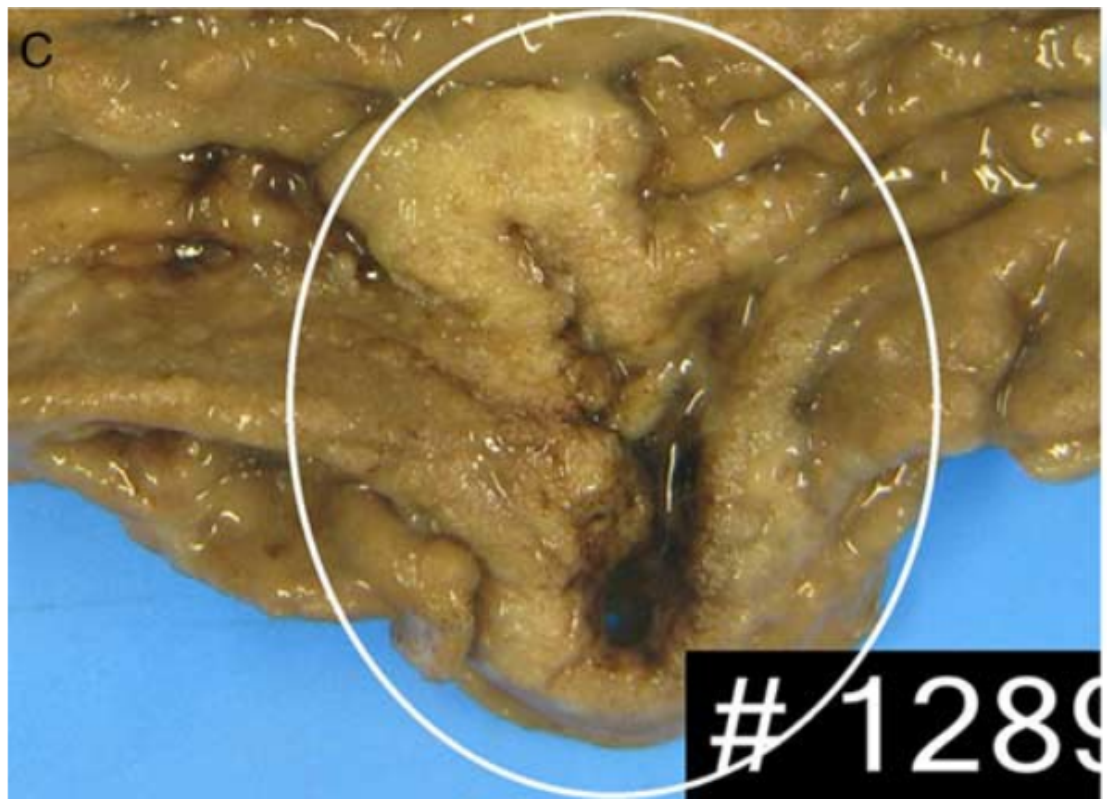
RESULTS

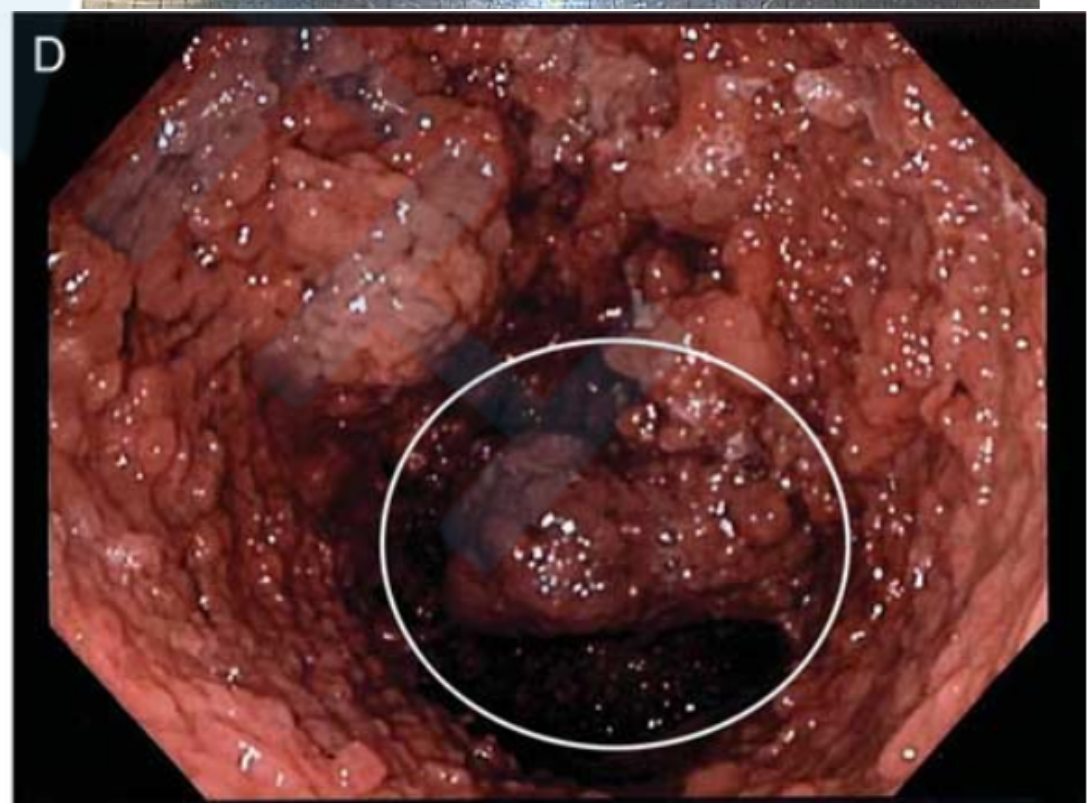
Carpeting polyposis(2 to 10 mm in size) sparing the antrum and lesser curve.(14 patients)

RESULTS

Dominant polyps (circled) in the setting of carpeting polyposis, between 15 and 35 mm.(5 patients)







RESULTS

TABLE 1. Endoscopic and Microscopic Features of 25 Patients With 51 Biopsy Episodes and 5 Gastrectomies

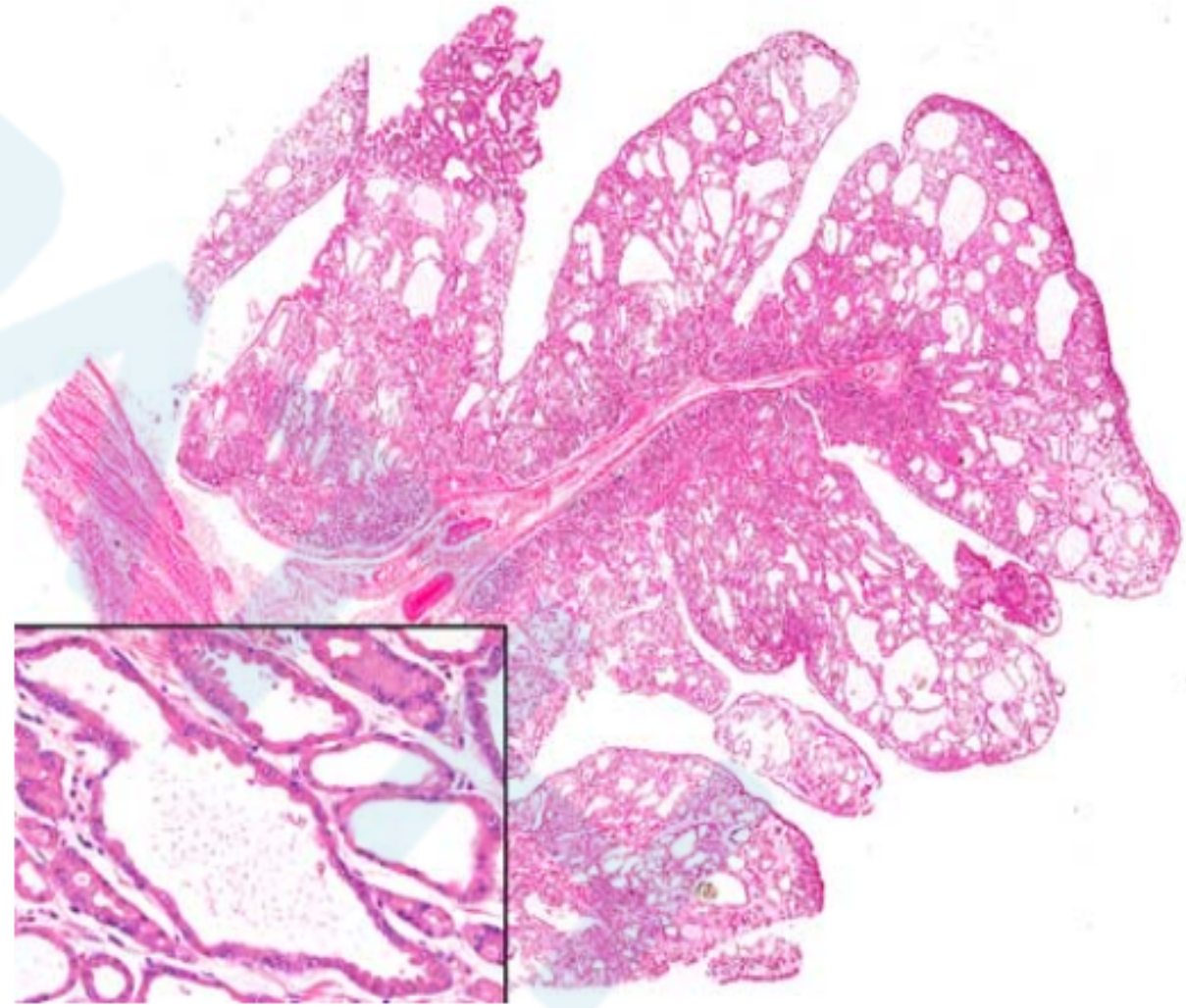
	Patients With Gastric Body Biopsy (N = 25)			Gastrectomies (N = 5)*	Total (N = 25)
Endoscopy	**Normal (N = 10)**	**Polyposis (N = 14)**	**Mass No Polyposis (N = 1)†**	**Polyposis (N = 5)**	**N = 25**
Fundic gland polyps	0	10	0	4	10
Hyperproliferative aberrant pits	0	12	0	5	13
Neoplastic lesions	0	8	1		9
Gastric adenoma	0	4	0	4‡	6§
"Flat" dysplasia associated with other polyps	0	3	0	5	8
Adenoma+adenocarcinoma	NA	0	1	0	1

*All 5 gastrectomy patients had a previous biopsy available.
†No polyposis seen at endoscopy.
‡Two adenomas were biopsied before gastrectomy.
§All 6 patients with a gastric adenoma also showed multifocal "flat" dysplasia.
NA indicates not available.

RESULTS

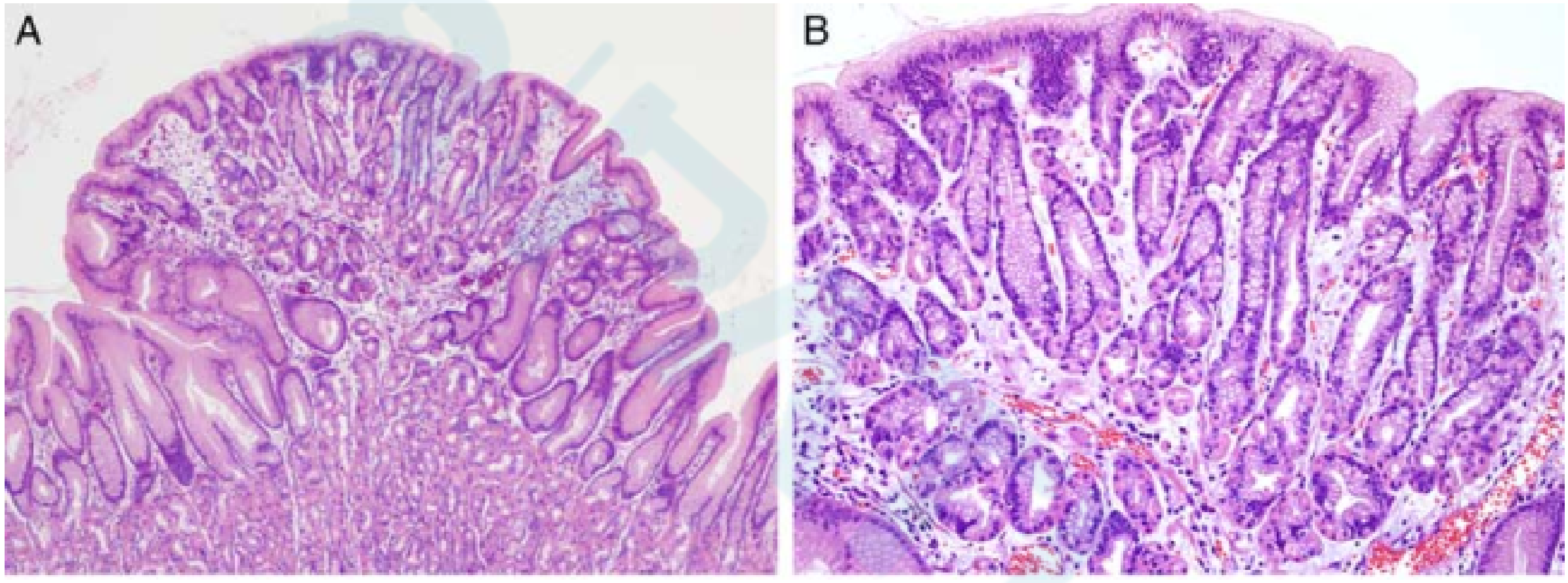
Fundic Gland Polyps (10/15 Patients)

Microcysts lined by fundic epithelium including oxyphilic cells



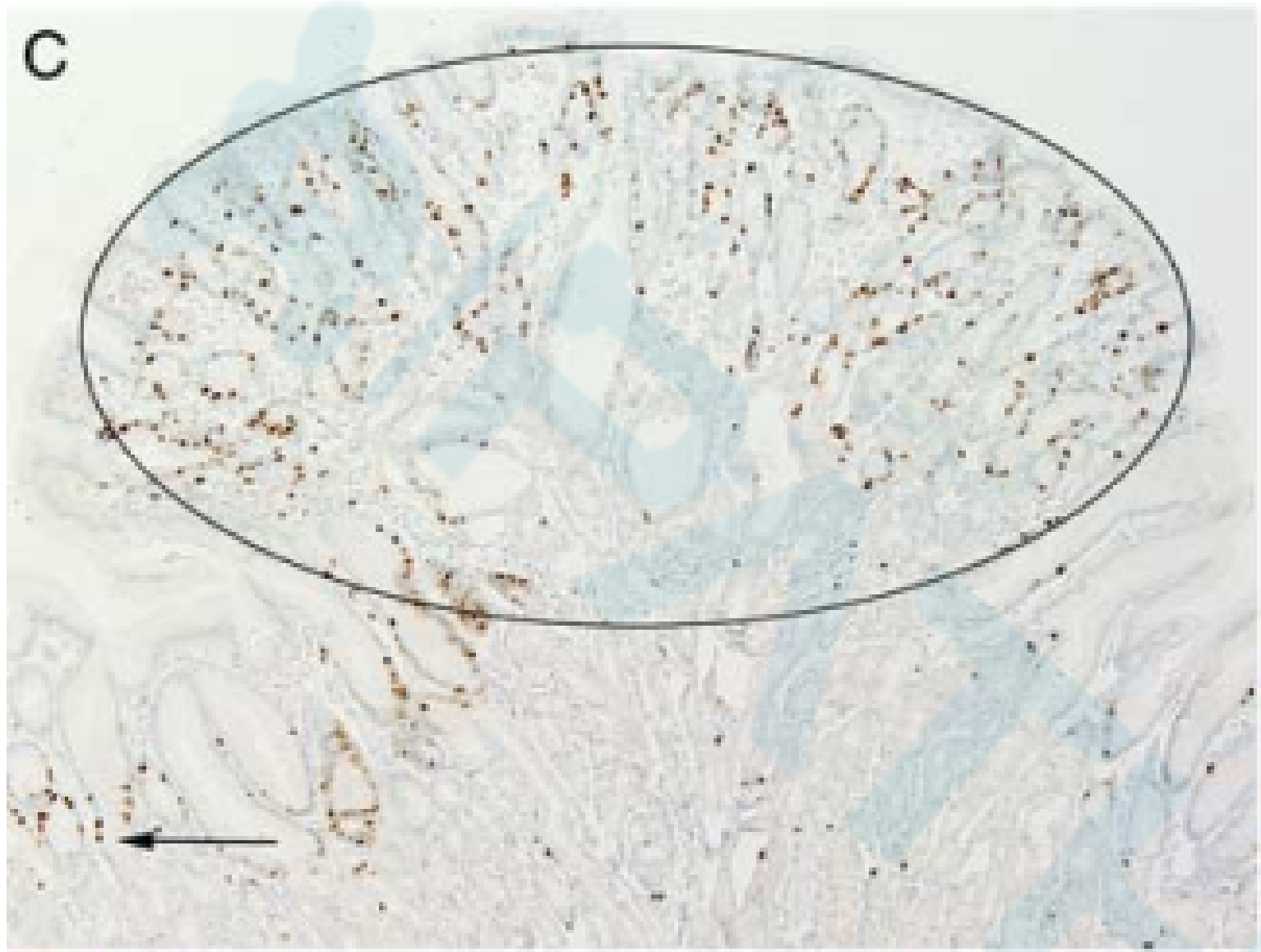
RESULTS

Hyperproliferative Aberrant Pits (12/15 Patients)



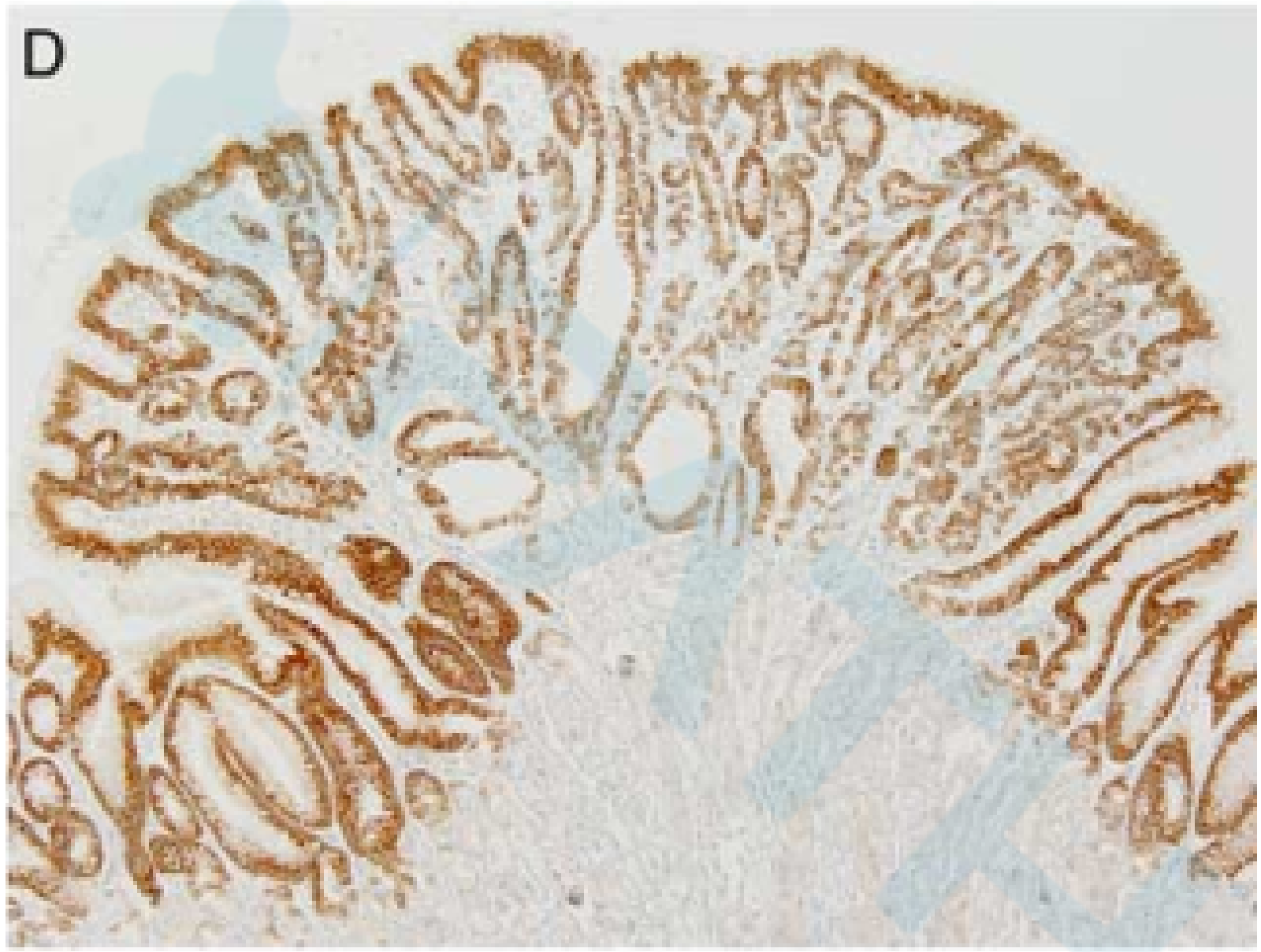
Disorganized proliferation of specialized/oxyntic glands high up in the mucosa involving the attenuated foveolar region around the gastric pits, forming a polypoid lesion.

RESULTS



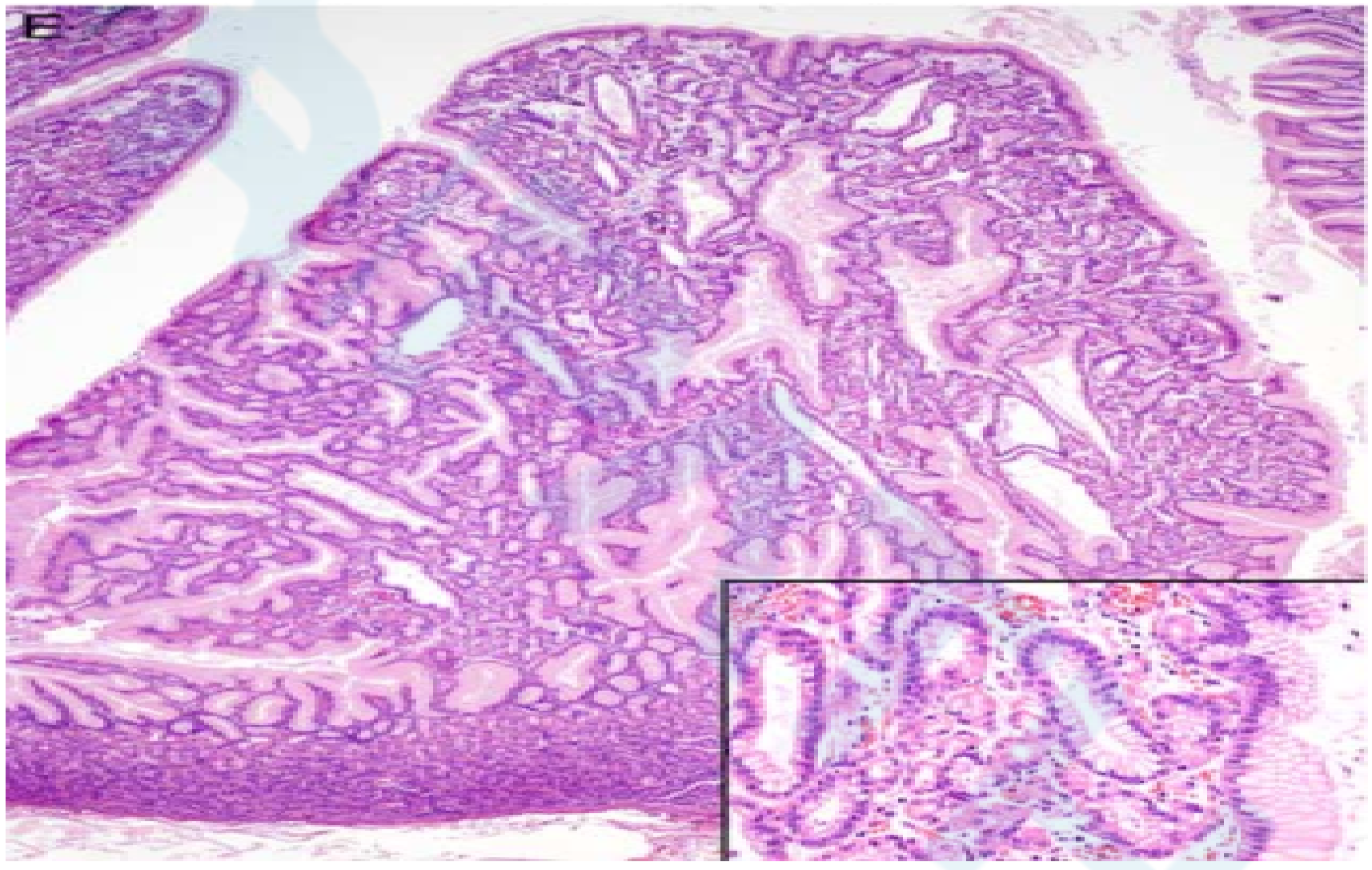
A Ki-67 immunostain showing heightened Ki-67 activity in the lesion (ellipse) when compared with the proliferative zone of the adjacent tubular neck region (arrow).

RESULTS



These appeared to be the earliest stage of polyp formation and were strongly positive for MUC5AC (Fig. 3D)

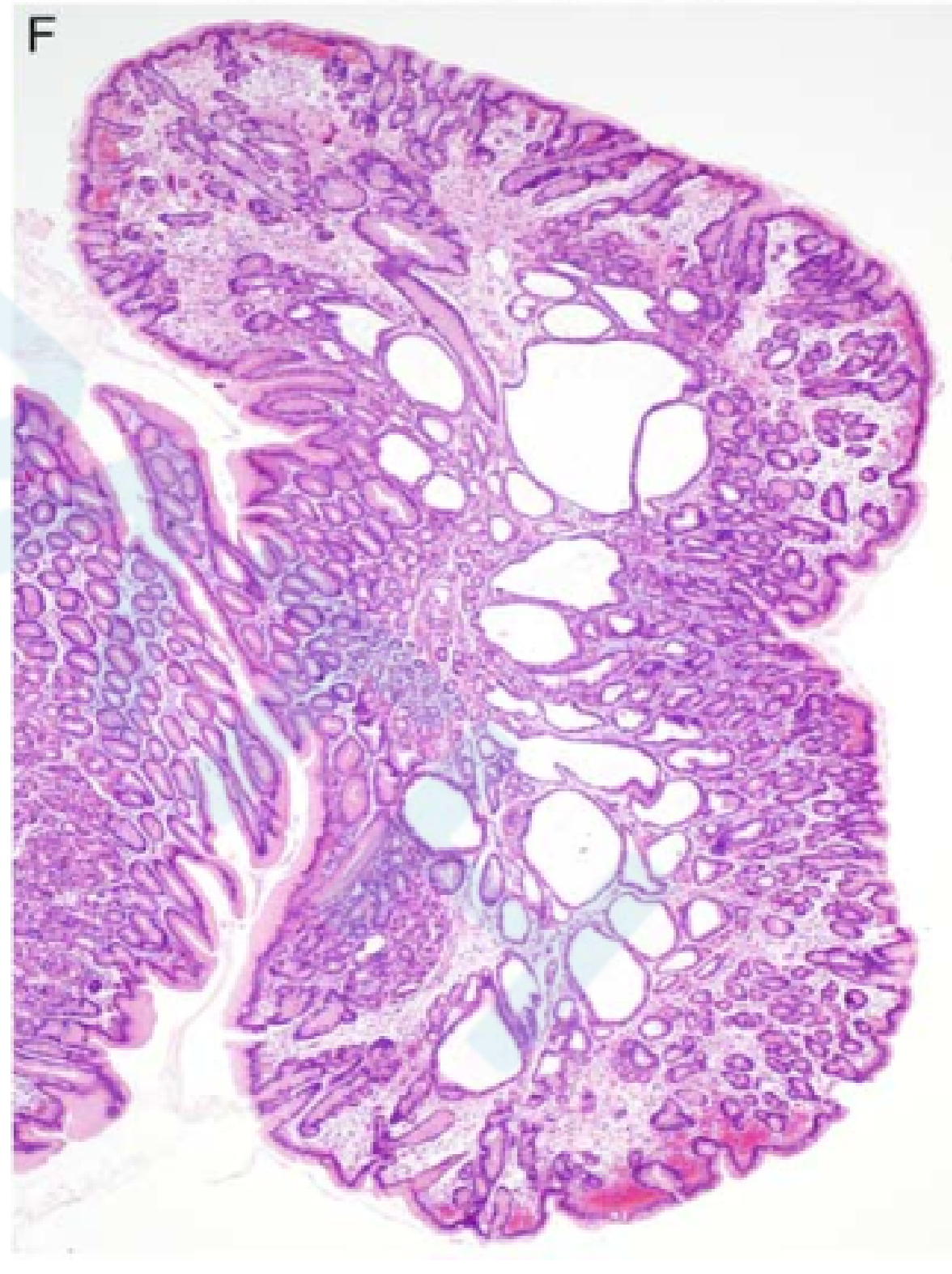
RESULTS



HPAP showing inverted foveolar hyperplasia, inset shows oxyntic cells adjacent to the hyperplastic foveolar compartment.

RESULTS

The HPAPs coexisted with FGP-like changes. (8 patients.)



RESULTS

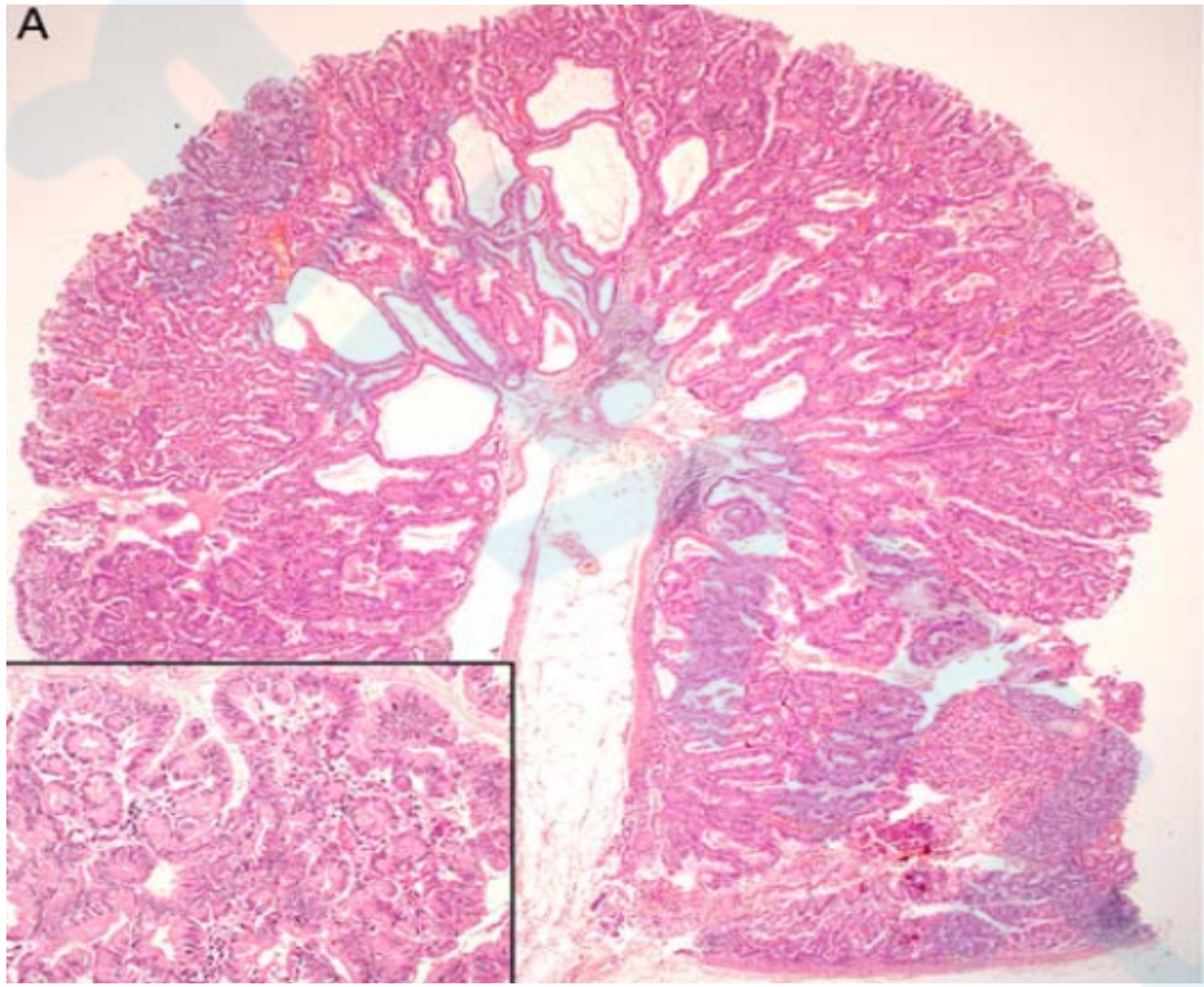
Neoplastic Lesions (9/15 Patients)

Dysplasia was noted in 3 settings:

1. Discrete gastric adenomas (6 cases),
2. Multifocal “flat” dysplasia in the setting of HPAP +/− FGP-like polyps (8 cases, 6 of these were the patients with an adenoma)
3. Adenomatous tissue associated with adenocarcinoma (1 case).

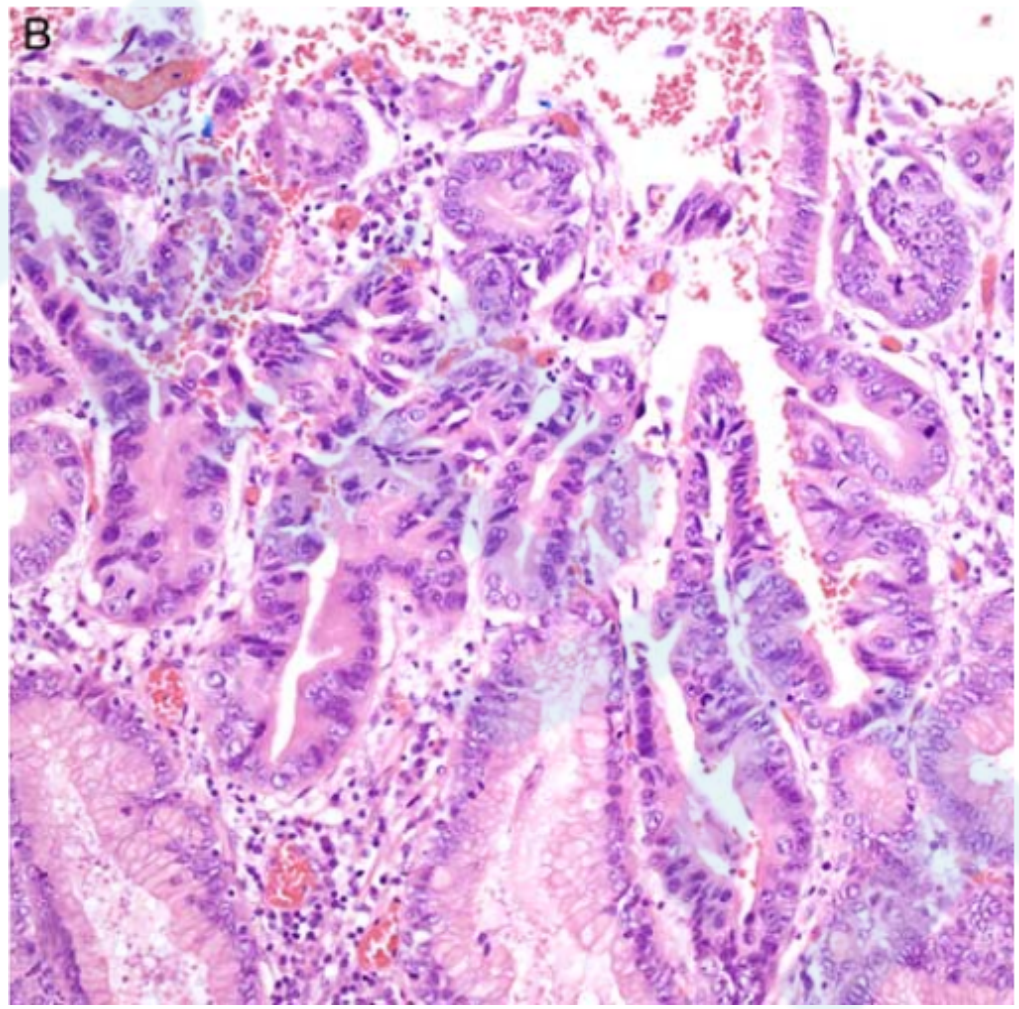
RESULTS

Gastric Adenomas (6/15 Patients)



The adenomas were composed of crowded glands lined by dysplastic epithelium that showed eosinophilic cytoplasm with predominantly basal, oval to round enlarged nuclei, conspicuous to prominent nucleoli and an apical mucin cap.

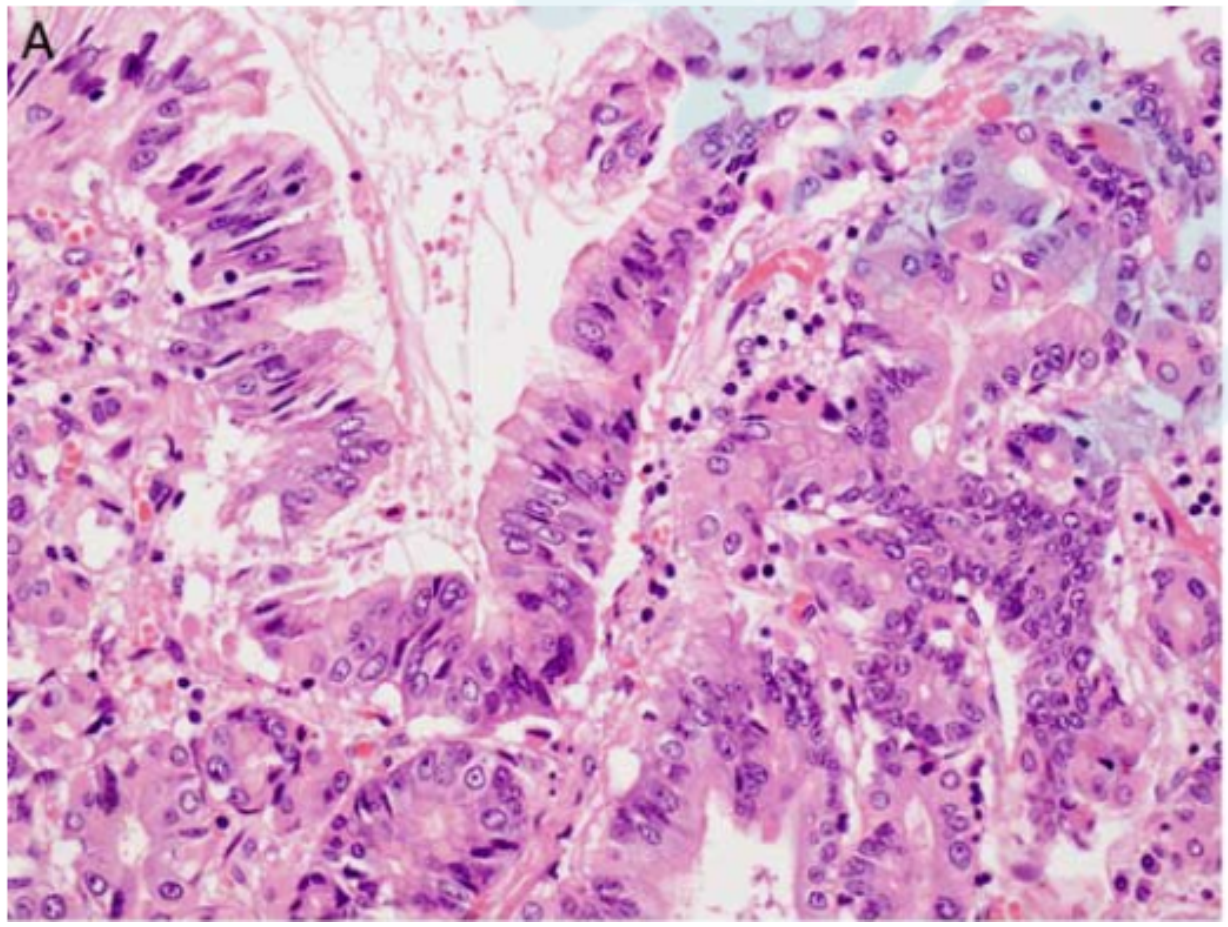
RESULTS

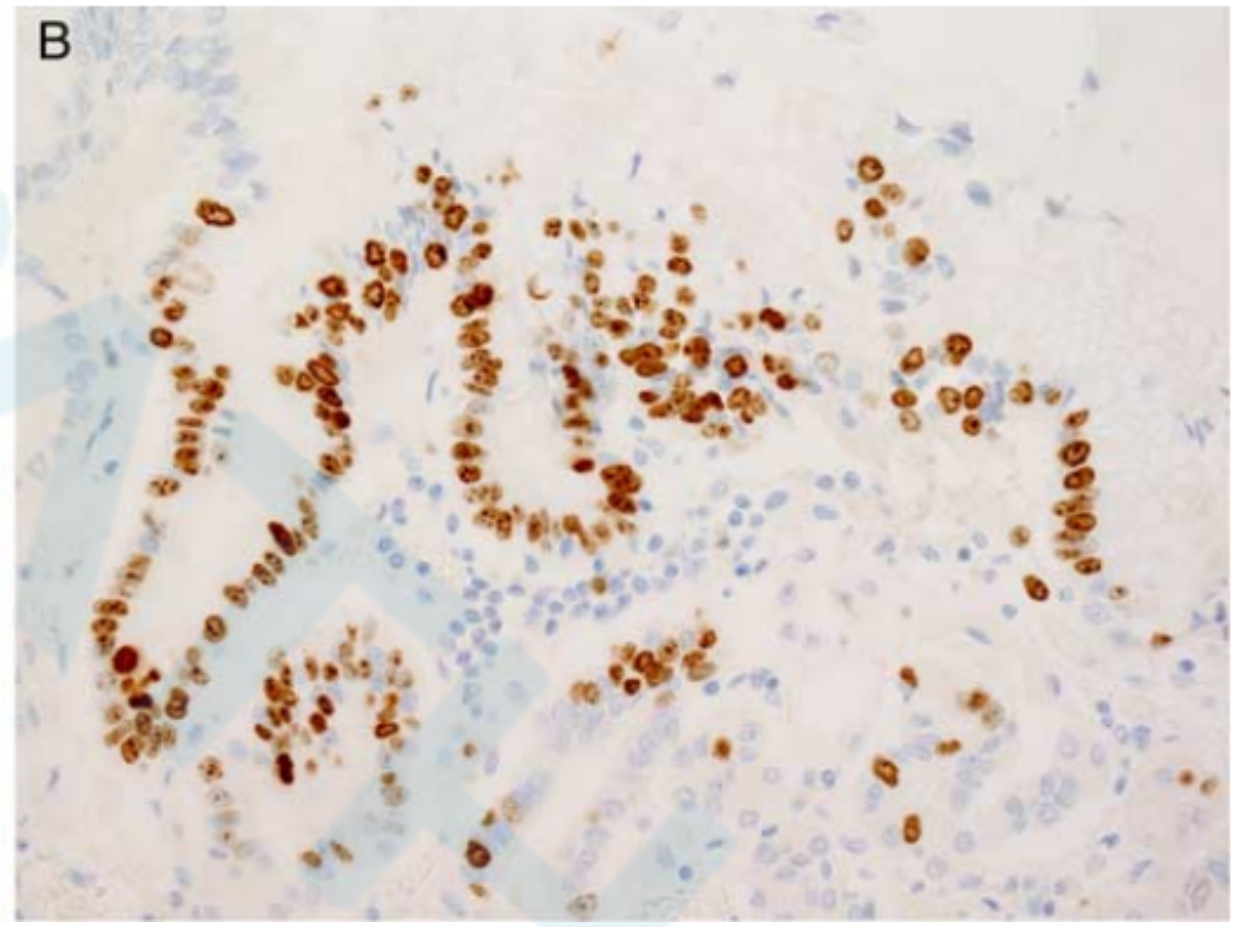


One adenoma was considered high grade as it focally showed more architectural complexity and crowding coupled with highgrade nuclear features comprising loss of polarity, rounder more vesicular nuclei, and prominent nucleoli as focal change in a background of low-grade dysplasia (Fig. 4B).

RESULTS

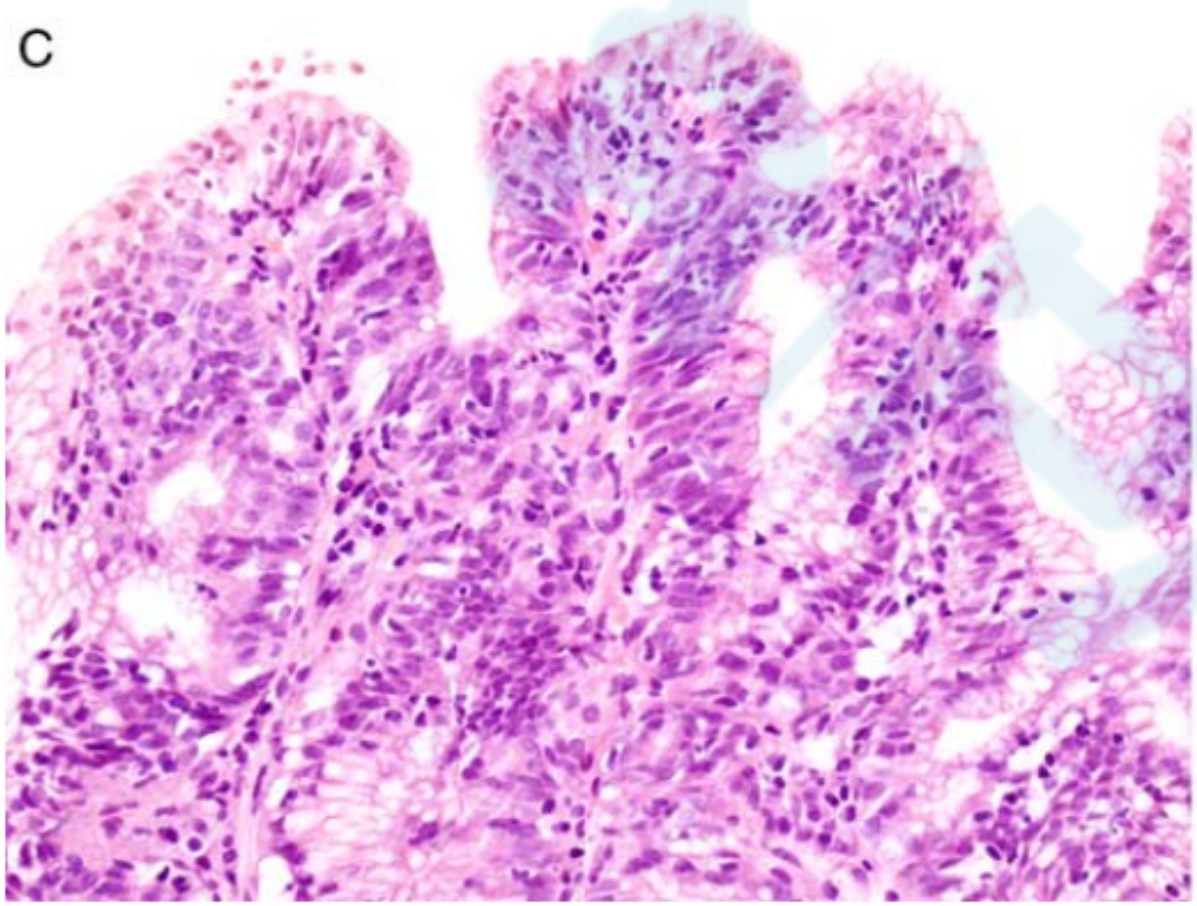
Multifocal “Flat” Dysplasia in the Setting of HPAP +/– FGP-like Polyps (8/15 Patients)





The dysplastic epithelium showed eosinophilic cytoplasm with mostly basal and oval to round enlarged nuclei and conspicuous to prominent nucleoli, similar to those changes described in adenomas (Figs. 5A, B)

RESULTS



One dysplastic lesion was considered high grade as it showed more nuclear crowding and stratification (Fig. 5C) and there was a marked increase in proliferative activity (Ki-67 staining) above baseline and above that seen in HPAPs (Fig. 5D).

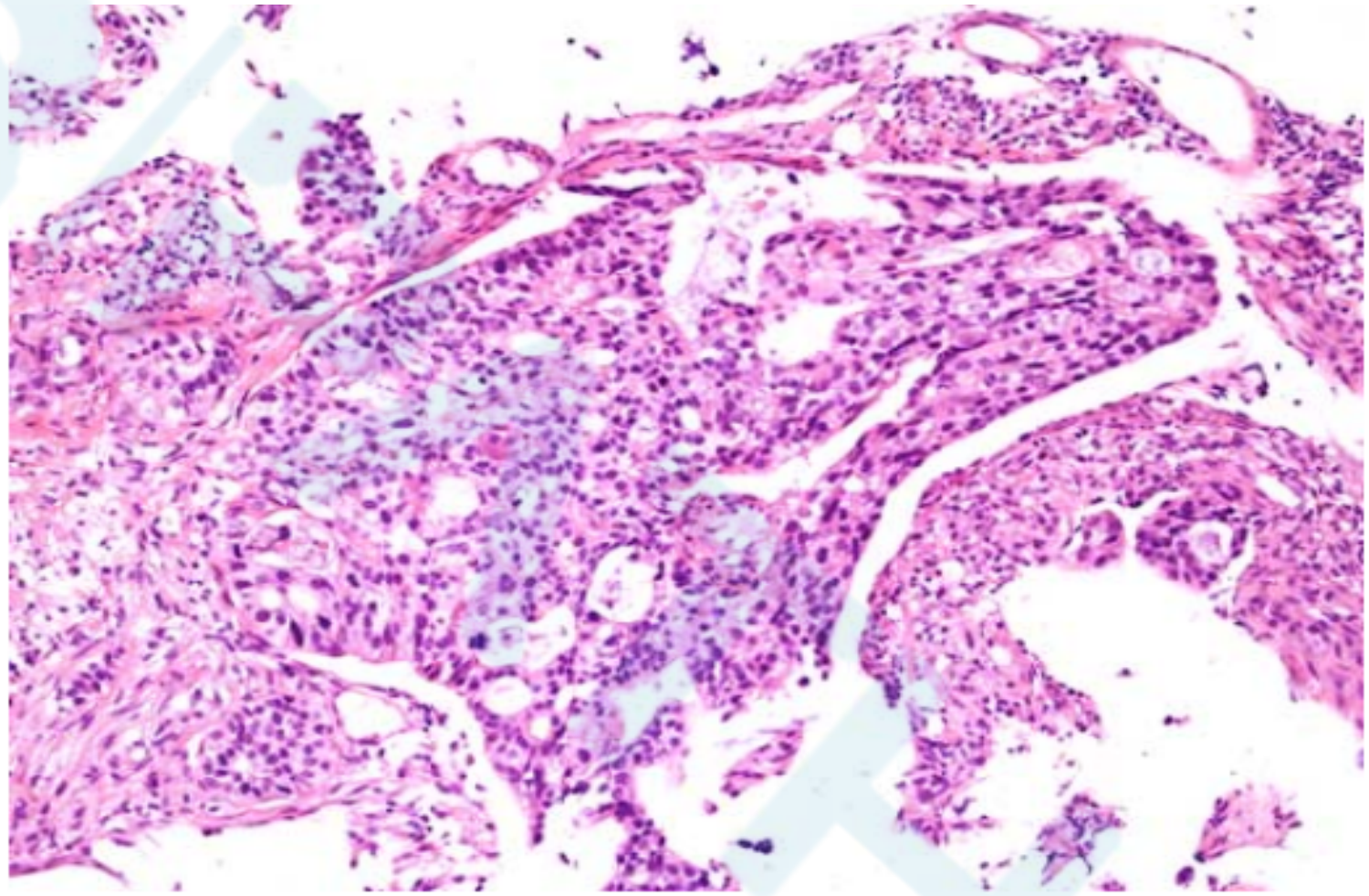
RESULTS

Adenoma (Dysplasia) Associated With Adenocarcinoma (1/15 Patient)

Included in the biopsy of adenocarcinoma were 2 fragments of adenomatous tissue similar in appearance to the gastric adenomas described above.

RESULTS

Adenocarcinoma (1/15 Patients)



The biopsies from this patient's “mass lesion” as described at endoscopy showed neoplastic mucosa only. The adenocarcinoma was of WHO tubular type (Fig. 6)

RESULTS

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RESULTS

TABLE 2. Immunohistochemical Profile and Proliferation Index in Polypoid Lesions Associated With GAPPS

	MUC2	MUC5AC	MUC6	CDX2	CD10	Beta Catenin	P53	Ki-67*
HPAP†	Negative	Positive	Positive deep	Variable positive	Negative	Negative	Positive	Increased
FGP‡	Negative	Positive	Negative	Variable positive	Negative	Negative	Negative	Normal
Adenoma	Negative	Positive	Positive focal	Variable positive	Negative	Negative	Variable positive	Increased
Dysplasia	Negative	Positive	Negative	Variable positive	Negative	Negative	Positive	Increased
Carcinoma	Negative	Positive	Negative	Variable positive	Negative	Negative	Positive	Increased

*Increased Ki-67 activity in the lesional area compared with the proliferative zone of the adjacent tubular neck region.
†Hyperproliferative aberrant pits.
‡Fundic gland polyps.

DISCUSSION

1. Morphologic changes: FGP-like polyps, (a separate lesion)
2. Hyperproliferative aberrant pits(HPAPs),(The earliest lesions and not be easily detectable endoscopically.a disordered proliferation **or** neoplastic in nature)
3. Fully developed gastric type adenomas
4. A WHO tubular type adenocarcinoma.

CONCLUSIONS

1. the spectrum of gastric pathology associated with GAPPS is wider than previously reported.
2. The earliest microscopic is the finding of HPAPs.
3. The dysplasia is of gastric phenotype.
4. The subsequent adenocarcinoma may follow the gastric pathway of carcinogenes.（we propose a morphologic progression from HPAPs to gastric type dysplasia through to carcinoma.）

THANK YOU