Duodenal gangliocytic paraganglioma: a rare case report

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Case Report

Keywords: gangliocytic paraganglioma, duodenum, immunohistochemistry, progesterone receptor, paraganglioma-ganglioneuroma

Posted Date: July 8th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-40551/v1

Abstract

Background Gangliocytic paraganglioma (GP) is quite rare, and origin and entity remain to be elucidated. Case presentation A 51-year-old male presented with a sessile polyp with smooth surface measured about 1cm in diameter in the descending portion of duodenum. Pathological examination displayed a neoplasm located in submucosa, infiltrating into lamina propria. The tumor consisted of epithelioid, ganglion-like and spindle cells admixing in a haphazard way. The epithelioid cells resembled paraganglioma in cytological and architectural features, the ganglion-like cells was scattered, and the spindle cells resembled neurofibroma. Syn, MAP-2 and CgA were positive in the epithelioid and ganglion-like cells in variety and NF highlighted the ganglion-like cells. S-100 and SOX-10 were positive in the sustentacular cells around the epithelioid cells and spindle cell proliferation. PR was also positive. Conclusions Origin of GP is presumed to be related with pancreas islet. GP is supposed to be distinguished with NET G1 and designated as paraganglioma-ganglioneuroma, a kind of composite paraganglioma.

Background

Paraganglioma always involves the extra-adrenal ganglions among the sympathetic or parasympathetic chain. Gangliocytic paraganglioma (GP), a distinct type of paragangliomas, is quite rare and up to three hundred cases have been reported since first described in 1957. Origin and entity of GP remain to be elucidated. We experienced a case of GP in the descending portion of duodenum. Herein, we presented the case and discussed with review of literature.

Case Presentation

A 51-year-old male presented with abdominal discomfort for several years. Physical and experimental examinations revealed no significant differences. Gastrointestinal endoscopy was performed and a sessile polyp in the descending portion of duodenum measured about 1 cm in diameter with smooth surface was found and excised (Fig. 1).

Microscopically the tumor was predominately located in submucosa and infiltrated into lamina propria focally, thus was covered with duodenal mucosa (Fig. 2). The tumor was composed of epithelioid cells, ganglion-like cells and spindle cells. The epithelioid cells were large in round or polygonal shape arranged in nest or zellballen pattern. They were of abundant eosinophilic cytoplasm and a round nucleus with inconspicuous nucleoli. Some were larger with granular cytoplasm and vesicular nuclei with prominent nucleoli.The ganglion-like cells were even larger with eosinophilic cytoplasm and out-standing eccentric vesicular nuclei. They were always scattered and not easily distinguished with the epithelioid cells. The both types of cells displayed mild cellular pleomorphism whereas were absent from mitoses. The spindle cells were bland and arranged in fascicular clusters just as that of neurofibroma. The three proportions were admixed in a haphazard way. Some distorted and enlarged glands were entrapped in the lesion. The tumor was absent from inflammation, necrosis and calcification.

Immunohistochemical study showed an extremely low index of Ki-67 which was less than 1 percent (Fig. 3). The neoplastic proliferation was negative for cytokeratin (CK, AE1/AE3), epithelial membrane antigen (EMA), LCA, HMB45, Melan A, CD30, CD117 and DOG-1. Synaptophysin (Syn) and microtubule associated protein-2 (MAP-2) was diffusely positive for the epithelioid cells and highlighted the ganglion-like cells due to more intensity. The staining pattern of chromogranin A (CgA) was similar, and yet the number and intensity were limited. The epithelioid cells were surrounded by S-100 and SOX-10 positive cells, just as chief cells were surrounded by sustentacular cells in paraganglioma. The ganglion-like cells stood out in staining of neurofilament (NF) since they were the only positive cells except the spindle cells. Neu-N was negative in both epithelioid and ganglion-like cells. Progesterone receptor (PR) was positive in some epithelioid cells whereas estrogen receptor (ER) was negative. S-100 and SOX-10 were also positive in the spindle cell proliferation. CD34 was positive in the spindle cells as well as endothelia. SMA and desmin stained muscularis mucosa, which displayed the tumor infiltrated into lamina propria.

The patient received no adjuvant therapies and remained no recurrence in two years' follow-up.

Discussion And Conclusions

GP is a rare neuroendocrine tumor and up to three hundred cases have been reported until now. GPs affect individuals ranging from 15 to 84 years old with mean of about 53 years old, and are a little more prevalent in males with a male-to-female ratio of 1.5:1 [1]. A majority of GPs were documented to be located in the duodenum, accounting for nearly 90%. Involvement of other sites, such as spinal cord, respiratory system and digestive tracts was also reported [2].

The presenting symptoms and complaints of GPs in digestive tracts include gastrointestinal bleeding, abdominal pain or anemia and so on, which have no reliably diagnostic signs. Imaging examinations always demonstrates a mass lesion [3].

GPs range in size from 0.5 cm to 10 cm with average 2.5 cm in maximum diameter. Pathological investigation always displays a well-circumscribed, non-encapsulatedtumor whereas some cases are infiltrative focally or even mostly. GPs in duodenum are located or anchored in submucosa, expanding to nearby lamina propria or muscularis propria [2]. Therefore, preoperative pathological diagnosis is difficult through endoscopic biopsy due to relatively deep location, and definite diagnosis requires resection of the mass [4].

GP consists of three distinct cellular elements, including the epithelioid, ganglion-like and spindle cells [5]. The epithelioid cells have eosinophilic abundant cytoplasm and a round nucleus with inconspicuous or conspicuous nucleoli. They arranged in nest or zellballen pattern. Immunohistochemically, Syn and CgA are positive, and S-100 and SOX-10 are positive in sustentacular cells around. In sum, they resemble paraganglioma in cytological, architectural and immunostaining features. The ganglion-like cells are larger than the epithelioid cells, and of abundant cytoplasm and eccentric vesicular nuclei with prominent round nucleoli. They are always scattered or sometimes merged into epithelioid or spindle cellular areas, individually or arranging in small clusters. The immunophenotypes of the ganglion-like cells are similar

with those of the epithelioid cells, while NF is positive uniquely. The spindle cells arrange in fascicular clusters, and are bland in morphology and positive for S-100 and SOX-10, which resemble neurofibroma. The neoplasm is absent from mitosis and necrosis.

The proportion of the three cellular types is variable. In tumors predominant of spindle cells, the differential diagnosis includes spindle cell neoplasms especially schwannoma and gastrointestinal stromal tumor (GIST) [6]. The presence of epithelioid and ganglion-like cells, although perhaps rare, is the most important clue against schwannoma. Negative immunohistochemical expression for DOG-1 and CD117 provides compelling evidence against GIST.

In tumors predominant of ganglion-like or epithelioid cells, the differential diagnosis includes epithelial tumors, melanoma and well-differentiated neuroendocrine tumors. The first two neoplasms are supposed to be excluded by immunohistochemistry of epithelial or melanic markers. Since the concept was introduced by the World Health Organization (WHO) classification in 2010, neuroendocrine tumor (NET) has been widely diagnosed according to mitotic activity and Ki-67 proliferation index. GP is generally classified among NETs [7]. However, diversity of GP is different from relative consistence of NET in morphology, and GP has a more indolent clinical behavior and improved prognosis than NET [8]. Thus, GP is supposed to be differentiated from NET Grade 1.

The entity of GP remains a problem. It is noted that paraganglioma is a distinct entity among NET menu, which is not graded according to proliferation index. Some authors pointed out that histological differences between pheochromocytoma-ganglioneuromas and GPs were not clear [9]. Some areas of ganglioneuroma or ganglion-like cells were reported to be present in paragangliomas. In our opinion, since pathology of GP is supposed to be divided into two neoplastic proportions, paraganglioma and ganglioneuroma, GP is preferred as paraganglioma-ganglioneuroma, a kind of composite paraganglioma. Thus immature ganglion cells are supposed to be explored to exclude possibility of paraganglioma-neuroblastoma, especially in the young cases.

Origin of GP need be elucidated. GP is always located in submucosa, inducing hypothesis of origin related with meissner plexus [10]. Recent studies and our report displayed that the epithelioid cells expressed PR just as the same as pancreatic isletcells, which indicated that GP may originate from pancreas islet remnant or ectopia [2].

Although clinical behavior of GP is usually benign, up to 10% of cases occurred regional lymph node metastasis and a few were reported to occur distant metastasis to bone, liver or pelvic cavity [11]. Age, tumor size and depth of invasion appear to be related with metastasis [2]. The general immunohistochemical prognostic factors in NETs, such as Ki-67, P53 and Bcl-2, are not indicative for malignant potential. It is noted that all the three cellular components are supposed to be present in metastasis. The patients with metastasis have favorable prognosis with long survival periods, whereas one case followed an aggressive clinical course and died of the disease [11]. Endoscopic resection of duodenal GP appears to be enough for most cases, while additional surgery was managed in cases for

positive margin. Adjuvant therapies, including chemotherapy and irradiation appear no effect and necessity even in cases with metastasis.

In conclusion, we presented a rare case of 51-year-old malewith GP as a polyp in the descending portion of duodenum. Pathological examination showed aneoplasm located in submucosa, infiltrating into lamina propria. The tumor was composed of epithelioid, ganglion-like and spindle cells. Syn, MAP-2 and CgA were positive in epithelioid and ganglion-like cells in variety and NF highlighted the ganglion-like cells. S-100 and SOX-10 were positive in the sustentacular cells around the epithelioid cells and spindle cell proliferation. PR was also positive. GP is supposed to be distinguished with NET G1 and designated as paraganglioma-ganglioneuroma, a kind of composite paraganglioma. Most GPs displayed benign clinical biological behaviors and a few occurred regional lymph node metastasis or distant metastasis. A large majority of cases follow favorable prognosis, even with metastasis.

Abbreviations

GP: Gangliocytic paraganglioma

EMA: epithelial membrane antigen

Syn: Synaptophysin

MAP-2: Microtubule associated protein-2

CgA: Chromogranin A

NF: Neurofilament

PR: Progesterone receptor

ER: Estrogen receptor

GIST: Gastrointestinal stromal tumor

NET: Neuroendocrine tumor

Declarations

Acknowledgements

Not applicable.

Authors' Contributions

JLand LW collected the clinical information, made the pathological diagnosis and made up the manuscript. PZ performed immunohistochemistry. All authors read and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

The dataset supporting the conclusion of this article is included within the article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the consent form is available for review by the Editor of Diagnostic Pathology.

Competing interests

The authors declare that they have no competing interests.

References

1. Okubo Y, Yoshioka E, Suzuki M, Washimi K, Kawachi K, Kameda Y, Yokose T. Diagnosis, pathological findings, and clinical management of gangliocytic paraganglioma: a systematic review. Front Oncol. 2018, 8:291.
2. Okubo Y, Wakayama M, Nemoto T, Kitahara K, Nakayama H, Shibuya K, Yokose T, Yamada M, Shimodaira K, Sasai D, Ishiwatari T, Tsuchiya M, Hiruta N. Literature survey on epidemiology and pathology of gangliocytic paraganglioma. BMC Cancer. 2011, 11:187.
3. Buetow PC, Levine MS, Buck JL, Pantongrag-Brown L, Emory TS. Duodenal gangliocytic paraganglioma: CT, MR imaging, and US findings. Radiology. 1997, 204(3):745-7.
4. Kwon J, Lee SE, Kang MJ, Jang JY, Kim SW. A case of gangliocytic paraganglioma in the ampulla of Vater. World J Surg Oncol. 2010, 8:42.
5. Perrone T, Sibley RK, Rosai J. Duodenal gangliocytic paraganglioma. an immunohistochemical and ultrastructural study and a hypothesis concerning its origin. Am J Surg Pathol. 1985, 9(1):31-41.
6. Loftus TJ, Kresak JL, Gonzalo DH, Sarosi GA Jr, Behrns KE. Duodenal gangliocytic paraganglioma: a case report and literature review. Int J Surg Case Rep. 2015, 8C:5-8.
7. Tatangelo F, Cantile M, Pelella A, Losito NS, Scognamiglio G, Bianco F, Belli A, Botti G. Duodenal gangliocytic paraganglioma, a rare entity among GEP-NET: a case report with immunohistochemical and molecular study. Diagn Pathol. 2014, 9:54.

8. Okubo Y. Gangliocytic paraganglioma: an overview and future perspective. World J Clin Oncol. 2019, 10(9):300-302.
9. de Montpréville VT, Mussot S, Gharbi N, Dartevelle P, Dulmet E. Paraganglioma with ganglioneuromatous component located in the posterior mediastinum. Ann Diagn Pathol. 2005, 9(2):110-4.
10. Shekitka KM, Sobin LH. Ganglioneuromas of the gastrointestinal tract. Relation to Von Recklinghausen disease and other multiple tumor syndromes. Am J Surg Pathol. 1994, 18(3):250-7.
11. Li B, Li Y, Tian XY, Luo BN, Li Z. Malignant gangliocytic paraganglioma of the duodenum with distant metastases and a lethal course. World J Gastroenterol. 2014, 20(41):15454-61.

Figures

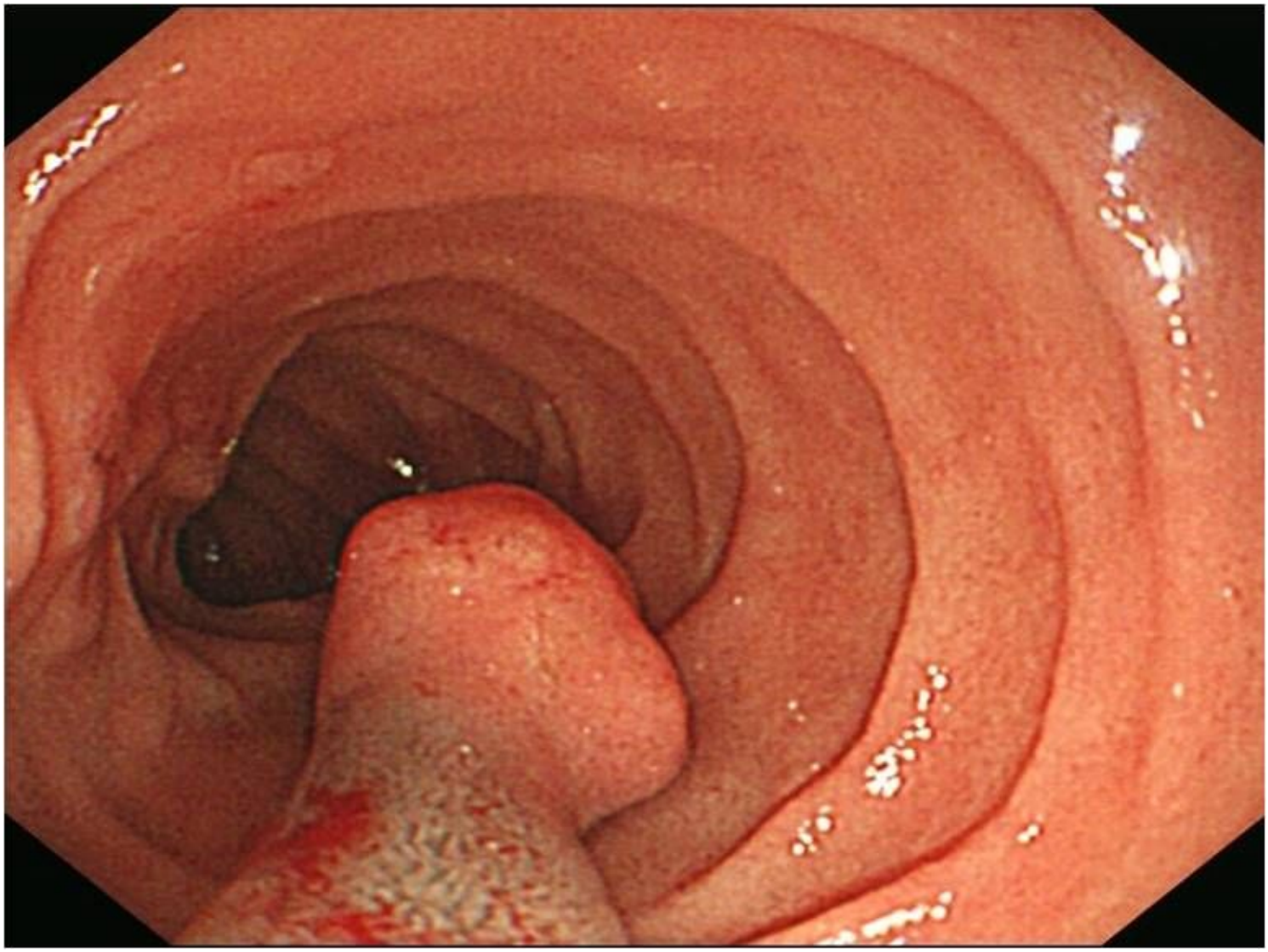

Figure 1

Asessilepolyp measured about 1cm in diameter with smooth surface was found in gastrointestinal endoscopy.

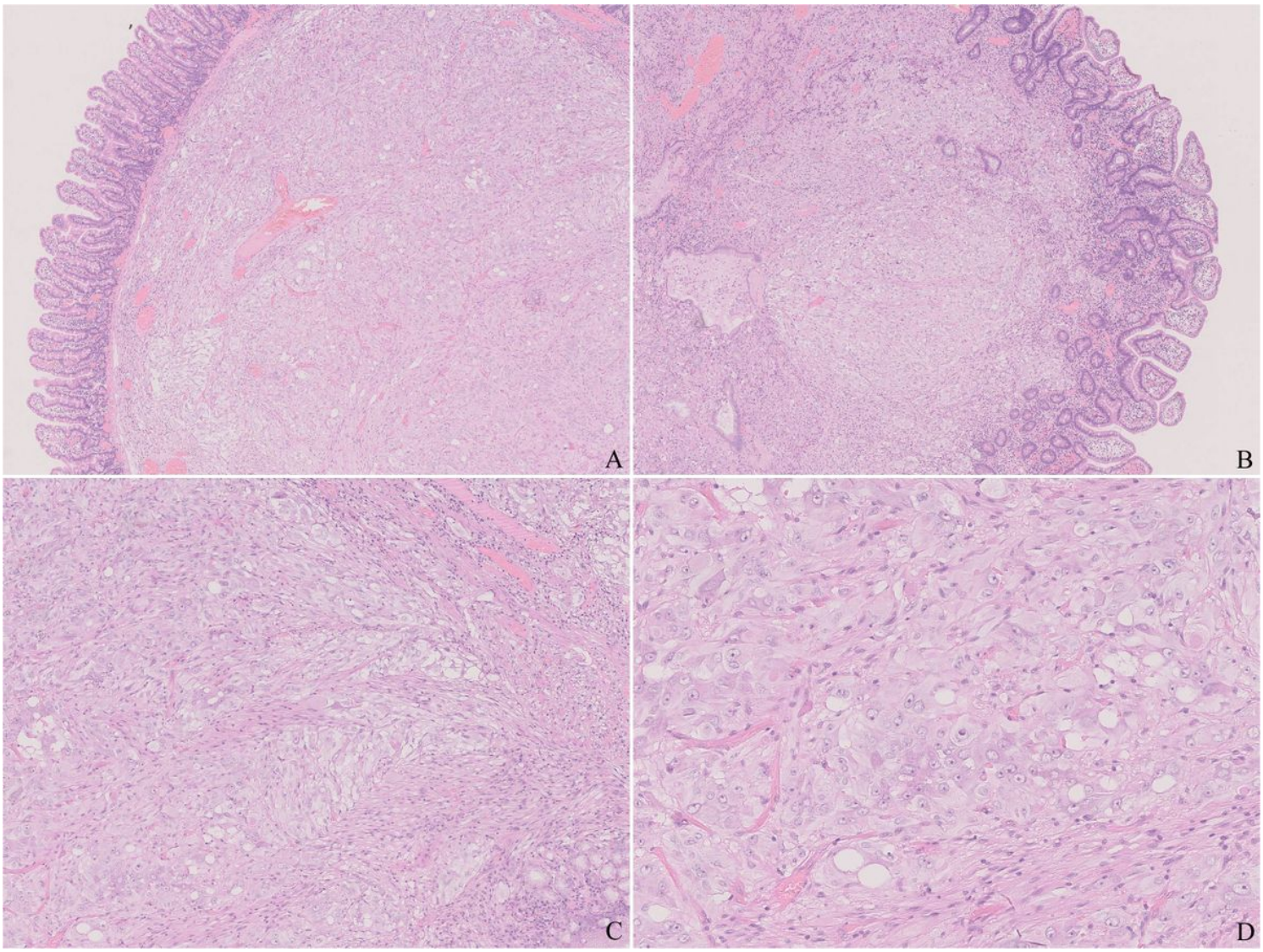

Figure 2

A. The tumor was well-circumscribed, non-encapsulatedandlocated in submucosa. B. The tumor infiltrated into lamina propria focally. C. The tumor was composed of epithelioid cells, ganglion-like cells and spindle cells. Note muscularis mucosae in the upper right different from the neoplastic spindle cells. D. The epithelioid cells have abundant eosinophilic cytoplasm and a round nucleus with inconspicuous or conspicuousnucleoli. Note the ganglion-like cell in the center, which was larger in shape and nucleus with prominent eccentric nuclei.

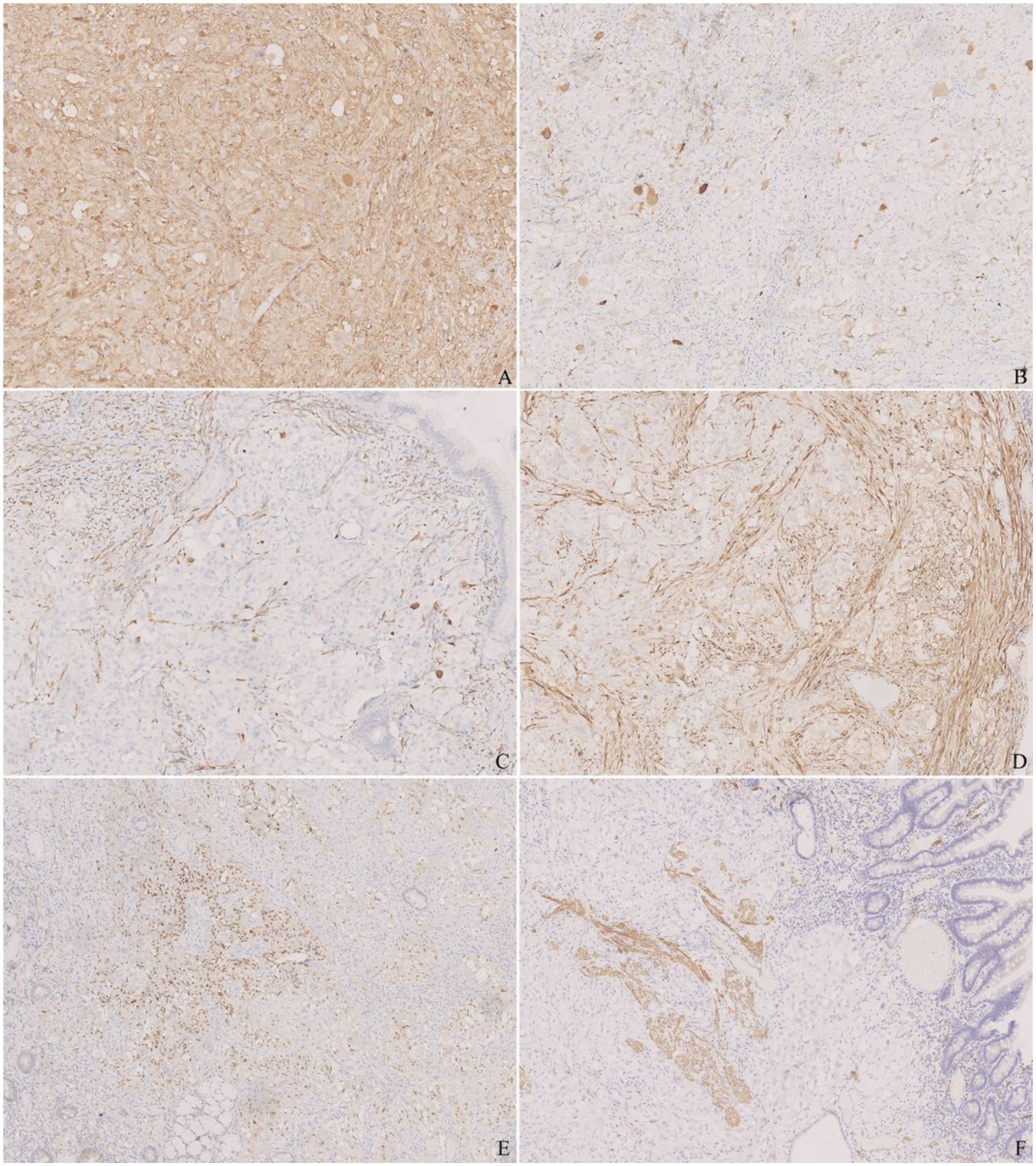

Figure 3

A. Syn was diffusely positive for the epithelioid cells and highlighted the ganglion-like cells. B. CgA was positive for the epithelioid cells and highlighted the ganglion-like cells, but the number of positive cells was less than that in Syn. C. NF stained some ganglion-like cells and neoplastic spindle cells. D. S-100 stained sustentacular cells around the epithelioid cells and the neoplastic spindle cells. E. PR was

positive in some epithelioid cells. F. Desmin stained muscularis mucosa, which displayed the tumor infiltrated into lamina propria.