Case Report **OPEN ACCESS**

Surgical management of endoscopically unresectable duodenal gangliocytic paraganglioma in a patient with partial upper gastrointestinal obstruction

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Abstract

Context: Gangliocytic paragangliomas are unusual and often misunderstood tumors that occur almost exclusively in the second portion of the duodenum, although they have been described in other sites such as the urinary bladder, spermatic cord, prostate, urethra, uterus and scalp. We describe our experience with the surgical management of an endoscopically unresectable gangliocytic paraganglioma located in the third part of the duodenum causing a partial upper gastrointestinal obstruction. **Case Report:** A fifty-two-year-old male presented to the Geisinger clinic with a four-year history of postprandial projectile vomiting associated with epigastric discomfort. Computed tomography scan revealed an oval-shaped filling defect in the third part of the duodenum. Endoscopic ultrasonography showed a 22 x 16 x 35 mm submucosal mass that was not amenable to an endoscopic resection. Exploratory laparotomy revealed an absence of extraduodenal involvement. A long-stalked tumor was successfully excised and extruded through a longitudinal duodenotomy. The pathology report showed a gangliocytic paraganglioma with negative lymph nodes. **Conclusions:** In patients presenting with prolonged recurrent attacks of vomiting, diagnostic workup to exclude anatomic causes is mandatory. Gangliocytic paraganglioma must be considered in the differential diagnosis of an intraduodenal tumor.

Keywords: Paraganglioma, duodenum, surgical management.

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Introduction

Gangliocytic paraganglioma is a rare neuroendocrine tumor arising from the parenchymal cell of the autonomic nervous system [1]. Nakamura T et al has reported that it occurs almost exclusively near the Ampulla of Vater even though it had been described in various locations such as the urinary bladder, gallbladder, uterus, scalp, spermatic cord, prostate, urethra, and mesentery [2-7]. These tumors are typically benign, however, they could metastasize to regional lymph nodes with unknown consequences [8].

Few published reports have shown excellent long-term results without evidence of recurrence or distant metastasis following local excision, prompting many gastroenterologists to pursue the less invasive endoscopic mucosal resection (EMR). However, for an endoscopically unresectable tumor, an open surgical resection is necessary. In this study, we describe our experience with an endoscopically unresectable gangliocytic paraganglioma in the third portion of the duodenum that required an open transduodenal surgical excision.

Case Report

A fifty-two-year-old male presented with a four-year history of intermittent upper epigastric discomfort and projectile vomiting following meals. Past medical and surgical histories were only significant for a laparoscopic cholecystectomy a year prior which failed to relieve his

symptoms. The patient underwent a computed tomography (CT) scan which demonstrated an oval-shaped filling defect in the third portion of the duodenum without evidence of metastatic disease [Fig. 1]. Octreotide scan revealed an increased activity in the target area. Serotonin and chromogranin assays, however, showed normal values. Upper gastrointestinal endoscopy [Fig. 2] and endoscopic ultrasonography using a radial probe [Fig. 3] discovered a 22 x 16 x 35 mm elongated smooth-edged heterogenous submucosal lesion extending down to the muscularis propria without evidence of nodal enlargement or invasion of the surrounding structures. Endoscopic fine needle aspiration biopsy initially suggested the diagnosis of gastrointestinal stromal tumor (GIST) based on cells positivity for synaptophysin [Fig.4], neuron specific enolase [Fig.5], and chromogranin [Fig.6] using immunoperoxidase staining. Differential diagnosis includes carcinoid tumor, paraganglioma, and adenocarcinoma of either the pancreatic head or the duodenum.

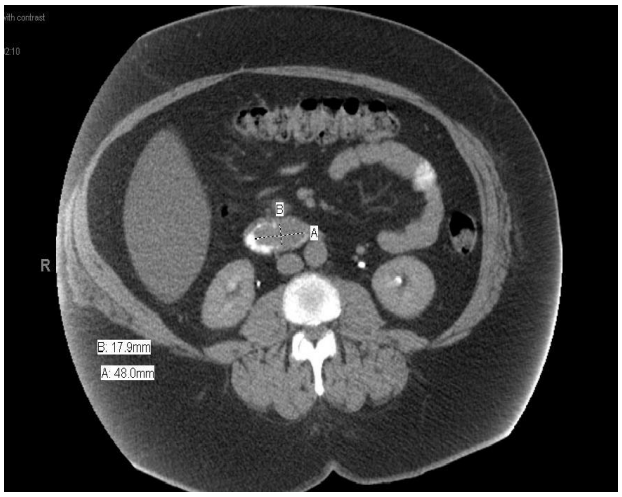

Fig. 1 CT scan figure with intravenous and oral contrast showing 17.9 x 48 mm filling defect in the third portion of the duodenum causing an upper gastrointestinal obstruction. No evidence of lymph nodes or adjacent organ metastasis seen.

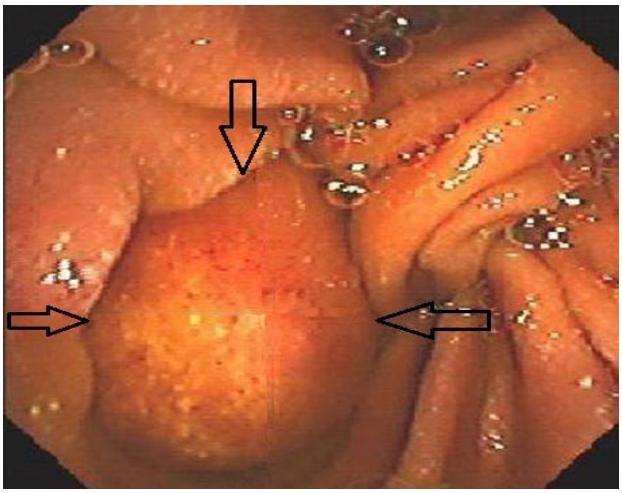

Fig. 2 Upper GI endoscopy figure showing the intraduodenal polypoid submucosal tumor with intact mucosa. No evidence of mucosal ulceration/bleeding seen.

Due to position, size, and abutment of the tumor into the muscularis propria, an endoscopic resection was not feasible. An exploratory laparotomy was performed in which a long-stalked tumor was successfully excised through a 4-cm longitudinal duodenotomy. No evidence of other intraabdominal pathology was seen.

The duodenotomy was primarily repaired followed by placement of a T-tube duodenostomy and a postpyloric nasogastric tube for duodenal decompression. Early in the postoperative period, the patient made a progressive recovery without events. The nasogastric tube was removed on postoperative day 5. Unfortunately, a pulmonary embolism occurred on POD 10 despite properly administered prophylactic anticoagulation. The final pathology report showed a completely excised gangliocytic paraganglioma with negative nodes.

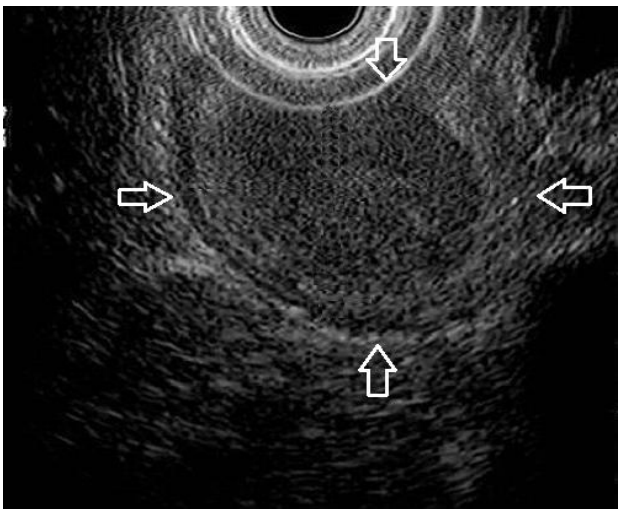

Fig. 3 Endoscopic ultrasound using a radial probe showing the tumor in the duodenal submucosa extending down to the muscularis propria.

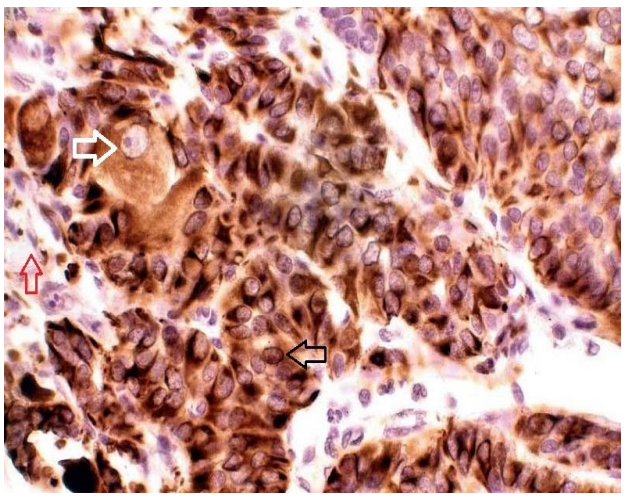

Fig. 4 Histopathologic appearance of the tumor demonstrating epitheloid, spindle and ganglion cells using synaptophysin neuroendocrine marker (Type of cells are indicated by the arrows). White arrow: Ganglion cell, Black arrow: Epitheloid cell, Red arrow: Spindle cell.

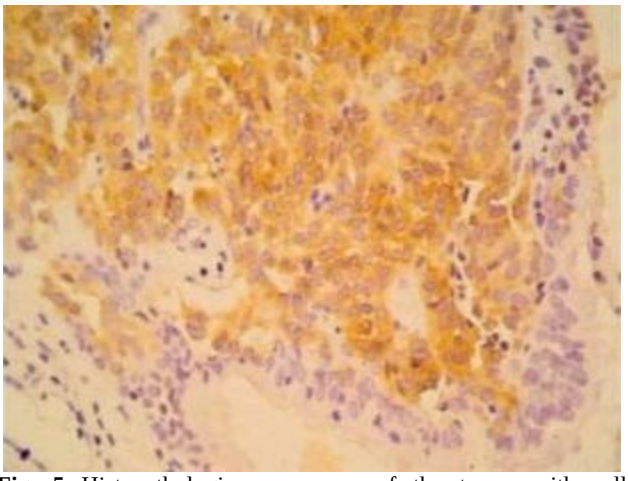

Fig. 5 Histopathologic appearance of the tumor with cell reactivity to neuron spesific enolase.

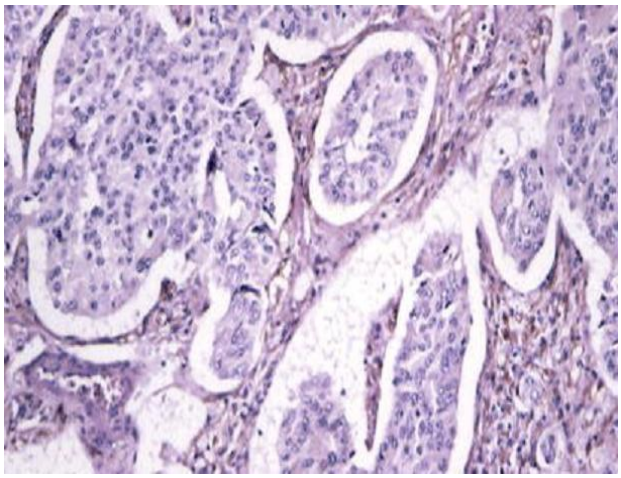

Fig 6. Histopathologic appearance of the tumor with cell reactivity to chromogranin.

Table 1. Literature review on previously published duodenal gangliocytic paragangliomas.

						Nodal		Immunohisto-chemical Findings		
Authors	Locations	Age	Sex	Clinical Presentation	Treat.	Metast.	Recurence	Epitheloid Cells	Ganglion Cells	Spindle Cells
Altavilla et al [9]	Ampulla of Vater	34/63 *	M	Epigastric discomfort and melena	Whipple	(-)	NO	SNP, CHG, NSE	SNP, NSE, NF	S-100, NSE, NF
Hashimoto et al [10]	Ampulla of Vater	47	M	Incidental finding	Whipple	(+)	NO	Cytokeratin	Not reported	S-100
Inai et al [13]	Ampulla of Vater	17	M	Massive hematemesis	Whipple	(+)	NO	NSE, NF	NSE, NF	S-100, NSE, NF
Dookan et al [16]	2nd part of duodenum	41	M	Abdominal pain	Whipple	(+)	YES	SNP	SNP	S-100, NSE, NF
Morita T et al [17]	2nd part of duodenum	53	M	Incidental finding	EMR	(-)	NO	CHG, NSE, SNP, NF	NSE, SNP	NSE, SNI NF
Scheithauer BW et al [18]	2nd (10 pat.)/3rd part of duodenum (1 pat.)	56**	M/F 8/3	Gastrointestinal bleeding	Local Resection	(-)	NO	SNP, CHG	Somatostation Serotonin	S-100
Sundararajan et al [19]	2nd part of duodenum	67	F	Common bile duct dilation	Whipple	(+)	NO	SNP, CHG	SNP	S-100
Sakuja et al [20]	Periampullary	33	M	R.hypochond. pain	Whipple	(-)	NO	CHG, Somatostatin	SNP, NSE	S-100, SNP
Collina et al [21]	2nd part of duodenum	71	F	Abdominal pain,vomitting weight loss	Whipple	(-)	NO	NSE, NF, CHG, Somatostatin	NSE, NF, Somatostatin,	S-100, NSE, NF
Wong A [22]	Periampullary	49	F	Melena	Whipple	(+)	NO	SNP, CHG, Cytokeratin	SNP	S-100
Sanchez-Perez MA [23]	2nd part of duodenum	70	F	Abdominal pain	Local Resection	(-)	NO	SNP, CHG, NF	NF	S-100, NF
Chen J [24]	Ampulla of Vater	67	M	Positive occult blood test, anemia	Local Resection	(-)	NO	NSE, NF	NSE, NF	S-100
Kwon J [25]	Ampulla of Vater	56	M	Melena	Whipple	(-)	NO	SNP,NSE	NSE	S-100
Okubo Y [26]	Ampulla of Vater	61	M	Melena	Whipple	(+)	NO	SNP, Somatostation	SNP	S-100
Barbareschi M at al [27]	Ampulla of Vater	56	F	Abdominal pain	Whipple	(-)	NO	SNP, Leu-7, Somatostatin	NF, CHG, Myelir Desmin,	S-100, Vimentin
Imai S et al [28]	2nd part of duodenum	65	F	Melena	Local Resection	(-)	NO	SNP, CHG	SNP	S-100
Kubota K et al [29]	Paraduodenum	58	F	Retroperitoneal mass	Whipple	(-)	NO	SNP, CHG	SNP	S-100
Ohtsuki Y et al [30]	Ampulla of Vater	65	M	Incidental finding	Whipple	(-)	NO	CHG, PP Somatostatin,	SNP, NSE, CD-56	S-100

* Report of 2 patients, age 34 and 63, ** Report of 11 patients, average age 56, EMR = Endoscopic Mucosal Resection, SNP =Synaptophysin, CHG = Chromogranin, NSE = Neuron Spesific Enolase, NF = Neurofilament, PP = Pancreatic Polypeptide.

Discussion

Gangliocytic paraganglioma is a neuroendocrine tumor derived from the autonomic nervous system ganglia. It is a rare but potentially malignant tumor that can be found in various locations. Other than as an incidental finding

during endoscopy or autopsy, gangliocytic paraganglioma most commonly presents as abdominal pain and upper gastrointestinal (GI) bleeding [7]. The average age of presentation is 54 with equal gender distribution [9]. On rare occasions, a clinical picture of obstructive jaundice is present. Right upper quadrant discomfort and dyspepsia frequently lead physicians to an incorrect diagnosis and treatment of peptic ulcer disease [10, 11].

On upper endoscopic evaluation, the tumor is usually polypoid, but may be sessile or pedunculated. Mucosal ulceration causing upper gastrointestinal hemorrhage can also occur. The average size is 2.9 cm (range 0.5 to 10)[12]. The lesions are typically well circumscribed, located submucosally, nonencapsulated and may involve the muscularis propria [1, 13]. Endoscopic ultrasound (EUS) has an accuracy of 70-90% in staging and it can reliably determine tumor depth or invasion to adjacent structures [14].Previously published reports on duodenal gangliocytic paragangliomas are summarized in Table 1.

Histologically, gangliocytic paraganglioma is characterized by a mixture of spindle cells, ganglion-like cells, and epitheloid cells. The presence of 3 cell types distinguishes gangliocytic paragangliomas from carcinoids which exclusively consist of epitheloid cells, and also from GIST that does not demonstrate the ganglion-like cells component. On immunohistochemical analysis, epitheloid cells show reactivity to the neuroendocrine markers such as chromogranin, synaptophysin, neurofilament, neuron spesific enolase (NSE) and somatostatin [11,12,15]. The ganglion cells share several immunohistochemical characters with the epitheloid cells in which they show reactivity with synaptophysin, neurofilament and NSE [13]. The spindle cells typically stain with S-100 protein.

Approximately 10-20% of duodenal paragangliomas behave in malignant fashion characterized by regional lymph node metastasis of the epitheloid cell component or local tumor recurrences [10,13,16]. Common sites of metastasis include the bone, liver, lung and central nervous system. Treatment modality for this tumor consists of an endoscopic resection, a local/limited surgical resection or the pancreaticoduodenectomy/Whipple procedure. Indications for performing the endoscopic mucosal resection for duodenal tumors are less well defined compared to those for esophageal and gastric tumors. There is no definitive guideline regarding the size of duodenal tumor for which an EMR or snare polypectomy should not be attempted. The following conditions preclude the EMR: Difficult access to the mass, tumor depth beyond the submucosal layer, inability to obtain an intact specimen for an accurate histopathologic evaluation of a potentially malignant lesion, and the presence of lymphovascular/surrounding structure invasion. Morita T et al reported a successful EMR for a 2.0 x 1.8 cm duodenal paraganglioma with absence of abnormal findings in the duodenal wall, regional lymph nodes, bile duct, and pancreatic duct [17].

When an endoscopic treatment fails to achieve an adequate tumor removal, a local surgical resection would be the next step before a Whipple procedure. This procedure is known to be complex with higher morbidity and mortality rates. Tumors located in the second portion of the duodenum with close proximity to the ampulla-common bile duct-pancreatic duct complex, however, have a higher chance of requiring a Whipple procedure as shown in Table 1. A complete preoperative workup including a high-quality CT scan is important since the presence of lymphovascular and surrounding structure invasion leaves pancreaticoduodenectomy as the only option for potential cure.

At the present time, Whipple procedure remains the main modality of treatment even though Scheithauer BW et al reported a favorable 8.3 year follow-up result without evidence of tumor recurrence or metastasis following a local excision or snare polypectomy in a total of 11 patients [18]. This new paradigm suggested that the less invasive treatment options such as endoscopic resection and limited/local surgical excision are appropriate, although a further randomized prospective clinical investigation is required [15,18,19].

Conclusion

In a patient presenting with prolonged recurrent attacks of vomiting, diagnostic workup to exclude anatomic causes is important. Gangliocytic paraganglioma must be considered in the differential diagnosis of an intraduodenal tumor. Local tumor excision via longitudinal duodenotomy followed by T-tube placement is an option for an endoscopically unresectable duodenal paraganglioma.

References

1. Lack E. Tumors of the adrenal gland and extra-adrenal paraganglioma. In: Atlas of tumor pathology, series 3, fasc 19. Washington DC: Armed Forces Institute of Pathology; 1997
2. Zhou M, Epstein Jl, Young RH. Paraganglioma of the urinary bladder; a lesion that may be misdiagnosed as urothelial carcinoma in transurethral resection specimens. Am J Surg Pathol 2004; 28:94-100.
3. Miller TA, Weber TR, Appleman HD. Paraganglioma of the gallbladder. Arch Surg 1972;105:637-639.
4. Young TW, Trasher TV. Nonchromaffin paraganglioma of the uterus. A case report. Arch Pathol Lab Med 1982; 106:608-609.
5. Saadat P, Cesnorek S, Ram R, et al. Primary cutaneous paraganglioma of the scalp. J Am Acad Dermatol 2006;54:S220-S223.
6. Shibahara J, Goto A, Niki T, at al. Primary pulmonary paraganglioma. Report of a functioning case with immunohistochemical and ultrastructural study. Am J Surg Pathol 2004;28:825-829.
7. Nwakakwa V, Kahaleh M, Bennett A, et al. EMR of ampullary gangliocytic paragangliomas. Gastrointest Endosc 2005;62(2):318-322.

8. Bucher P, Mathe Z, Buhler L, et al. Paraganglioma of the ampulla of Vater: a potentially malignant neoplasm. Scand J Gastroenterol 2004; 3:291-295.
9. Altavilla G, Charelli S, Fassina A. Duodenal periampullary paraganglioma: report of two cases with immunohistochemical and ultrastructure study. Ultrastruc Pathol 2001; 25:137-145.
10. Hashimoto S, Kawasaki S, Matasuzawa K, et al. Gangliocytic paraganglioma of the papilla of Vater with regional lymph node metastasis. Am J Gastroenterol 1992; 87: 1216-1218.
11. Burke AP, Helwig EB. Gangliocytic paraganglioma. Am J Clin Pathol 1989; 92:1-9.
12. Hamid QA, Bishop AE, Rode J, et al. Duodenal gangliocytic paragangliomas: a study of 10 cases with immunocytochemical neuroendocrine markers. Hum Pathol 1986; 17: 1151-1157.
13. Inai K, Kobuke T, Yonehara S, et al. Duodenal gangliocytic paraganglioma with lymph node metastasis in a 17-year-old-boy. Cancer 1989; 63: 2540-2545.
14. Ingram M, Arregui ME. Endoscopic ultrasonography. Surg Clin N Am 2004; 84: 1036-1059.
15. Smithline AE, Hawes RH, Kopecky KK, et al. Gangliocytic paraganglioma, a rare cause of upper gastrointestinal bleeding. Endoscopic ultrasound findings presented. Dig Dis Sci 1993; 39:173-177.
16. Dookhan DB, Miettinen M, Finkel G, et al. Recurrent duodenal gangliocytic paraganglioma with lymph node metastases. Histopathology 1993; 22: 399-401.
17. Morita T, Tamura S, Yokoyama Y, et al. Endoscopic Resection of a Duodenal Gangliocytic Paraganglioma. Dig Dis Sci 2007; 52:1400-1404.
18. Scheithauer BW, Nora FE, LeChago J, et al. Duodenal gangliocytic paraganglioma. Clinicopathologic and immunocytochemical study of 11 cases. Am J Clin Pathol 1986; 86: 559-565.
19. Sundararajan V, Robinson-Smith T, Lowy AM. Duodenal gangliocytic paraganglioma with lymph node metastasis. A case report and review of the literature. Arch Pathol Lab Med 2003; 127:e139-e141.
20. Sakuja P, Malhotra V, Gondal R, et al. Periampullary gangliocytic paraganglioma. J Clin Gastroenterol 2001; 33:154-156.
21. Collina G, Maiorana A, Trentini GP. Duodenal paragangliocytic paraganglioma. Case report with immunohistochemical study on expression of keratin polypeptides. Histopathology 1991;19:476-478.
22. Wong A, Miller AR, Metter J. Locally Advanced duodenal gangliocytic paraganglioma treated with adjuvant radiation therapy: case report and review of the literature. World J Surg Oncol 2005; 3:15.
23. Sanchez-Perez MA, Luque-de-leon E, Munoz-Juarez M, et al. Duodenal gangliocytic paraganglioma. Can J Surg 2009; 52: E27–E28.
24. Chen J, Sharon E, Morgenstern S, et al. Local surgical resection of gangliocytic paraganglioma of the duodenal papilla. IMAJ 2009;11:311-312.
25. Kwon J, Lee SE, Kang MJ, et al. A case of gangliocytic paragangloma in the ampulla of Vater. World J Surg Oncol 2010; 8:42.
26. Okubo Y, Yokose T, Tuchiya M, et al. Duodenal gangliocytic paraganglioma showing lymph node metastasis: A rare case report. Diagn Pathol 2010; 5: 27.
27. Barbareschi M, Frigo B, Aldovini D, et al. Duodenal gangliocytic paraganglioma. Report of a case and review of the literature. Virchow Arch A Pathol Anat Histopathol 1989; 416 (1):81-99.
28. Imai S, Kajihara Y, Komaki K, et al. Paraganglioma of the duodenum: a case report with radiological findings and literature review. Br J Radiol 1990; 63(756): 975-977.
29. Kubota K, Kato S, Mawatari H, et al. Risky endoscopic ultrasonography-guided fine-needle aspiration for asymptomatic retroperitoneal tumors. Dig Endosc 2010; 22(2):144-146.
30. Ohtsuki Y, Watanabe R, Kimura M, et al. Immunohistochemical and electron microscopic studies of a case of duodenal gangliocytic paraganglioma. Med Mol Morphol 2009; 42(4): 245-249.