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Gangliocytic paraganglioma: An overview and future perspective

Yoichiro Okubo

ORCID number: Yoichiro Okubo (0000-0002-7079-4454).

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Yoichiro Okubo, Department of Pathology, Kanagawa Cancer Center, Yokohama, Kanagawa 241-8515, Japan

Corresponding author: Yoichiro Okubo, MD, PhD, Assistant Professor, Department of Pathology, Kanagawa Cancer Center, 2-3-2 Nakao, Asahi-Ku, Yokohama, Kanagawa 241-8515, Japan. yoichiro0207@hotmail.com

Telephone: +81-45-5202222

Fax: +81-45-5202202

Abstract

Gangliocytic paraganglioma (GP) is rare neuroendocrine tumor (NET) with a good prognosis that commonly arising from duodenum. Although the tumor is characterized by its unique triphasic cells (epithelioid, spindle, and ganglion-like cells), the proportions of these three tumor cells vary widely from case to case, and occasionally, morphological and immunohistochemical similarities are found between GP and NET G1 (carcinoid tumors). Further, GP accounts for a substantial number of duodenal NETs. Therefore, GP continues to be misdiagnosed, most often as NET G1. However, GP has a better prognosis than NET G1, and it is important to differentiate GP from NET G1. In this article, I wish to provide up-to-date clinicopathological information to help oncologists gain better insight into the diagnosis and clinical management of this tumor.

Key words: Neuroendocrine tumor; Gangliocytic paraganglioma; Progesterone receptor; Pancreatic polypeptide; Literature survey

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Core tip: Although gangliocytic paraganglioma (GP) has been regarded as a rare neuroendocrine tumor (NET), GP accounts for a significant number of duodenal NETs. Morphological and immunohistochemical similarities between GP and NET G1 often lead to misdiagnoses of both. However, the prognosis is often better for patients with GP than for those with NET G1. Therefore, it is important to differentiate GP from NET G1. This editorial provides up-to-date data on the clinicopathological characteristics of GP and emphasizes the importance of confirming progesterone receptor and pancreatic polypeptide immunoreactivity for differentiating GP from NET G1.

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INTRODUCTION

Gangliocytic paraganglioma (GP) is rare tumor with a good prognosis that commonly arising from the small intestine (especially, duodenum). Gastrointestinal neuroendocrine tumors (NETs) have a low, but gradually increasing, incidence worldwide^[1]. Specifically, the overall prognosis for patients with gastrointestinal NETs has improved and has been favorable^[2], but some investigators have reported 5-year survival rates of patients with NET G1 of approximately 80%^[3]. Although few patients with liver metastases^[4-7] and one with fatal GP^[6] have been reported, GP shows a benign course more frequently than NET G1.

Thus, it is important to distinguish between GP and NET G1. However, morphological and immunohistochemical similarities between GP and NET G1 may lead to misdiagnosis^[8,9]. Thus, oncologists, clinicians, and pathologists should be aware of the concept of GP because our previous study suggests that GP accounts for a consistent proportion of NETs arising from the duodenum^[10]. In this editorial, I would like to discuss the overview and future perspectives of GP, on the basis of our up-to-date systematic review.

Data from 263 patients with GP were collected and analyzed^[11]. The vast majority of GPs arose in the duodenum (89.7%). The mean age of patients with GP was 53.5 years. A slight male-to-female predominance was observed, with a ratio of approximately 3:2. Gastrointestinal bleeding and abdominal pain were commonly reported (47.9% and 44.7%, respectively), and many patients were asymptomatic. The mean tumor size was 25.7 mm, and notably, the proportion of the three characteristic GP cells (epithelioid, spindle, and ganglion-like cells) varied considerably from case to case. For a correct diagnosis of GP, pathologists should be aware of the histopathological heterogeneity of this tumor.

Lymph node and liver metastases were observed in approximately 10% and 1% of patients with GP, respectively. Notably, our statistical analysis showed that the depth of invasion was the most significant risk factor for lymph node metastases (tumor size has little effect on lymph node metastasis)^[11]. These findings and the associated histological heterogeneity indicate that GP may have hamartomatous characteristics.

To date, pancreaticoduodenectomy is the generally preferred treatment for GP. However, since GP grows slower than NET G1, less invasive procedures (especially endoscopic procedures) have gradually increased in popularity^[12]. In fact, in our systematic review, 27 patients underwent endoscopic procedures and showed favorable outcomes, with the exception of one patient who required additional surgery because of a positive surgical margin.

However, to perform less invasive procedures, a definite diagnosis of GP before surgery is essential. Unfortunately, it is difficult to diagnose GP based on a usual biopsy because of the inaccessibility of the tumor (GP is often in a submucosal layer or deeper) and the similarities between GP and NET G1. To solve the first problem, a boring biopsy may be effective because it obtains submucosal tissue. In fact, some patients were successfully diagnosed with GP following multiple boring biopsies^[13]. To solve the second problem, I wish to emphasize the usefulness of immunohistochemical examination of pancreatic polypeptide and progesterone receptor levels. GP epithelioid cells show positivity for both markers, and NET G1 shows negativity, and this difference helps distinguish between GP and NET G1. The main differences between GP and NET G1 are summarized in [Table 1](#).

CONCLUSION

Occasionally, GP is misdiagnosed as NET G1, and immunohistochemical examinations of progesterone receptor and pancreatic polypeptide levels help differentiate GPs. Accurate GP identification will facilitate the use of less invasive treatment procedures.

Table 1 Differences in gangliocytic paraganglioma and gastrointestinal neuroendocrine tumor G1

	Gangliocytic paraganglioma	Gastrointestinal neuroendocrine tumor G1
Predominant site of the primary tumor	Duodenum (approximately 90%)	Small intestine, but duodenal is relatively rare
5-yr survival rates	Excellent (approximately 100%)	Good (approximately 80%)
Incidence	Extremely rare	Relatively rare, but gradually increasing, incidence worldwide
Morphological findings obtained by surgery	Epithelioid, spindle, and ganglion-like cells	Nesting, trabecular pattern, and/or rosette formation with nuclear palisading
Immunohistochemistry (pancreatic polypeptide and progesterone receptor)	Epithelioid cells show positive reactivity for both.	Tumor cells show negative reactivity for both
Perspective	Accurate diagnosis of gangliocytic paraganglioma will facilitate the use of less invasive treatment procedures	

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