CASE REPORT

Open Access

Primary grade 2 neuroendocrine tumor of the ileal mesentery: a case report

Shigemi Morishita[1*], Shinichi Yoshida[1], Yasufumi Kamatani[1], Shinya Suzuhigashi[1], Masaki Kitou[1] and Takuma Nasu[2]

Abstract

Background: The prevalence and incidence of neuroendocrine tumors (NETs) are increasing worldwide. Primary mesenteric NETs are extremely rare. Solid tumors that arise in the mesentery are typically metastatic. We present an extremely rare case of a primary grade 2 NET (NET G2) in the ileal mesentery.

Case presentation: A 54-year-old man was referred to our hospital for further examination of a previously diagnosed right mesenteric tumor. Mild tenderness was noted on the right side of the abdomen, but there were no palpable masses. Fluorodeoxyglucose-positron emission tomography (FDG-PET) revealed slight FDG uptake (maximum standardized uptake value, 2.0) in the right abdomen, and a benign or low-grade malignant tumor was suspected. We extracted the ileal mesenteric tumor with an ileal resection (90 cm). The cut surface of the $55 \times 33 \times 33$ mm^3 tumor was pale yellowish-white. Immunohistochemistry revealed diffuse staining for synaptophysin and chromogranin A, and focal staining for CD56. The Ki-67 index was 3%. The final pathological diagnosis was NET G2. The patient's postoperative course was uneventful, and he developed no recurrence 1.5 years after surgery. Postoperative antitumor therapy was not performed for this patient because the histological diagnosis was NET G2, and it was determined that the tumor could be completely resected by surgery.

Conclusions: We report an extremely rare case of primary ileal mesenteric NET. Mesenteric tumors that show slight FDG uptake on FDG-PET examination should be considered well-differentiated NET.

Keywords: Neuroendocrine tumor G2, Mesenteric tumor, Ileum

Background

Neuroendocrine neoplasm (NEN) is a rare disease with a gradually increasing prevalence [1]. NENs are divided into well-differentiated neuroendocrine tumors (NETs) and poorly differentiated neuroendocrine carcinomas (NECs), based on the degree of tissue differentiation. Furthermore, according to the World Health Organization (WHO) classification 2019, it is classified as NET G1, G2, G3, and NEC G3 based on Ki-67, which is a proliferation marker that reflects prognosis (Table 1). We present an extremely rare case of a primary grade 2 NET (NET G2) in the ileal mesentery that demonstrated benign or low-grade malignant characteristics on preoperative fluorodeoxyglucose-positron emission tomography (FDG-PET).

Case presentation

A 54-year-old man was referred to our hospital after his previous doctor thoroughly examined him for right-sided abdominal pain. His previous diagnosis based on computed tomography (CT) was a right mesenteric tumor. Mild tenderness was noted on the right side of the abdomen, but there were no palpable masses. His medical history included diabetes mellitus and hypertension. Blood chemistry tests showed mild elevation of liver enzymes levels and elevated blood glucose and hemoglobin A1c
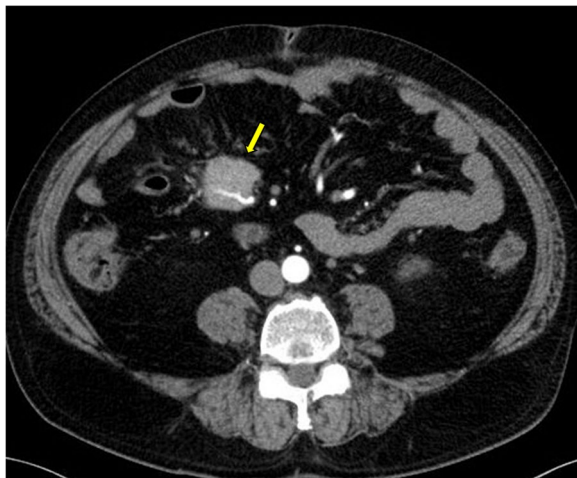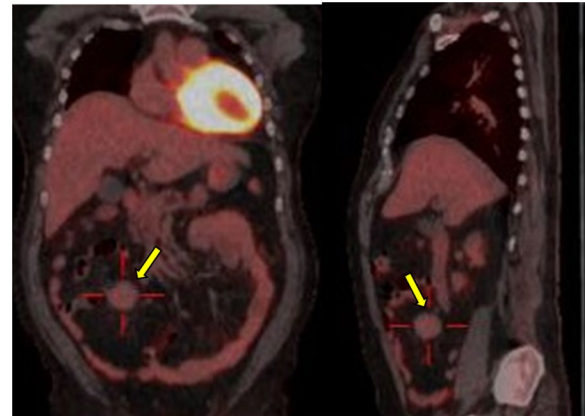
*Correspondence: sitamori1957@gmail.com
[1] Department of Surgery, Kagoshima Seikyou General Hospital, 5-20-10 Taniyama-chuou, Kagoshima City, Kagoshima 891-0141, Japan
Full list of author information is available at the end of the article

Morishita *et al. Surgical Case Reports*　　(2022) 8:146

Page 2 of 6

Table 1 Incidence of NEN in Japan in 2016 [3]

Primary tumor site	Diagnosed number in 2016	Adjusted incidence/100,000 people in 2016
Pancreas	1136	0.697
GI-NEN	5399	2.835
Esophagus	262	0.098
Stomach	1042	0.482
Duodenum	442	0.195
Jejunum/ileum	97	0.046
Appendix	105	0.074
Colon	278	0.118
Rectum	3173	1.835
All cases	6735	3.532

GI gastrointestinal

Fig. 2 Slight fluorodeoxyglucose uptake (maximum standardized uptake value, 2.0) in the right abdomen (arrows). A benign or low-grade malignant tumor was suspected

Fig. 1 Contrast-enhanced computed tomography of the abdomen reveals a mesenteric lobulated mass with an artery running through the center (arrow)
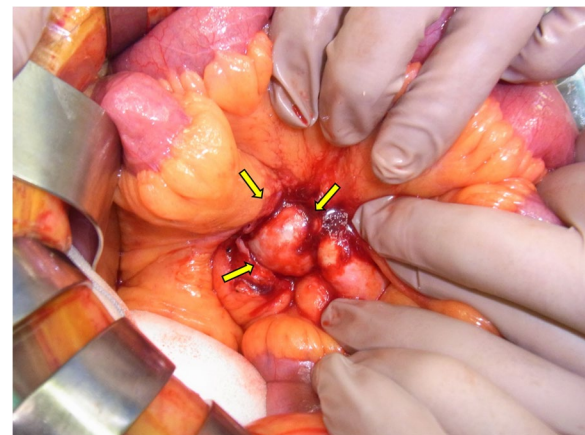
Fig. 3 The tumor is located in the mesentery of the ileum and retracted into the mesentery (arrows)

levels, which are associated with diabetes mellitus. The tumor marker carcinoembryonic antigen level was mildly elevated at 6.2 ng/mL. Contrast-enhanced abdominal CT revealed a mesenteric lobulated mass with an artery running through the center (Fig. 1). FDG-PET revealed slight FDG uptake (maximum standardized uptake value, 2.0) in the right abdomen; hence, a benign or low-grade malignant tumor was suspected (Fig. 2).

Based on the imaging findings, we suspected a malignant mesenchymal tumor, and because the tumor was painful, surgery was performed to diagnose and treat it. The tumor was located in the mesentery of the ileum and retracted into the mesentery (Fig. 3). Surgery was performed via a laparotomy. Initially, the small mesenteric

mass was resected along with the surrounding mesentery (Fig. 4a). However, resection of the tumor and mesentery resulted in impaired blood flow to the ileum in that area, and eventually, a 90-cm ileum was also resected (Fig. 4c). The cut surface of the $55 \times 33 \times 33$ mm^3 tumor was pale yellowish-white (Fig. 4b). Anastomotic reconstruction was performed using an instrumental functional end-to-end anastomosis. Our intraoperative search did not reveal any small bowel tumor, and an additional search of the resected ileum did not reveal any tumor. Thus, we diagnosed the patient with a primary ileal mesenteric tumor rather than a metastatic tumor.

Histological examination showed proliferative infiltration of atypical cells of unequal size and irregular spore structure. Some atypical cells infiltrated the surrounding
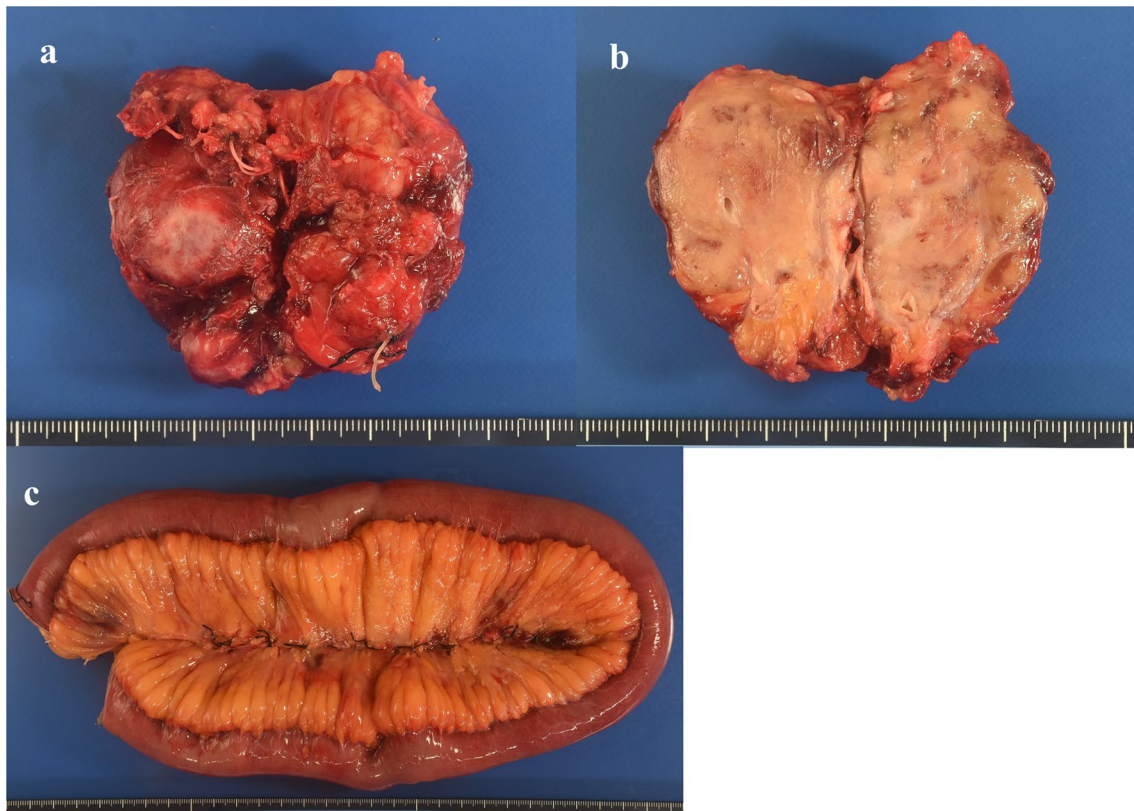
Fig. 4 Resected specimens. **a** Tumor resected together with the surrounding mesentery. The tumor size is 55 × 33 × 33 mm^3. **b** The cut surface is pale yellowish-white. **c** Additional resected ileum (90 cm). It is congested, but no tumor is found

adipose tissues (Fig. 5a) and proliferating atypical cells had round nuclei and a relatively abundant cytoplasm with pale eosinophilia. There were narrow fibrovascular interstitial spaces between atypical cell foci (Fig. 5b).

Immunohistochemical staining was positive for CD56 (Fig. 6a), chromogranin A (Fig. 6b), and synaptophysin (Fig. 6c). The Ki-67 index was 3% (Fig. 6d). The final pathological diagnosis was NET G2.
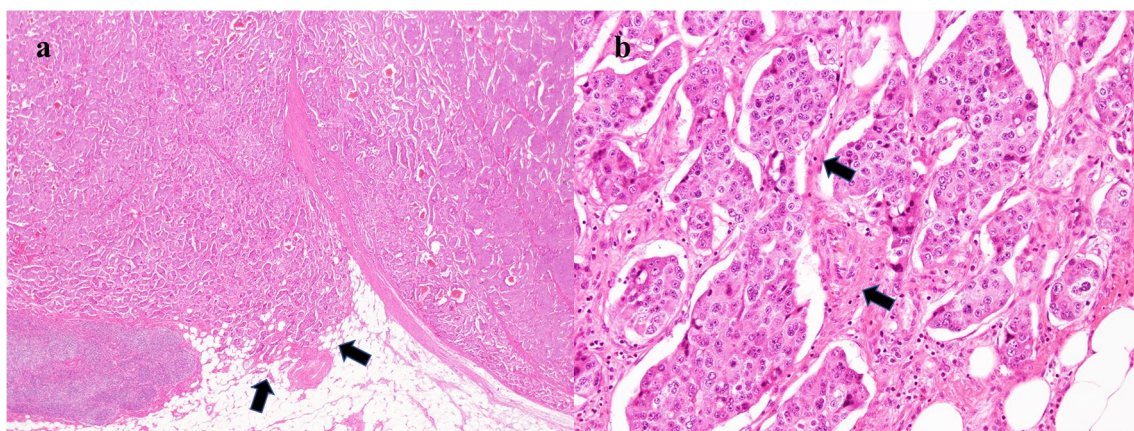

Fig. 5 Histopathological findings (H&E). **a** (× 40) Proliferative infiltration of atypical cells of unequal size and irregular spore structure. Some of them infiltrate the surrounding adipose tissue (arrows). **b** (× 200) Proliferating atypical cells have round nuclei and relatively abundant cytoplasm with pale eosinophilia. There are narrow fibrovascular interstitial spaces between atypical cell foci (arrows)
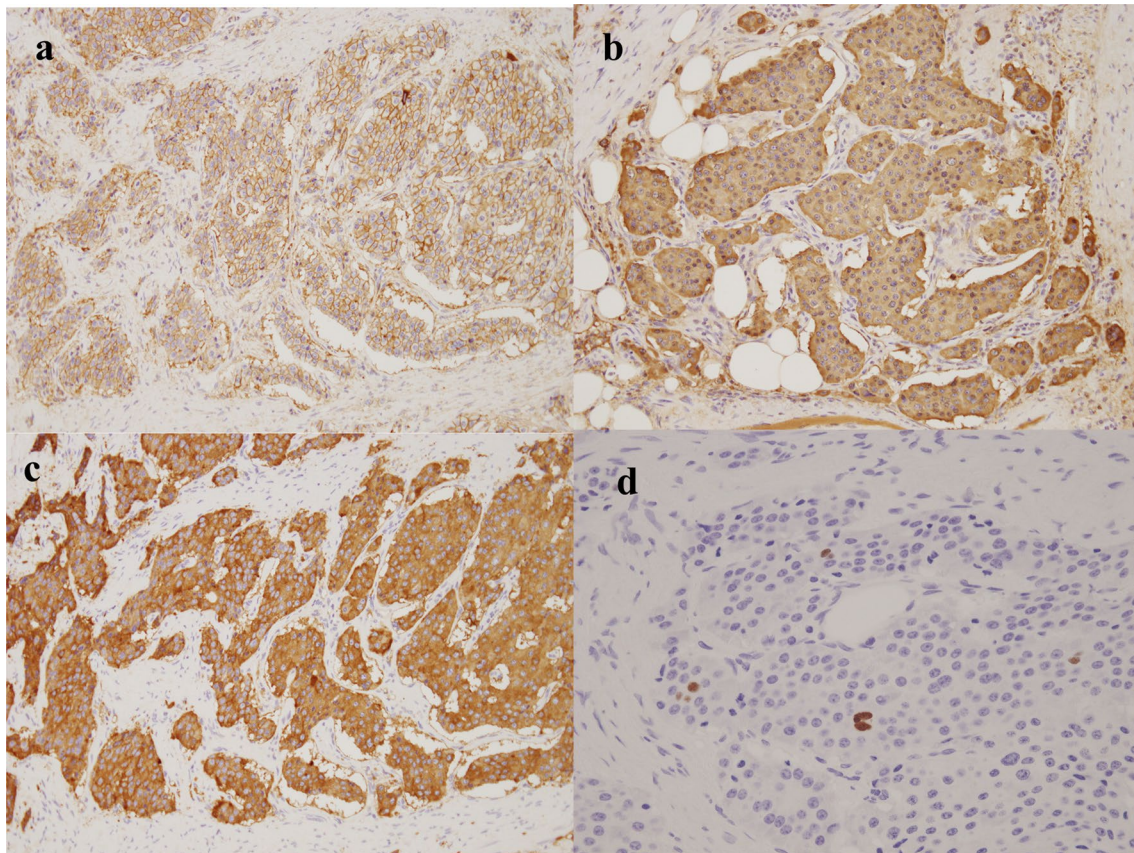
Morishita *et al. Surgical Case Reports*   (2022) 8:146

Page 4 of 6

Fig. 6 Immunohistochemical staining is positive for the following: **a** (× 200) CD56. **b** (× 200) chromogranin A. **c** (× 200) synaptophysin. **d** (× 400) The Ki-67 index is 3%

The patient's postoperative course was good, and he was discharged 10 days after the surgery. The patient developed no recurrence for 1.5 years. Postoperative antitumor therapy was not performed for this patient because the histological diagnosis was NET G2, and it was determined that the tumor could be completely resected by surgery.

Discussion

NETs are rare neoplasms. They arise from cells of the diffuse endocrine system, which are mainly dispersed throughout the gastrointestinal, pancreatic, and respiratory tracts. Neuroendocrine cells are derived from the epithelial and neuroectodermal cells. NETs are positive by silver staining and express synaptophysin, neuron-specific enolase, and chromogranin A.

The worldwide prevalence and incidence of NETs have recently increased. The incidence of NET was 1.09 per 100,000 people in 1973 and increased to 6.98 per 100,000 people in 2012 in the United States [2]. Based on data derived from the National Cancer Registry in Japan, the total number of patients treated for gastro-entero-pancreatic NENs (GEP-NENs) in 2016 was 6735, and the age-adjusted overall incidence was 3.53 per 100,000 people. The age-adjusted incidence of each primary NEN is presented in Table 1 [3]. Approximately half of the GEP-NENs involved the rectum (1.82 per 100,000 people), followed by the pancreas (0.697 per 100,000 people). The incidence of ileal NEN is 1% of the total GEP-NENs [3].

True primary solid tumors of the mesentery include NETs, fibromatoses, neurofibromas, teratomas, germ cell tumors, and primary neoplasms composed of smooth muscle, blood vessels, or fat [4]. Primary mesenteric NETs are very unusual, although secondary mesenteric involvement is common, reported as 40–80%, respectively [5]. We present an extremely rare case of an ileal mesenteric NET with benign or low-grade malignant characteristics on preoperative FDG-PET.

NETs are a subtype of NENs that are defined as epithelial neoplasms with predominant neuroendocrine differentiation. Because neuroendocrine cells are widely distributed throughout the body, NENs can arise in various locations, including the respiratory and digestive

Morishita *et al. Surgical Case Reports*   (2022) 8:146

Page 5 of 6

Table 2 Classification and grading criteria for NEN (2019) [8]

Terminology	Differentiation	Grade	Mitotic rate (mitoses/10 HPF)	Ki-67 index
NET G1	Well differentiated	Low	< 2	< 3%
NET G2		Intermediate	2–20	3–20%
NET G3		High	> 20	> 20%
NEC small-cell type (SCNEC)	Poorly differentiated	High	> 20	> 20%
NEC large-cell type (LCNEC)			> 20	> 20%
MiNEN	Well or poorly differentiated	Variable	Variable	Variable

Table 3 Resected cases of primary small intestinal mesenteric NETs [5, 12–20]

No	Author	Year	Age/sex	Location	Size (mm)	Grade	Operation
1	Barnard	1984	74/M	Ileum	60 × 55	NA	Ileal resection
2	Stone	1993	48/F	Jejunum	40 × 32	NA	Tumor resection
3	Tsubaki	2003	73/F	Ileum	45 × 35	NA	Tumor resection
4	Yamanuha	2009	52/M	Ileum	20 × 20	NA	Ileal resection
5	Park	2013	73/F	Jejunum	82 × 73	G1	Tumor resection
6	Sakai	2013	56/F	Ileum	40 × 35	G1	Tumor resection
7	Jida	2014	59/M	Jejunum	77 × 77	G1	Jejunal resection
8	Ikenaga	2014	59/F	Jejunum	24 × 20	G1	Jejunal resection
9	Yasuda	2017	72/M	Jejunum	40 × 40	G1	Tumor resection
10	Tsuji	2019	56/F	Jejunum	16 × 16	G2	Laparoscopic tumor resection
11	Our case	2020	55/M	Ileum	55 × 33	G2	Ileal resection

NA not available

systems [6]. The WHO previously proposed a classification scheme for digestive NENs that divides them into three categories based on mitotic count and Ki-67 labeling index value: NET G1, NET G2, and NEC [7]. In particular, a mitotic count of < 2 per 10 high-power fields (HPFs) and/or Ki-67 index of < 3% corresponds to NET G1, a mitotic count of 2–20 per 10 HPFs and/or Ki-67 index of 3–20% corresponds to NET G2, and a mitotic count of > 20 per 10 HPFs and/or Ki-67 index of > 20% corresponds to NEC. In 2019, the WHO revised its former classification scheme and established a well-differentiated subtype of NET G3 from cases previously classified as NEC (Table 2) [8].

The current gold standard for functional imaging of NETs is somatostatin receptor scintigraphy (SRS) with 111In-diethylenetriaminepentaacetic acid-octreotide [9]. Which is a proliferation marker reflecting the prognosis. FDG-PET is the most widely used nuclear medicine technique for functional imaging of cancer. However, FDG-PET has never been routinely used for imaging NETs, and its diagnostic performance remains unclear. The overall sensitivity rates of diagnostic imaging for NETs were reported to be 89% and 58% for SRS and FDG-PET, respectively [10]. FDG-PET is not sensitive in detecting low-grade primary gastrointestinal NETs.

Tumor differentiation can be used to guide the selection of nuclear imaging modalities for staging of gastrointestinal and pancreatic NETs. SRS appears to be more sensitive than FDG-PET for well-differentiated NETs, whereas FDG-PET demonstrates superior sensitivity for poorly differentiated NETs [11]. The tumor presented by us was diagnosed as a benign or low-grade malignant tumor on preoperative FDG-PET. Based on the final pathological diagnosis, the tumor was diagnosed as NET G2. If SRS could have been performed preoperatively in our case, it may have been diagnosed as an NET with strong accumulation at the tumor site. When a neoplastic lesion of the small intestine or mesentery is diagnosed, it is possible that the tumor is an NET, but it is often difficult to confirm the tumor diagnosis preoperatively. However, if FDG-PET and SRS can be performed simultaneously at the time of tumor diagnosis, it may be possible to diagnose NETs, including GRADE.

Surgery is the mainstay treatment for localized gastrointestinal NETs, and may be curative in cases of R0 resection. To our knowledge, only 10 cases of primary small intestinal mesenteric NETs have been reported in the literature [5, 12–20] (Table 3). Of the 11 patients, including this patient, there were five men and six women, with

Morishita *et al. Surgical Case Reports*   (2022) 8:146

Page 6 of 6

a mean age of 61.3 (range, 48–74) years. Tumors were localized in the jejunal mesentery in six cases and in the ileal mesentery in five cases. As far as the grade classification of these 11 cases is known, there were no highly malignant G3 cases. Of these 11 surgical procedures, tumor resection was performed in five cases, and small bowel resection including the mesentery, was performed in six cases. In addition, one of the five tumor resections was laparoscopic. Regarding the surgical approach, we initially considered observing the lesion using laparoscopy. However, due to the irregular shape of the tumor and the fact that the tumor was invading the mesentery, we ultimately opted for laparotomy.

Conclusions

Herein, we report an extremely rare case of primary ileal mesenteric NET resection. The preoperative diagnosis of a small intestinal mesenteric tumor is difficult. However, if FDG-PET shows a small accumulation in the tumor, the possibility of a well-differentiated NET G2 should be considered.

Abbreviations

NEN: Neuroendocrine neoplasm; NET: Neuroendocrine tumor; NEC: Neuroendocrine carcinoma; WHO: World Health Organization; NET G2: Grade 2 neuroendocrine tumor; FDG-PET: Fluorodeoxyglucose-position emission tomography; CT: Computed tomography; GEP-NENs: Gastro-entero-pancreatic neuroendocrine neoplasms; HPF: High-power fields; SRS: Somatostatin receptor scintigraphy.

Author contributions

SM wrote the manuscript. The other authors reviewed the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Informed consent was obtained from the patient for the publication of this case report.

Competing interests

The authors have no conflicts of interest to declare.

Author details

[1]Department of Surgery, Kagoshima Seikyou General Hospital, 5-20-10 Taniyama-chuou, Kagoshima City, Kagoshima 891-0141, Japan. [2]Department of Pathology, Kagoshima Seikyou General Hospital, 5-20-10 Taniyama-chuou, Kagoshima City, Kagoshima 891-0141, Japan.

References

1. Ito T, Igarashi H, Nakamura K, Sasano H, Okusaka T, Takano K, et al. Epidemiological trends of pancreatic and gastrointestinal neuroendocrine tumors in Japan: a nationwide survey analysis. J Gastroenterol. 2015;50:58–64.
2. Dasari A, Shen C, Halperin D, Zhao B, Zhou S, Xu Y, et al. Trends in the incidence, prevalence, and survival outcomes in patients with neuroendocrine tumors in the United States. JAMA Oncol. 2017;3:1335–42.
3. Masui T, Ito T, Komoto I, Uemoto S, Group JPS. Recent epidemiology of patients with gastro-entero-pancreatic neuroendocrine neoplasms (GEP-NEN) in Japan: a population-based study. BMC Cancer. 2020;20:1104.
4. Jaffer S, Harpaz N. Mesenteric paraganglioma: a case report and review of the literature. Arch Pathol Lab Med. 2002;126:362–4.
5. Park IS, Kye BH, Kim HS, Kim HJ, Cho HM, Yoo C, et al. Primary mesenteric carcinoid tumor. J Korean Surg Soc. 2013;84:114–7.
6. Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol. 2008;26:3063–72.
7. Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO classification of tumors of the digestive system. Lyon: IARC Press; 2010.
8. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, et al. The 2019 WHO classification of tumours of the digestive system. Histopathology. 2020;76:182–8.
9. Koopmans KP, Neels ON, Kema IP, Elsinga PH, Links TP, de Vries EG, et al. Molecular imaging in neuroendocrine tumors: molecular uptake mechanisms and clinical results. Crit Rev Oncol Hematol. 2009;71:199–213.
10. Binderup T, Knigge U, Loft A, Mortensen J, Pfeifer A, Federspiel B, et al. Functional imaging of neuroendocrine tumors: a head-to-head comparison of somatostatin receptor scintigraphy, 123I-MIBG scintigraphy, and 18F-FDG PET. J Nucl Med. 2010;51:704–12.
11. Squires MH, Volkan Adsay N, Schuster DM, Russell MC, Cardona K, Delman KA, et al. Octreoscan versus FDG-PET for neuroendocrine tumor staging: a biological approach. Ann Surg Oncol. 2015;22:2295–301.
12. Barnardo DE, Stavrou M, Bourne R, Bogomoletz WV. Primary carcinoid tumor of the mesentery. Hum Pathol. 1984;15:796–8.
13. Tsubaki MKH, Yamanaka M, Matsuoka K. A case of primary carcinoid tumor of the mesentery. J Jpn Surg Assoc. 2003;64:2613–7.
14. Stone NN, Atlas I, Kim US, Kwan D, Leventhal I, Waxman JS. Renal angiomyolipoma associated with neurofibromatosis and primary carcinoid of mesentery. Urology. 1993;41:66–71.
15. Yamanuha J, Ballinger R, Coon D, Navin J. Carcinoid tumor presenting as a primary mesenteric mass: a case report and review of the literature. Hawaii Med J. 2009;68:137–9.
16. Sakai NIF, Seki M, Itoh H, Suwa T, Miyazaki M. A case of neuroendocrine tumor originating from the mesentery of the jejunum. J Jpn Surg Assoc. 2013;74:1899–903.
17. Jida MTN, Ohashi R. A case of resected primary jejunal mesenteric carcinoid tumor. J Jpn Surg Assoc. 2014;75:467–72.
18. Ikenaga M, Kim H, Matsuura Y, Hitora T, Hirota M, Murakami M, et al. A case of mesenteric carcinoid tumor (Neuroendocrine tumor: NET G1) with liver metastasis, coexisted with rectal cancer. J Jpn Coll Surg. 2014;39:971–8.
19. Yasuda A, Kitagami H, Kondo Y, Nonoyama K, Watanabe K, Fujihata S, et al. Primary mesenteric neuroendocrine tumor that changed its internal composition from cystic to solid: a case report. Clin J Gastroenterol. 2017;10:18–22.
20. Tsuji A, Tomiyasu T, Kuramoto K, Iizaka M, Inomata Y, Baba H. Laparoscopic resection of a neuroendocrine tumor arising from the mesentery: a case report. J Jpn Surg Assoc. 2019;80:1152–7.