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## Bilocal recurrence of a neuroendocrine carcinoma of the small intestine: A case report

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## ABSTRACT

**INTRODUCTION:** Neuroendocrine tumors of the small intestine represent about half of all small intestine neoplasms. Recurrence after surgery with curative intention is frequently observed but recurrence rate has not yet been described or analyzed sufficiently.

**PRESENTATION OF CASE:** In this case bilocal recurrence 4 years after curative surgery of an ileocecal neuroendocrine carcinoma was observed in a 64 year old female. Diagnosis and follow-up was carried out as proposed in current ENETS guidelines using somatostatin receptor scintigraphy for primary diagnosis and Ga-DOTATOC-PET/CT in follow-up.

**DISCUSSION:** We can confirm that PET/CT for somatostatin receptor imaging shows good sensitivity in detecting neuroendocrine neoplasms and should be preferred for diagnostic, if available. For individual adaptation of follow-up procedures, as far as time intervals and preferred imaging methods are concerned, research on recurrence rate and long term outcome after curative surgery should be extended.

**CONCLUSION:** Livelong follow-up after surgical resection of neuroendocrine tumors is necessary and Ga-DOTA/TOC-PET/CT should be the method of choice, if available.

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## 1. Introduction

With an incidence of 0.29/100.000 the malignant forms of neuroendocrine neoplasms of the small intestine are a rather rare entity.<sup>1–4</sup> Though they represent about 30–50% of all small intestine neoplasms and hence are of high clinical importance.<sup>1</sup> Current literature does not present precise data on recurrence rate in low grade neuroendocrine tumors (NET).<sup>3–7</sup> The tumor proliferation rate, measured with help of Ki-67 has not only been established for grading neuroendocrine tumors, but it is also of prognostic value for possible tumor recurrence. Following the ENETS guidelines close follow-up is necessary even after complete tumor resection and even in slow proliferating tumors. In this case report we present a 64 year old female with recurrence of a slow proliferating neuroendocrine tumor (Ki-67 < 1%) in two locations of the small intestine at the same time.

## 2. Presentation of case

A 64 year old female with several carcinomas in her family history (among others colorectal and gastric) underwent annually

screening tests including measurement of CA-19.9. In January 2009 an asymptomatic elevation of CA-19.9 (80.3 ku/l) lead to an abdominal CT scan revealing a lesion with hypertrophic and hypervascular wall of the small intestinal. Reanalysis with CT scan after 3 months verified a hypodense, intraluminal lesion, 14 mm in diameter. Diagnostic laparoscopy with segmental gut resection was performed and an intraoperative pathologic examination requested. Histological findings classified the resected tumor as a high differentiated neuroendocrine carcinoma with local lymph node involvement (pT4, N1 (4/9), L1, V0, G1, R0). In consequence Chromogranin A levels have been measured postoperatively, not showing pathologic values (43 µg/l). Further staging analysis using somatostatin receptor scintigraphy (SRS) did not indicate any metastasis.

Due to the slow proliferation rate (Ki-67 < 1%) semiannual follow-up examinations including CT scan and measurements of Chromogranin A levels were carried out like proposed in the current ENETS guidelines.<sup>3,4</sup> CT scan in December 2012 revealed hypertrophy of the intestinal wall again, this time in two locations simultaneously. With the patient asymptomatic and tumor markers at normal levels, active surveillance was performed for further 6 months and finally Ga-DOTATOC-PET/CT was done, verifying two intraluminal lesions of the small intestine measuring 15 mm in diameter (Figs. 1 and 2). Therefore diagnostic laparoscopy with resection of the two affected gut segments via mini-laparotomy was performed. The tumors were localized in the proximal ileum, about 100 cm oral from the ileocecal region, with a distance of

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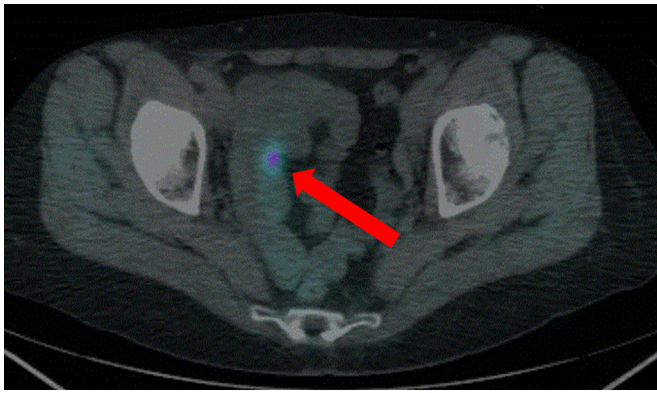


Fig. 1. DOTATOC-PET/CT 06/2013 showing first location of tumor recurrence.

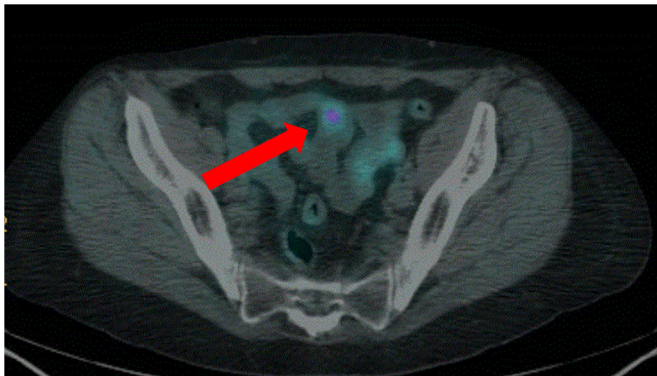


Fig. 2. DOTATOC-PET/CT 06/2013 showing second location of tumor recurrence.

25 cm between each other. This time histological exams classified the tumors as high differentiated neuroendocrine carcinomas, the proximal one even with regional lymph node involvement (pT2, pN1 (1/1), G1 and pT1, pN0, G1) (Fig. 3). Proliferation rate was slow again with Ki-67 less than 1%.

### 3. Discussion

Tumor grading in this case described a high differentiated and slow proliferating NET with Ki-67 < 1%. Despite low proliferation and high differentiation we found a bilocal tumor recurrence. With a distance of 25 cm between the two lesions we can assume an

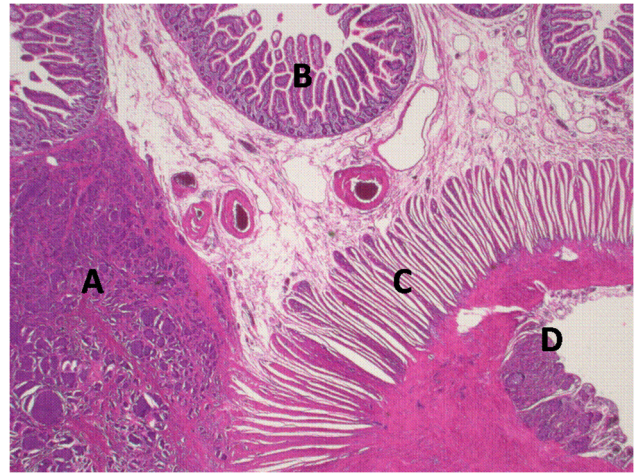


Fig. 4. Typical histological appearance of neuroendocrine carcinoma, 12× zoom: (A) tumor, (B) mucosa, (C) muscularis propria, (D) serosa.

independent process of growth. A case of bilocal recurrence has not yet been described explicitly and is rather uncommon. Regarding recurrence of NET after surgical R0 resection only two publications are considered in current guidelines. Moertel described that only 23% of the patients that underwent curative surgery were free of disease after 25 years.<sup>5</sup> Second one is Pape et al. who present 52 cases of tumor recurrence after surgical R0 resection in 139 patients (37.4%).<sup>6</sup> Due to such a lack of long-term results further studies on recurrence rate and typical localization should be made (Fig. 4).

Diagnostic procedures and operative treatment in this case were performed according to ENET guidelines with follow-up imaging every 6–12 months. Between the two tumor manifestations in 2009 and 2013 technical development led to a change in diagnostic procedures. Following ENETS guidelines in 2007 SRS has been proposed for imaging of neuroendocrine tumors. Latest guidelines from 2012 prefer Ga-DOTATOC-PET/CT, if available, because of its higher sensitivity.<sup>3,4,8–11</sup> Therefore SRS has been used in 2009 whereas PET-CT revealed tumor recurrence in 2013. Both times tumor manifestation has been recognized in early state. As PET-CT provides higher sensitivity, detection of two additional but preexisting lesions which had been missed by SRS in 2009 is theoretically possible but rather unlikely. For instance assume a bilocal recurrence after curative surgical treatment.

### 4. Conclusion

According recurrence rate of neuroendocrine tumors only few data is presented in current literature and hence considered in common guidelines. Coming research should focus on recurrence rate and long-time outcomes, especially after R0 resection, of neuroendocrine tumors so that follow-up procedures could be adapted. Following the ENETS guidelines lifelong follow-up is essential and Ga-DOTATOC-PET/CT should nowadays be the diagnostic item of choice, if available. Even in this case of bilocal tumor recurrence early tumor detection was possible.

### Conflict of interest

We certify that there is no conflict of interest.

### Funding

We certify that no funding was received by the authors.

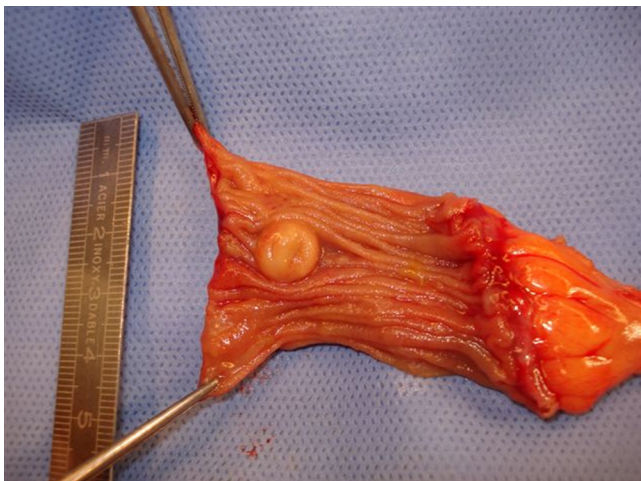


Fig. 3. Macroscopic appearance of neuroendocrine tumor recurrence.

## Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Author contribution

Literature research, data collection, writing of case report: Peiffer S. Oncologic consultant, review: Cathomas R. Surgery, follow-up consultations: Villiger P.

## References

1. Niederle MB, Hackl M, Kaserer K, Niederle B. Gastroenteropancreatic neuroendocrine tumours: the current incidence and staging based on the WHO and European Neuroendocrine Tumour Society classification: an analysis based on prospectively collected parameters. *Endocr Relat Cancer* 2010;**17**:909–18.
2. 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 tumours in 35,825 cases in the United States. *J Oncol* 2008;**26**:3063–72.
3. Pape UF, Perren A, Niederle B, Gross D, Gress T, Costa F, et al. ENETS consensus guidelines for the management of patients with neuroendocrine neoplasms from the Jejunum-Ileum and the Appendix including goblet cell carcinomas. *Neuroendocrinology* 2012;**95**:135–56.
4. Arnold R, Chen Y, Costa F, Falconi M, Gross D, Grossmann AB, et al. ENETS consensus guidelines for the standards of care in neuroendocrine tumours: follow-up and documentation. *Neuroendocrinology* 2009;**90**:227–33.
5. Moertel CG. Karnofsky memorial lecture. An odyssey in the land of small tumors. *J Clin Oncol* 1987;**5**:1502–22.
6. Pape U, Berndt U, Müller-Nordhorn J, Böhmig M, Roll S, Koch M, et al. Prognostic factors of long-term outcome in gastroenteropancreatic neuroendocrine tumours. *Endocr Relat Cancer* 2008;**15**:1083–97.
7. Haug AR, Cindea-Drimus R, Auernhammer CJ, Reincke M, Beuschlein F, Wängler B, et al. Neuroendocrine tumour recurrence: diagnosis with 68Ga-DOTATATE PET/CT. *Radiology* 2013;**270**(2):517–25.
8. Putzer D, Gabriel M, Kendler D, Henninger B, Knoflach M, Kroiss A, et al. Comparison of (68)Ga-DOTA-Tyr(3)-octreotide and (18)F-fluoro-L-dihydroxy-phenylalanine positron emission tomography in neuroendocrine tumour patients. *Q J Nucl Med Mol Imaging* 2010;**54**(February (1)):68–75.
9. Gabriel M, Decristoforo C, Kendler D, Dobrozemsky G, Heute D, Uprimny C, et al. 68 Ga-DOTA-Tyr3-octreotide PET in neuroendocrine tumours: comparison with somatostatin receptor scintigraphy and CT. *J Nucl Med* 2007;**48**:508–18.
10. Kayani I, Bomanji JB, Groves A, Conway G, Gacinovic S, Win T, et al. Functional imaging of neuroendocrine tumours with combined PET/CT using 68 Ga-DOTATATE (DOTA-DPhe1, Tyr3-octreotate) and 18F-FDG. *Cancer* 2008;**112**:2447–50.
11. Ruf J, Heuck F, Schiefer J, Denecke T, Elgeti F, Pascher A, et al. Impact of multiphase 68 Ga-DOTATOC-PET/CT on therapy management in patients with neuroendocrine tumours. *Neuroendocrinology* 2010;**91**:101–9.

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