Polish Annals of Medicine

Journal homepage: https://www.paom.pl

Case Report

Synchronous early rectal adenocarcinoma and neuroendocrine tumour: A treatment strategy

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Article info

Article history
Received: January 21, 2024
Accepted: March 4, 2024
Available online: April 22, 2024

Keywords
Carcinoid tumour
Neuroendocrine tumour
Rectal adenocarcinoma
Synchronous tumours

Doi
https://doi.org/10.29089/paom/185641

Abstract

Introduction: Synchronous colorectal adenocarcinoma with neuroendocrine tumour (NET) are a unique combination of tumours. These may be incidental lesions, usually a histopathological diagnosis rather than a clinical diagnosis from symptoms, examination or even gross appearances.

Aim: This paper aims to highlight our management strategy on manging a middle-aged woman with synchronous rectal adenocarcinoma and NET.

Case study: A 53-year-old woman presented with lower gastrointestinal bleeding with constitutional symptoms. Clinical examination and colonoscopy revealed a classical rectal adenocarcinoma, confirmed via biopsy. However, the final histopathology reports of the resected tumour revealed an early rectal adenocarcinoma with synchronous NET.

Results and discussion: We review the relevant literature and a discussion regarding guidelines available for diagnosis, follow-up and surveillance of this rare case.

Conclusions: There are no current guidelines for surveillance colonoscopy after detecting gastrointestinal NET, particularly synchronous tumours. NET may be another colorectal cancer risk factor with similar mutations and common genetic markers. Clinicians should consider doing a colonoscopy when or if their patients are diagnosed with any gastrointestinal NET. Detection of any NET warrants a thorough evaluation of the whole colon for colorectal cancer and close surveillance so that timely management can be achieved.

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1. INTRODUCTION

Synchronous colorectal carcinoma is characterized as the occurrence of more than one primary colorectal cancer in a single patient.[1] Although neuroendocrine tumour (NET) is not rare, it has been uncommonly seen correlated with synchronous or metachronous colorectal carcinoma.[2] Synchronous NET with colorectal cancers have only been reported a few times.[3] The NET was first described in 1867 by Langhans and most commonly occurs in the rectum and appendix.[4] This type of tumour is described as a composite carcinoid tumour. As per Gibbs, rectal carcinoid tumours have been histologically classified into 3 main types: composite carcinoid, true carcinoid or argentaffinoma, and atypical or non-argentaffin carcinoid.[5] We highlight a 53-year-old woman with synchronous rectal adenocarcinoma and NET and we discuss our management strategy for managing this case.

2. CASE STUDY

A 53-year-old woman presented with per-rectal bleeding associated with altered bowel habits for 1 month. She also had a significant loss of weight and appetite. On further history, she is a non-smoker, with no significant family history of malignancy or any significant risk factors. Clinically, she was anaemic and appeared cachexic, but not icteric. No cervical or inguinal lymphadenopathy was palpated. There were no abdominal masses felt, and per-rectal examination was unremarkable. She was mildly anaemic, with the rest of the parameters within the normal range. During her index admission, a colonoscopy detected a mass at the upper rectum (Figure 1). A biopsy of the lesion revealed a rectal adenocarcinoma. There were no distant metastases visualised upon staging computed tomography (CT).

The patient then underwent a laparoscopic anterior resection with a covering ileostomy. The final histopathological diagnosis revealed the presence of rectal adenocarcinoma pT1N0Mx, stage 1 with mesorectal NET, grade 2 (Figure 2). Given her result, she does not require any chemotherapy postoperatively. Her postoperative serum chromogranin A and CEA were not elevated. A surveillance colonoscopy after 6 months after surgery, revealed a nodule at the anastomotic line. However, histopathology was revealed to be a benign inflammatory lesion. Her ileostomy was then reversed. Post reversal of ileostomy, she developed anal canal stenosis. She has been on repeat colonoscopy with CRE dilatation, and a surveillance CT scan. After 12 months, the patient was asymptomatic and the latest surveillance CT revealed no local recurrence.

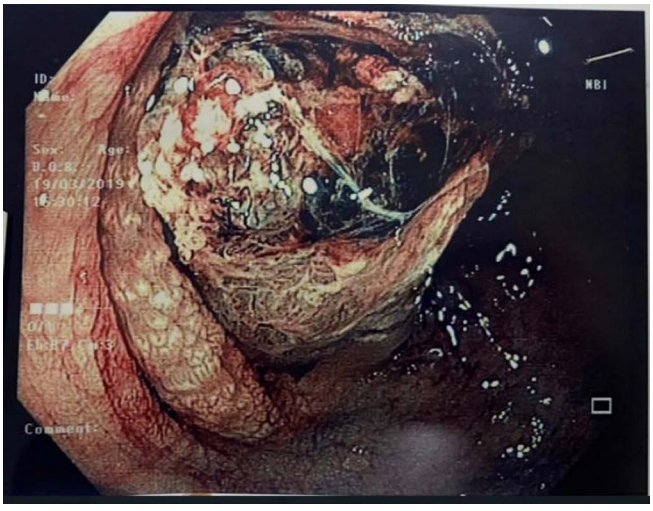

Figure 1. Endoscopic image of a mass at the upper rectum 18 cm from the anal verge.

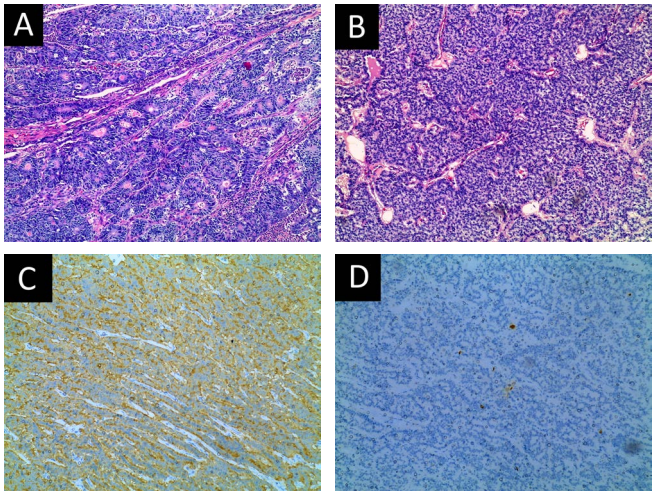

Figure 2. The histopathological diagnosis: rectal adenocarcinoma pT1N0Mx, stage 1 (A) with mesorectal neuroendocrine tumour, grade 2 (B). The immunohistochemical study: focal positivity towards (C) synaptophysin haematoxylin and eosin (HE) x10 and (D) chromogranin HE (magnification ×10).

3. RESULTS AND DISCUSSION

The composite of NET and adenocarcinoma of the rectum develops when the two components show histological transition. According to Kanno et al., only about 10 cases were reported in English literature on the possibility of composite carcinoid tumours similar to our case.[6] However, according to the latest classification of gastrointestinal NETs by the World Health Organization, it is classified into 2 categories, (1) previously known as gastrointestinal tract carcinoid tumours, they are well-differentiated NETs (2) poorly differentiated NETs, which carry poorer prognosis.[7] This classification has been adopted worldwide to avoid a conundrum between clinicians and pathologists. NETs are now further divided into 3 groups based on the degree of differentiation, grading, Ki-67 index, and mitotic rate.[8]

NETs are considered uncommon, having a 0.5% incidence of all newly diagnosed malignancies, with the gastrointestinal tract being the most prevalent location.[8] Pearson

and Fitzgerald reported the first recorded case of synchronous carcinoid and non-carcinoid gastrointestinal neoplasms in 1949.[9] The presence of a carcinoid tumour raises the possibility of synchronous colorectal cancer.[10] The relationship between colorectal adenocarcinoma and NET is unknown.[10] A case of positive CK20 in NET was detected along with a synchronous colorectal carcinoma, where this was a common marker detected in colorectal adenocarcinoma.[11]

According to the European Neuroendocrine Tumor Society in 2016, there are newer treatment options for NET with no involvement of muscularis propria, namely endoscopic resection by simple polypectomy or endoscopic mucosal resection with band ligation.[12] Endoscopic submucosal dissection and transanal endoscopic microsurgery should be done for those with incomplete resection margins.[12] At the moment there are no guidelines for the surveillance of synchronous tumors.[13] Frequent surveillance follow-up should be employed given their correlation with synchronicity potential.

The treatment approach for this case was only considering the adenocarcinoma of the rectum initially where anterior resection was done for this case and was staged as pT1N0MX, whereby the incidental findings of the 'mesorectal node' that histologically and immunohistochemically evident of NET (G2) considered did not alter the course of managing this case. This patient was followed up 3 monthly for the first 2 years, with a colonoscopy done at 6 months postoperatively. Chromogranin A levels were not repeated, as the patient was not keen to incur the cost involved. MDT discussion with the oncology team concluded that a yearly endoscopic surveillance to be done. The multiphase CT showed no evidence of distant metastasis, only a nodule at the anastomotic line.

Ultrasound, CT, and magnetic resonance imaging are often unable to detect the tumours.[14] A positron emission tomography (PET)/CT imaging with a ^{68}Ga-labelled somatostatin analogue has emerged as an essential tool for NET.[14] In this case report, we believe that performing a PET scan on this patient will be beneficial to look for occult NET as the NET was discovered in the single node from the resected specimen. The role of PET scan in this case is crucial because NET lesions are always small in size with variable anatomical location and low metabolic rate; as conventional imaging modalities of such tumours are often challenging. Ideally, 6–12 monthly levels of chromogranin A should be repeated to further monitor the recurrence of the NET lesion.

4. CONCLUSIONS

(1) There are no current guidelines for surveillance colonoscopy after detecting gastrointestinal NET, particularly synchronous tumours.
(2) NET may be another colorectal cancer risk factor with similar mutations and common genetic markers.
(3) Clinicians should consider doing a colonoscopy when or if their patients are diagnosed with any gastrointestinal NET.
(4) Detection of any NET warrants a thorough evaluation of the whole colon for colorectal cancer and close surveillance so that timely management can be achieved.

Acknowledgment
We would like to thank the Director-General of Health Malaysia for his permission to publish this article as a case report.

Conflict of interest
Authors declare that there is no conflict of interest.

Funding
None declared.

References
1 Parra-Medina R, Moreno-Lucero P, Jimenez-Moreno J, Parra-Morales AM, Romero Rojas A. Neuroendocrine neoplasms of gastrointestinal tract and secondary primary synchronous tumors: A systematic review of case reports. Casualty or causality? *Plos One*. 2019;14(5):e0216647. https://doi.org/10.1371/journal.pone.0216647.
2 Michna MK, Bichalska-Lach M, Rudzki M, Waniczek D. A rare case of a trifocal synchronous colon cancer in a 65-year old patient. *Pol Ann Med*. 2023;30(2):140–143. https://doi.org/10.29089/paom/161659.
3 Prommegger R, Ensinger C, Steiner P, Sauper T, Profanter C, Margreiter R. Neuroendocrine tumors and second primary malignancy – a relationship with clinical impact? *Anticancer Res*. 2004;24(2C):1049–1051.
4 Langhans T. Über einen drüsenpolyp im Ileum. *Virchows Arch Pathol Anat*. 1867;38:550–560.
5 GIBBS NM. The histogenesis of carcinoid tumours of the rectum. *J Clin Pathol*. 1963;16(3):206–214. https://doi.org/10.1136/jcp.16.3.206.
6 Kanno-Okada H, Mitsuhashi T, Mabe K, Shimoda T, Matsuno Y. Composite neuroendocrine tumor and adenocarcinoma of the rectum. *Diagn Pathol*. 2017;12(1):85. https://doi.org/10.1186/s13000-017-0674-8.
7 Popa O, Taban SM, Pantea S, et al. The new WHO classification of gastrointestinal neuroendocrine tumors and immunohistochemical expression of somatostatin receptors 2 and 5. *Exp Ther Med*. 2021;22(4):1179. https://doi.org/10.3892/etm.2021.10613.
8 Sweetser SR. Gastric neoplasms and gastroenteric and pancreatic neuroendocrine tumors. In: Sweetser SR, ed. *Mayo Clinic Gastroenterology and Hepatology Board Review*. 5th Ed. New York: Oxford University Press; 2015. https://doi.org/10.1093/med/9780197679753.003.0006.

[9] Pearson CM, Fitzgerald PJ. Carcinoid tumors; A re-emphasis of their malignant nature; Review of 140 cases. *Cancer.* 1949;2(6):1005–1026. https://doi.org/10.1002/1097-0142(194911)2:6%3C1005::aid-cncr2820020608%3E3.0.co;2-1.

[10] Solcia E, Kloppel G, Sobin LH. *Histological typing of endocrine tumours*. 2nd ed. New York: Springer; 1999: 160.

[11] Kato T, Terashima T, Tomida S, et al. Cytokeratin 20-positive large cell neuroendocrine carcinoma of the colon. *Pathol Int*. 2005;55(8):524–529. https://doi.org/10.1111/j.1440-1827.2005.01864.x.

[12] Ramage JK, De Herder WW, Delle Fave G, et al. Vienna Consensus Conference participants: ENETS consensus guidelines update for colorectal neuroendocrine neoplasms. *Neuroendocrinology*. 2016;103(2):139–143. https://doi.org/10.1159/000443166.

[13] Habal N, Sims C, Bilchik AJ. Gastrointestinal carcinoid tumors and second primary malignancies. *J Surg Oncol*. 2000;75(4):310–316. https://doi.org/10.1002/1096-9098(200012)75:4%3C306::aid-jso14%3E3.0.co;2-3.

[14] Sharma P, Singh H, Bal C, Kumar R. PET/CT imaging of neuroendocrine tumors with (68)Gallium-labeled somatostatin analogues: An overview and single institutional experience from India. Indian *J Nucl Med*. 2014;29(1):2–12. https://doi.org/10.4103%2F0972-3919.125760.