

World Journal of *Clinical Cases*

World J Clin Cases 2017 November 16; 5(11): 390-406





CASE REPORT

- 390 Natural killer cells activity in a metastatic colorectal cancer patient with complete and long lasting response to therapy
Ottiano A, Napolitano M, Capozzi M, Tafuto S, Avallone A, Scala S
- 397 Case of gastric neuroendocrine carcinoma showing an interesting tumorigenic pathway
Uesugi N, Sugimoto R, Eizuka M, Fujita Y, Osakabe M, Koeda K, Kosaka T, Yanai S, Ishida K, Sasaki A, Matsumoto T, Sugai T
- 403 Acid suppressive therapy improved symptoms due to circumferential cervical inlet patch with proton pumps (H^+/K^+ -ATPase)
Yamada T, Tsuji A, Onoue S, Kaneko M, Tanioka F, Osawa S, Saida Y

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Giovanni Conzo, MD, Associate Professor, DU di Scienze Anestesiologiche Chirurgiche e dell'Emergenza, Azienda Ospedaliera Universitaria, Scuola di Medicina e Chirurgia, Seconda Università degli Studi di Napoli, Napoli 80131, Italy

AIM AND SCOPE

World Journal of Clinical Cases (*World J Clin Cases*, *WJCC*, online ISSN 2307-8960, DOI: 10.12998) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

The primary task of *WJCC* is to rapidly publish high-quality Autobiography, Case Report, Clinical Case Conference (Clinicopathological Conference), Clinical Management, Diagnostic Advances, Editorial, Field of Vision, Frontier, Medical Ethics, Original Articles, Clinical Practice, Meta-Analysis, Minireviews, Review, Therapeutics Advances, and Topic Highlight, in the fields of allergy, anesthesiology, cardiac medicine, clinical genetics, clinical neurology, critical care, dentistry, dermatology, emergency medicine, endocrinology, family medicine, gastroenterology and hepatology, geriatrics and gerontology, hematology, immunology, infectious diseases, internal medicine, obstetrics and gynecology, oncology, ophthalmology, orthopedics, otolaryngology, pathology, pediatrics, peripheral vascular disease, psychiatry, radiology, rehabilitation, respiratory medicine, rheumatology, surgery, toxicology, transplantation, and urology and nephrology.

INDEXING/ABSTRACTING

World Journal of Clinical Cases is now indexed in PubMed, PubMed Central.

FLYLEAF

I-V

Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Li-Min Zhao*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Li-Jun Cui*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Giuseppe Di Lorenzo, MD, PhD, Professor, Genitourinary Cancer Section and Rare-Cancer Center, University Federico II of Napoli, Via Sergio Pansini, 5 Ed. 1, 80131, Naples, Italy

Jan Jacques Michiels, MD, PhD, Professor, Primary Care, Medical Diagnostic Center Rijnmond Rotterdam, Bloodcoagulation, Internal and Vascular Medicine, Erasmus University Medical Center, Rotterdam, Goodheart Institute and Foundation, Erasmus Tower, Veennos 13, 3069 AT, Erasmus City, Rotterdam, The Netherlands

Sandro Vento, MD, Department of Internal Medicine, University of Botswana, Private Bag 00713, Gaborone, Botswana

Shuhei Yoshida, MD, PhD, Division of Gastroenterology, Beth Israel Deaconess Medical Center, Dana 509, Harvard Medical School, 330 Brookline Ave, Boston, MA 02215, United States

EDITORIAL BOARD MEMBERS
All editorial board members resources online at <http://www.wjnet.com/2307-8960/editorialboard.htm>

EDITORIAL OFFICE
Xiu-Xia Song, Director
World Journal of Clinical Cases
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjnet.com>

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive,
Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjnet.com

Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjnet.com>

PUBLICATION DATE
November 16, 2017

COPYRIGHT
© 2017 Baishideng Publishing Group Inc. Articles published by this Open Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non-commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.f6publishing.com>

Case of gastric neuroendocrine carcinoma showing an interesting tumorigenic pathway

Noriyuki Uesugi, Ryo Sugimoto, Makoto Eizuka, Yasuko Fujita, Mitsumasa Osakabe, Keisuke Koeda, Takashi Kosaka, Shunichi Yanai, Kazuyuki Ishida, Akira Sasaki, Takayuki Matsumoto, Tamotsu Sugai

Noriyuki Uesugi, Ryo Sugimoto, Makoto Eizuka, Yasuko Fujita, Mitsumasa Osakabe, Kazuyuki Ishida, Tamotsu Sugai, Department of Diagnostic Molecular Pathology, School of Medicine, Iwate Medical University, Morioka 020-8505, Japan

Keisuke Koeda, Akira Sasaki, Department of Surgery, School of Medicine, Iwate Medical University, Morioka 020-8505, Japan

Takashi Kosaka, Shunichi Yanai, Takayuki Matsumoto, Division of Gastroenterology, Department of Internal Medicine, School of Medicine, Iwate Medical University, Morioka 020-8505, Japan

ORCID number: Noriyuki Uesugi (0000-0002-4388-6660); Ryo Sugimoto (0000-0002-9486-0823); Makoto Eizuka (0000-0003-4815-1273); Yasuko Fujita (0000-0002-3988-9076); Mitsumasa Osakabe (0000-0002-1797-3189); Keisuke Koeda (0000-0002-9302-302X); Takashi Kosaka (0000-0001-6091-7214); Shunichi Yanai (0000-0003-1871-2412); Kazuyuki Ishida (0000-0002-2804-4588); Akira Sasaki (0000-0002-1346-5312); Takayuki Matsumoto (0000-0001-9786-3854); Tamotsu Sugai (0000-0002-4896-3557).

Author contributions: Uesugi N, Sugimoto R, Eizuka M, Fujita Y, Osakabe M, Ishida K and Sugai T designed the study; Koeda K, Sasaki A, Kosaka T, Yanai S and Matsumoto T collected the patients' clinical data; Uesugi N and Sugai T analyzed the data and wrote the paper.

Informed consent statement: The patient and his family has provided permission to publish these features of his case, and the identity of the patient has been protected.

Conflict-of-interest statement: The authors declare that there are no conflicts of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and

the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Tamotsu Sugai, MD, Professor, Department of Molecular Diagnostic Pathology, Iwate Medical University, 19-1, Morioka 020-8505, Japan. tsugai@iwate-med.ac.jp
Telephone: +81-19-6515111
Fax: +81-19-6291436

Received: May 31, 2017

Peer-review started: June 3, 2017

First decision: June 27, 2017

Revised: July 13, 2017

Accepted: September 12, 2017

Article in press: September 13, 2017

Published online: November 16, 2017

Abstract

Here, we report a case of gastric neuroendocrine carcinoma showing an interesting tumorigenic pathway. A 57-year-old Japanese woman presented with epigastric tenderness, and distal gastrectomy was performed. In the surgical specimen, histologically, the tumor tissue was composed of three subtypes of tumor components showing different histological architecture and cellular atypia, diagnosed as neuroendocrine tumor (NET) G2, NET G3, and neuroendocrine carcinoma (NEC) components. Immunohistochemically, the Ki-67-positive rates of NET G2, NET G3, and NEC components were 6.5%, 99.5% and 88.1%, respectively. Although allelic imbalance (AI) on chromosomes 1p, 3p, 8q, TP53, 18q and 22q was commonly found in all components, AI of 4p was found in NET G3 and NEC components (but not in the NET G2 component). In contrast, AIs of 5q and 9p were found in only the NEC

component. Thus, we showed the progression from NET G2 to NEC, via NET G3, within the same tumor.

Key words: Stomach; Neuroendocrine tumor G2; Neuroendocrine tumor G3; Neuroendocrine carcinoma

© The Author(s) 2017. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Gastric neuroendocrine carcinoma (NEC) is typically generated by dedifferentiation of adenocarcinoma cells to endocrine cells. However, we experienced a case of gastric NEC possibly generated from the neuroendocrine tumor (NET) component. The present case demonstrated an unconventional carcinogenic pathway in neuroendocrine tumorigenesis. In addition, we analyzed allelic imbalance in NET and NEC components and provided important insights into neuroendocrine carcinogenesis.

Uesugi N, Sugimoto R, Eizuka M, Fujita Y, Osakabe M, Koeda K, Kosaka T, Yanai S, Ishida K, Sasaki A, Matsumoto T, Sugai T. Case of gastric neuroendocrine carcinoma showing an interesting tumorigenic pathway. *World J Clin Cases* 2017; 5(11): 397-402 Available from: URL: <http://www.wjgnet.com/2307-8960/full/v5/i11/397.htm> DOI: <http://dx.doi.org/10.12998/wjcc.v5.i11.397>

INTRODUCTION

Neuroendocrine neoplasms of the digestive system are classified as neuroendocrine tumors (NETs) or neuroendocrine carcinomas (NECs) based on assessment of the pro-liferative fraction and morphological criteria in the 2010 World Health Organization (WHO) classification. Furthermore, NET can be divided into three tiers (G1, G2, and G3) based on the mitotic count and Ki-67 labeling index^[1]. NEC of the stomach is composed of proliferation of poorly differentiated tumorous endocrine cells with marked cellular atypia^[1]. In general, gastric NEC may be generated by dedifferentiation of adenocarcinoma cells to endocrine cells, and it is possible that gastric NETs and NECs may have different tumorigenic pathways^[1,2]. Here, we report a case of gastric NEC generated from a NET component, with immunohistochemical and molecular studies.

CASE REPORT

A 57-year-old Japanese woman presented with epigastric tenderness. Gastroendoscopy showed a growing lesion (size, 16 mm × 11 mm) in the greater curvature of the upper gastric body, and the mucosa adjacent to the lesion showed atrophic gastritis. Histopathological examination of a biopsy sample revealed NEC. *Helicobacter pylori* were not detected

by Giemsa staining. In addition, serum levels of chromogranin A and gastrin were not measured. The patient subsequently underwent distal gastrectomy. One year after surgery, liver metastasis was found in abdominal computed tomography examination, and chemotherapy was performed.

Pathological findings

In low-magnification images, tumor cells were distributed in two lesions. One lesion was constructed by tumor cell proliferation within the submucosal layer, and another lesion was found in the muscle layer; these two lesions were discontinuous (Figure 1A).

Microscopic examination revealed that the tumor tissue was composed of three subtypes of tumor components as follows. The first component was composed of cuboidal epithelial cells with uniform, oval nuclei showing fine nuclear chromatin and arranged in a trabecular growth pattern with focal rosettes. Tumor cells had very few mitotic figures [< 2 per 10 high-powered fields (HPF)] and no necrosis. This component corresponded to the NET G2 component (Figure 1B). The second component consisted of diffuse proliferation of tumor cells with small nuclei showing irregular, dense nuclear chromatin and high mitotic counts, corresponding to the NET G3 component (Figure 1C). The third component was composed of diffuse proliferation of tumor cells with large, irregular, coarse nuclei, high mitotic counts, and geographic necrosis, similar to the large cell NEC component (Figure 1D). Although the transition between the NET G2 component and the NET G3 component was confirmed, the submucosal lesion and intramuscular lesion were separated by the muscle layer (Figure 1A). Marked lymph vessel and venous invasion were observed in the submucosal layer, as determined by D2-40 immunohistochemical staining and EVG staining (Figure 1A, inset).

In addition, the mucosa adjacent to the tumor showed atrophic gastritis with intestinal metaplasia, but not type A gastritis. No endocrine cell micronests were found in the surrounding mucosa.

Immunohistochemical study

Immunohistochemical examination was performed using an auto-immunostaining system (Dako EnVision System, Denmark) for neuroendocrine differentiation, cell proliferation activity, p53 overexpression, and mucin phenotype (Muc2, Muc5AC, Muc6, CD10). The positive rate of Ki-67 was calculated using an APERIO virtual slide system (AT2; Leica Biosystems, United States).

All tumor components were immunopositive for chromogranin A, synaptophysin, and CD56, and decreased immunoreactivity was found in the NEC component. Differences in Ki-67-positive rates were

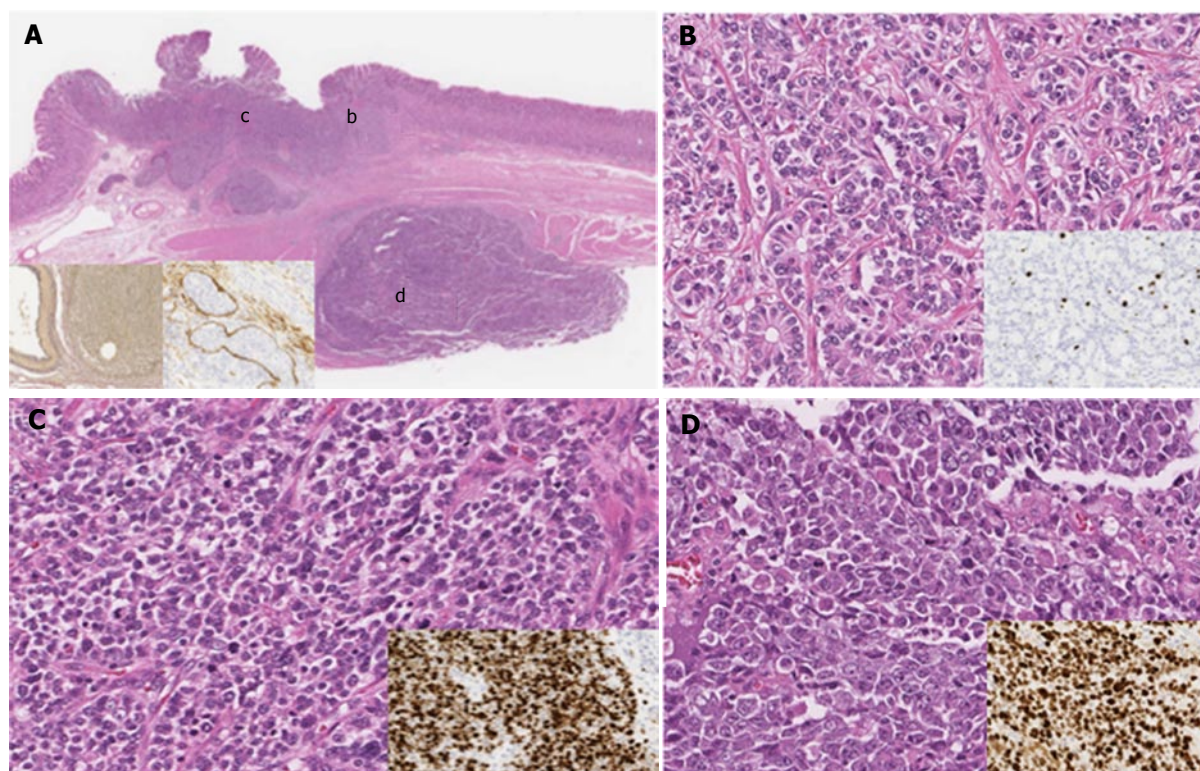


Figure 1 Histological findings of an HE-stained section of a resected specimen. A: Low-magnification image of the surgical specimen. The tumor component was composed of two lesions (a submucosal lesion and an intramucosal lesion). These two lesions were separated by muscle layer (inset: left, EVG staining; right, D2-40 immunohistochemical staining); B: NET G2 component (inset: Ki-67 positive rate, 6.5%); C: NET G3 component (inset: Ki-67 positive rate, 99.5%); D: Large cell NEC component (inset: Ki-67 positive rate, 88.1%). NEC: Neuroendocrine carcinoma; NET: Neuroendocrine tumor.

found among NET G2, NET G3, and NEC components (NET G2, 6.5%; NET G3, 99.5%; NEC, 88.1%). Overexpression of p53 protein was not found in any component. With regard to the mucin phenotype, no mucin markers were expressed in any tumor component (Table 1).

Molecular findings

DNA from NET G2, NET G3, and NEC components was extracted separately. PCR-allelic imbalance (AI) analyses were performed using a thermal cycler (GeneAmp PCR System 9600; Perkin-Elmer, CA, United States) according to previously reported procedures^[3]. AIs on chromosomes 1p, 3p, 4p, 5q, 8p, 9p, 13q, 17p, 18p, and 22q were examined using 22 highly pleomorphic microsatellite markers (D1S228, D1S548, D3S2402, D3S1234, D4S2639, D4S1601, D5S107, D5S346, D5S299, D5S82, D8S201, D8S513, D8S532, D9S171, D9S1118, D13S162, TP53, D18S487, D18S34, D22S274, D22S1140, and D22S1168).

In addition, PCR-MSI analysis was performed as described previously^[4]. Five different loci were assessed for MSI, including all those recommended by the Bethesda panel for colon cancer (BAT25, BAT26, D5S346, D2S123, and D17S250)^[4].

DNA methylation at the six specific promoters originally described by Yagi and colleagues was

quantified^[5]. Methylation of three markers (RUNX3, MINT31, and LOX) was analyzed, and samples with at least two methylated markers were defined as highly methylated epigenotype (HME) tumors. The remaining tumors were also screened for methylation at three other markers (NEUROG1, ELMO1, and THBD) and were defined as intermediate methylation epigenotype (IME) tumors if they had at least two methylated markers out of the three markers proposed as a second panel. Tumors not classified as HME or IME were designated as low methylation epigenotype (LME).

In the present case, DNA methylation status was LME, and MSI was not found in all tumor components. AIs at 1p, 3p, 8q, TP53, 18q and 22q were commonly found in all tumor components. Although AI of 4p was found in NET G3 and NEC components, it was not observed in the NET G2 component. In addition, AIs at 5q and 9p were found in the NEC component only (negative for NET G2 and G3 components; Figure 2).

DISCUSSION

Most cases of gastric NEC may be developed from endocrine precursor cell clones occurring in preceding adenocarcinoma components^[1,2]. In the present case, histological examination revealed that the tumor

Table 1 Summary of immunohistochemical analysis

Antibody	Clone	Dilution	Source	NET G2 component	NET G3 component	NEC component
Chromogranin A	DAK-A3	1:100	DAKO, CA, Unites States	Positive	Positive	Weakly positive
Synaptophysin	SY38	1:20	DAKO, CA, Unites States	Positive	Positive	Weakly positive
NCAM	1B6	1:100	DAKO, CA, Unites States	Positive	Positive	Weakly positive
Ki-67	MIB-1	1:50	DAKO, CA, Unites States	6.50%	99.50%	88.10%
p53	DO-7	1:100	Novocastra, United Kingdom	Negative	Negative	Negative
Muc2	Ccp58	1:200	Novocastra, United Kingdom	Negative	Negative	Negative
Muc5AC	CLH2	1:100	Novocastra, United Kingdom	Negative	Negative	Negative
Muc6	CLH5	1:100	Novocastra, United Kingdom	Negative	Negative	Negative
CD10	56C6	1:50	Novocastra, United Kingdom	Negative	Negative	Negative

NEC: Neuroendocrine carcinoma.

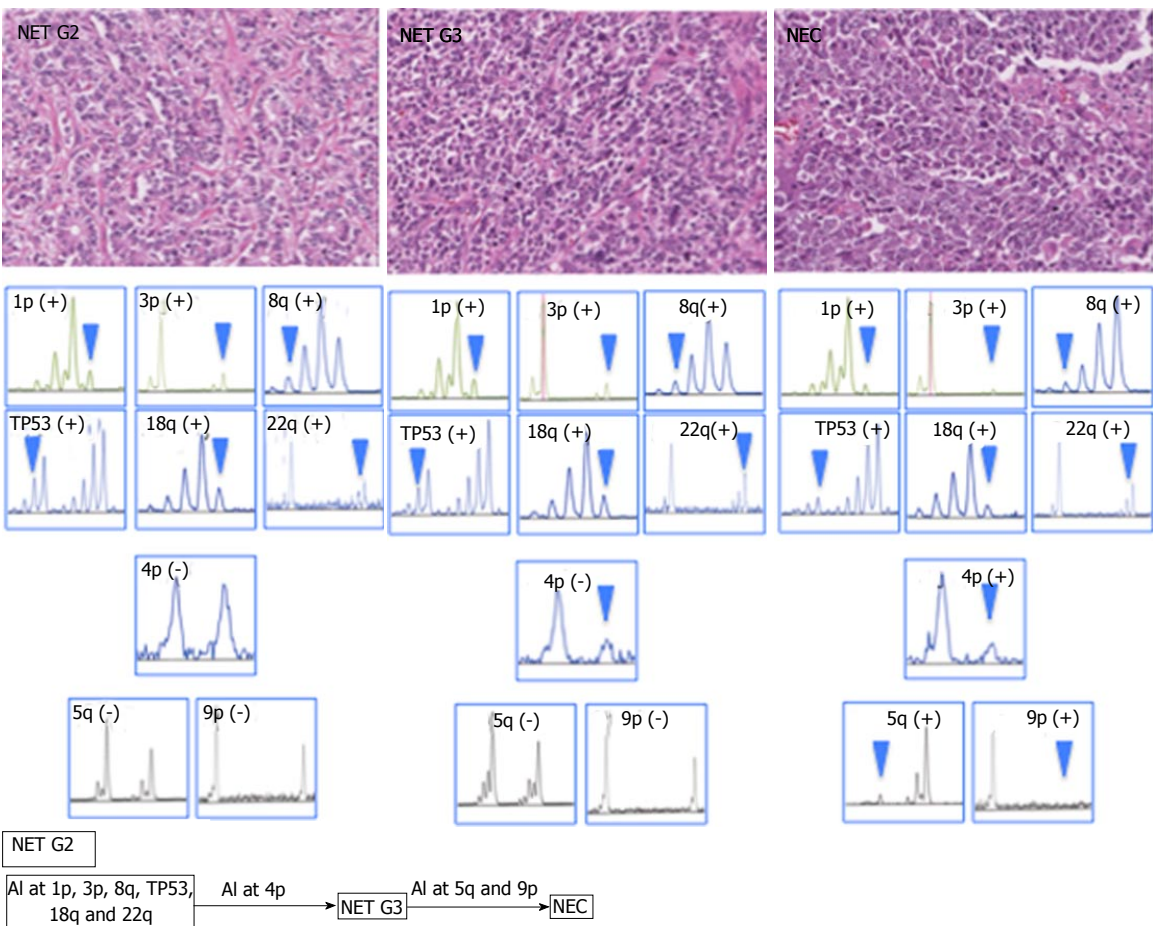


Figure 2 Accumulation of allelic imbalance through the progression from neuroendocrine tumor G2 to neuroendocrine tumor G3 to neuroendocrine carcinoma in the present case. Als at 1p, 3p, 8q, TP53, 18q, and 22q were common in three components (NET G2, NET G3, and NEC). Al at 4p was acquired during the progression from NET G2 to G3. Als at 5q and 8q were found during progression from NET G3 to NEC. NEC: Neuroendocrine carcinoma; NET: Neuroendocrine tumor; Al: Allelic imbalance.

tissue was composed of three subtype components. In addition, the transition between NET G2 and G3

components was confirmed. No adenocarcinoma components were found in serial sections of all specimens. Although a clear transition between the NET and NEC components was not found, we assumed that the tumor mass in the muscle layer may be an intramural metastasis because the tumor tissue showed marked vessel invasion (Figure 1A). Therefore, we speculated that the morphological change from NET to NEC could have occurred through the process of tumor progression. Additionally, NEC may arise from the NET component, suggesting that the tumor may have developed through an unconventional pathway in neuroendocrine tumorigenesis in our case^[2].

With regard to the tumorigenesis of the NET G2 component, although serum chromogranin A and gastrin had been measured, no endocrine cell micronests or findings of type A gastritis were observed in the mucosa adjacent to the tumor. Therefore, we assumed that the tumor in this case may be sporadic NET, namely non-endochromaffin-like cell tumor, defined as type 3 tumor by Rindi *et al.*^[1].

In previous reports, most cases of gastric NEC with an adenocarcinomatous component were found to exhibit immunopositivity of mucin markers, and the mucin phenotype of the NEC component was found to correspond with that of the adenocarcinoma component^[2,6]. In our case, both the NET and NEC components showed negative immunoreactivity for all mucin markers examined. Thus, it was unlikely that the NEC component was generated from adenocarcinoma in the present case.

Furthermore, Nishikura *et al.*^[7] reported that most cases of NEC with an adenocarcinoma component showed p53 mutations, consistent with the adenocarcinoma component. This finding strongly supported the hypothesis that most cases of gastric NEC are developed from precursor cell clones that occur in a preceding adenocarcinoma component.

The molecular features of NET and NEC have not been clarified^[8]. In the present case, AIs at 1p, 3p, 8q, TP53, 18q, and 22q were commonly found in three components (NET G2, NET G3, and NEC). These findings supported that the tumor in our case had been generated by progression from the NET G2 to NEC component. In contrast, AI at 4p was acquired during the progression from NET G2 to G3. In addition, AIs at 5q and 8q play an important role in the development from NET G3 to NEC. These findings suggested that acquisition of multiple AIs contributed to the progression from NET to NEC (Figure 2).

In conclusion, we experienced a case of gastric NEC possibly generated from the NET component. The present case demonstrated an unconventional carcinogenic pathway in neuroendocrine tumorigenesis, providing important insights into neuroendocrine carcinogenesis.

COMMENTS

Case characteristics

Gastric neuroendocrine carcinoma showing unconventional tumorigenic pathway.

Clinical diagnosis

Gastric carcinoma

Laboratory diagnosis

Gastric carcinoma.

Imaging diagnosis

Gastric carcinoma.

Pathological diagnosis

Gastric neuroendocrine carcinoma

Treatment

Distal gastrectomy

Peer-review

This is an interesting case of gastric neuroendocrine carcinoma showing a tumorigenic pathway. This report presents a case of gastric NEC possibly generated from NET component by analyzing allelic imbalance and shows unconventional carcinogenic pathway in neuroendocrine tumorigenesis.

REFERENCES

- 1 **Bosman FT**, Carneiro F, Hruban RH. WHO Classification of Tumours of the Digestive System. Lyon: IARC Press, 2010
- 2 **Domori K**, Nishikura K, Ajioka Y, Aoyagi Y. Mucin phenotype expression of gastric neuroendocrine neoplasms: analysis of histopathology and carcinogenesis. *Gastric Cancer* 2014; **17**: 263-272 [PMID: 23828549 DOI: 10.1007/s10120-013-0281-7]
- 3 **Sugai T**, Habano W, Jiao YF, Toyota M, Suzuki H, Tsukahara M, Koizuka H, Akasaka R, Koeda K, Wakabayashi G, Suzuki K. Molecular analysis of single isolated glands in gastric cancers and their surrounding gastric intestinal metaplastic mucosa. *Oncol Rep* 2010; **23**: 25-33 [PMID: 19956861]
- 4 **Sugai T**, Habano W, Uesugi N, Jiao YF, Nakamura S, Abe K, Takagane A, Terashima M. Three independent genetic profiles based on mucin expression in early differentiated-type gastric cancers--a new concept of genetic carcinogenesis of early differentiated-type adenocarcinomas. *Mod Pathol* 2004; **17**: 1223-1234 [PMID: 15154009 DOI: 10.1038/modpathol.3800170]
- 5 **Kaneda A**, Yagi K. Two groups of DNA methylation markers to classify colorectal cancer into three epigenotypes. *Cancer Sci* 2011; **102**: 18-24 [PMID: 21159060 DOI: 10.1111/j.1349-7006.2010.01712.x]
- 6 **Takenaka Y**, Tsukamoto T, Mizoshita T, Ogasawara N, Hirano N, Otsuka T, Ban H, Nakamura T, Yamamura Y, Kaminishi M, Tatematsu M. Gastric and intestinal phenotypic correlation between exocrine and endocrine components in human stomach tumors. *Histol Histopathol* 2007; **22**: 273-284 [PMID: 17163401 DOI: 10.14670/HH-22.273]
- 7 **Nishikura K**, Watanabe H, Iwafuchi M, Fujiwara T, Kojima K, Ajioka Y. Carcinogenesis of gastric endocrine cell carcinoma: analysis of histopathology and p53 gene alteration. *Gastric Cancer* 2003; **6**: 203-209 [PMID: 14716513 DOI: 10.1007/s10120-003-0249-0]
- 8 **Leotlela PD**, Jauch A, Holtgreve-Grez H, Thakker RV. Genetics of neuroendocrine and carcinoid tumours. *Endocr Relat Cancer* 2003;

Uesugi N *et al.* Gastric neuroendocrine carcinoma

10: 437-450 [PMID: 14713256 DOI: 10.1677/erc.0.0100437]

P-Reviewer: Fukuchi M, Tsolakis AV, Yang F **S-Editor:** Gong ZM
L-Editor: A **E-Editor:** Zhao LM





Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

