

Collision tumours are defined as the rare condition in which two histologically distinct neoplasms grow concurrently in the same location. In a 64-year-old male patient, with sharply defined borders. Adenocarcinomas are the most common tumours of the stomach. Other types of tumours can occasionally accompany gastric adenocarcinomas. Foci of adenocarcinoma and neuroendocrine carcinoma were identified in adjacent areas in a 64-year-old male patient who had undergone total gastrectomy due to adenocarcinoma of the gastric cardia. Of the seven metastatic lymph nodes, three were affected by adenocarcinoma and four were affected by neuroendocrine carcinoma. Based on this patient case, we discussed gastric collision tumours in the light of the literature.

Key words: gastric collision tumor, adenocarcinoma, neuroendocrine carcinoma.

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Gastric collision tumour of adenocarcinoma and neuroendocrine carcinoma

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Introduction

Collision tumours are defined as rare conditions in which two histologically distinct neoplasms grow concurrently in the same location with sharply defined borders. Adenocarcinoma is the most common tumour of the stomach. Although lymphomas are the most common coexisting tumours, carcinoid, neuroendocrine and stromal tumours may also accompany gastric adenocarcinomas [1–4]. Lymph node metastases of gastric collision tumours are mostly in the form of adenocarcinomas. The coexistence of a gastric adenocarcinoma and neuroendocrine tumour is rare [2, 5–12]. Herein, we present a patient, who had undergone surgery with the pre-diagnosis of gastric adenocarcinoma, in whom a coexisting neuroendocrine tumour was identified; some of the metastatic lymph nodes were affected by adenocarcinoma and some by the neuroendocrine tumour. We discussed this case in light of the available literature.

Case report

A 64-year-old male patient was admitted to the Department of Gastroenterology of Mersin University Faculty of Medicine with complaints of fatigue, loss of appetite, early satiety and flatulence in the epigastric region, persisting for four months. He had lost 10 kg in weight within the last four months. He had a history of smoking a pack of cigarettes a day for 40 years. There was no family history of any type of cancer. His physical examination revealed tenderness over the umbilicus. All laboratory parameters were within normal limits except for mild anaemia (haemoglobin 11.7 mg/dl). Serum levels of carcinoembryonic antigen (CEA) and calcium 19.9 were also within normal limits. Upper gastrointestinal system endoscopy revealed a fragile, vegetative mass starting from the 35th cm of the oesophagus from the incisors and surrounding the oesophagogastric junction. This complicated the passage of the endoscope into the stomach. An ulcerative, vegetative, fragile mass extending to the minor curvature was identified in the gastric cardia, and multiple biopsies were obtained. Examination of the biopsy specimens revealed gastric adenocarcinoma. On computed tomography (CT) a mass lesion that was more prominent in the gastric cardia, extending to the fundus, minor curvature and distal oesophagus and causing remarkable luminal narrowing particularly in the gastric cardia was observed. No distant organ metastasis was identified (Figs. 1 and 2).

The patient underwent total gastrectomy, Roux-en-Y anastomosis and splenectomy. Concurrent administration of adjuvant chemotherapy was planned. The patient is currently in the 4th month of treatment.



Fig. 1. Mass lesion causing remarkable luminal narrowing in the gastric cardia



Fig. 2. Lesion causing luminal narrowing in the gastric cardia and a metastatic lymph node

Pathological findings

Gross examination of the surgical specimen revealed a 6 cm × 4.5 cm × 1.8 cm ulcerative and vegetative mass located at a minimum distance of 0.8 cm from the proximal surgical margin and surrounded by the gastric wall. Macroscopically, the adenocarcinoma component of the tumour showed infiltration into the fat tissue. The colour of the cut surface of the tumour was grey-white, and the tumour extended to the serosa. Twenty-seven lymph nodes were resected together with the gastric sample. Microscopic examination of the surgical specimen stained with haematoxylin and eosin (H&E) revealed two different tissue types (Fig. 3). One of the components was an endocrine tumour composed of small cells forming solid, trabecular glands. These cells had granular eosinophilic cytoplasm, round or oval shaped, centrally located nuclei and distinct nucleoli. The value for the Ki67 labelling index was 10% and the mitotic index was 3/10 HPF. The other component was an adenocarcinoma composed of cells with extracellular mucin, mainly forming glandular and cribriform structures. Immunohistochemically, the endocrine component of the tumour showed positive staining with synaptophysin and chromogranin (Clone SP11, 1 : 50 and

Clone SP12, 1 : 25, NeoMarkers, Fremont, CA) (Fig. 4). It was observed that these tissues did not coalesce with each other in front of the tumour. Both tumour components invaded the serosa. The proximal surgical margin was invaded by the adenocarcinoma component of the tumour, but the distal surgical margin was intact. There was perineural invasion of the adenocarcinoma component as well; however, no vascular invasion was observed. Seven of the resected lymph nodes were metastatic, three of which were affected by adenocarcinoma and four by neuroendocrine carcinoma (Figs. 5, 6 and 7). Based on these findings, the patient was diagnosed with a collision tumour composed of an adenocarcinoma and an endocrine tumour.

Discussion

In the present patient case, two different types of carcinoma (adenocarcinoma and neuroendocrine carcinoma) were simultaneously identified in a single gastric tumour and in the metastatic lymph nodes affected by the same tumour. Neuroendocrine carcinomas account for 2% of tumours of the gastrointestinal system [13–15]. Their prevalence varies among populations. The most commonly involved organs in the Western population

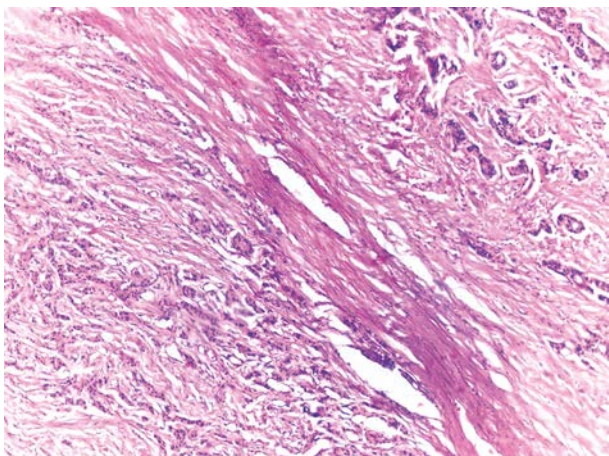


Fig. 3. Endocrine and adenocarcinoma components of the tumor (H&E, 40×)

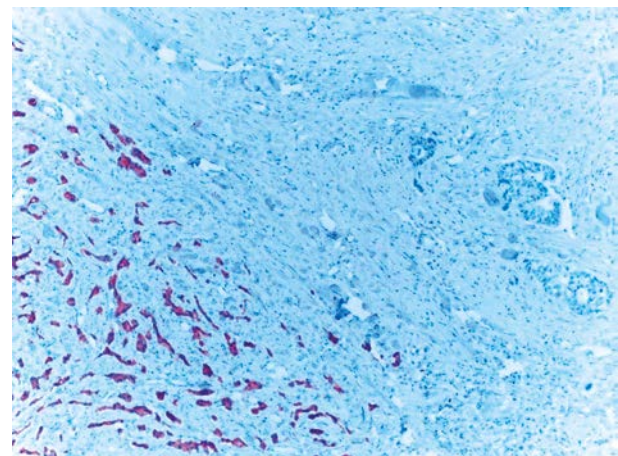


Fig. 4. Endocrine tumor showing positive staining with synaptophysin (synaptophysin, 40×)

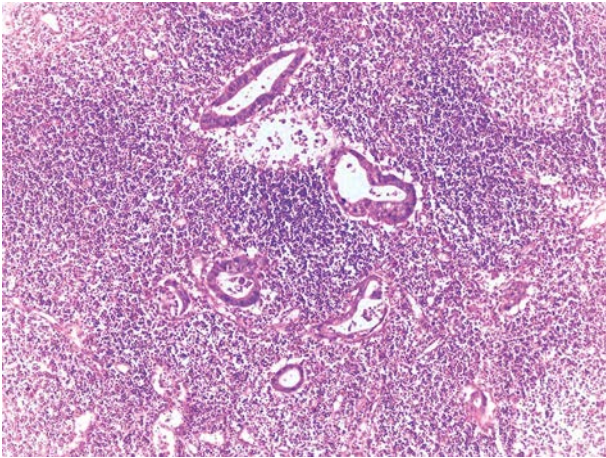


Fig. 5. Metastatic adenocarcinoma in the lymph node (H&E, 100×)

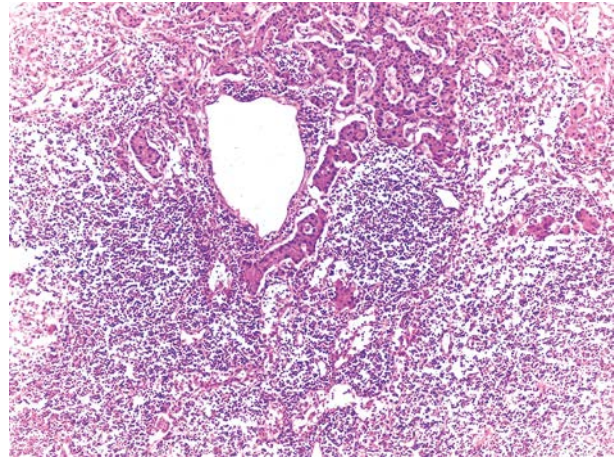


Fig. 6. Metastatic neuroendocrine tumor in the lymph node (H&E, 100×)

include the small intestine (36%), appendix (26%) and rectum (17%). Neuroendocrine carcinomas of the stomach are quite rare, with an incidence of 4% [15]. In the Japanese population, gastric involvement ranks second (27.3%) after rectal involvement [16]. A grading scheme endorsed by the World Health Organization (WHO) for NETs of the digestive system classifies well-differentiated NETs into 2 categories: low grade (G1) and intermediate grade (G2) [17]. The Ki67 labelling index is one of the factors of prognostic significance in well-differentiated NETs [18]. The 2010 WHO classification uses a Ki67 labelling cut-off value of < 3% to define low grade (G1), 3–20% for intermediate grade (G2) and > 20% for high-grade (G3) NETs. Mitotic activity shows the inherent proliferative potential of NETs. Based on the 2010 WHO classification, the cut-off value to define poorly differentiated gastroenteropancreatic neuroendocrine carcinoma is now 20/10 HPF. According to the WHO classification system, our patient had grade 2, well differentiated neuroendocrine carcinoma. But with the component of adenocarcinoma we could name it as a mixed adenoneuroendocrine carcinoma (MANEC).

To the best of our knowledge, the coexistence of gastric epithelial and non-epithelial tumours (collision tumour) has been reported in 57 cases in 49 different publications in the literature written in English. Table 1 shows the distribution of collision tumours that accompany gastric adenocarcinoma, indicating that lymphomas are the most common coexisting tumours (38%).

As can be seen in detail in Table 2, the coexistence of adenocarcinoma and neuroendocrine carcinoma has been reported in only nine cases. The age, gender and prognostic characteristics of these patients were similar to those of patients with other gastric tumours. The present patient is the 10th case reported in the literature. The only case of a collision gastric tumour reported in Turkey was a patient with coexisting adenocarcinoma and gastrointestinal stromal tumour [19]. The present case report will be the first in Turkey describing a coexisting gastric adenocarcinoma and neuroendocrine tumour.

It is known that a substantial portion of patients with pernicious anaemia have hypergastrinaemia and related

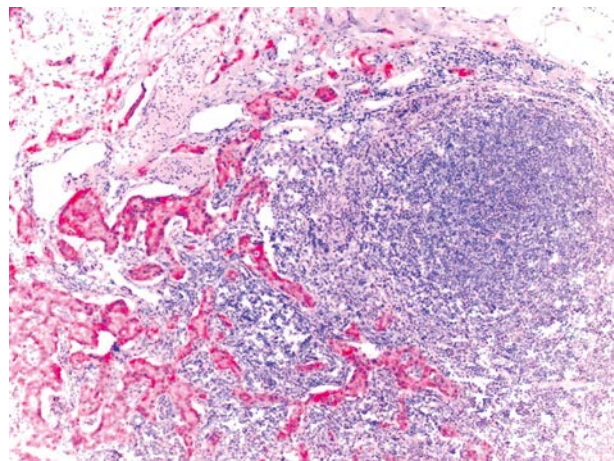


Fig. 7. Metastatic endocrine tumor showing positive staining with synaptophysin (synaptophysin, 100×)

endocrine cell proliferation [13]. The present patient case had neither pernicious anaemia nor endocrine cell proliferation. The serum gastrin level of the patient was within the normal range.

It is generally difficult to differentiate collision and composite tumours. A collision tumour is the coexistence of more than one type of neoplastic tissue in the same tumour, with sharply defined borders. A composite tumour is the presence of different types of tumour in mixed formation [16, 18]. According to these definitions, our case represents a collision tumour because there are two elements adjacent to one another without intermixing.

In such cases the most significant problem is encountered during the initial biopsy. If the biopsy specimen reveals only the neuroendocrine component, the therapy schema will be totally changed. Therefore, taking biopsies from multiple sites is important.

Of course, the prognosis for such patients is associated with the depth of invasion and lymph node involvement. But which part of the tumour affects the prognosis more than the other is unclear. There is not enough data to speculate.

Table 1. Distribution of collision-composite tumours that accompany gastric adenocarcinomas

Tumour type	Lymphomas	Neuroendocrine tumours	Oesophageal squamous cell carcinoma	Gastrointestinal stromal tumours	Sarcomas	Gastrinomas	Others	Total
No. of patients	22 (38%)	9 (17%)	7 (12%)	7 (12%)	3 (5.5%)	2 (3.5%)	7 (12%)	57 (100%)

Table 2. Summary of cases with a collision/composite tumour composed of adenocarcinoma and neuroendocrine carcinoma

No.	Age (years), gender	Tumour localization	Author
1	50, male	body	Yamashina, 1985 [5]
2	69, female	body	Chodankar, 1989 [6]
3	49, female	body	Morishita, 1991 [7]
4	72, female	unknown	Corsi, 1995 [8]
5	66, female	cardia	Camuñas Mohinelo, 1997 [20]
6	84, male	cardia	Morishita, 2005 [10]
7	48, male	body	Jayaraman, 2005 [11]
8	56, male	body	Mróz, 2009 [12]
9	50, male	body	Jang, 2010 [2]
10	64, male	cardia	present case

We are of the opinion that the presentation of this rare entity will contribute to the understanding of the behaviour and biology of gastric tumours.

Authors declare no conflict of interest.

References

- Bi R, Sheng W, Wang J. Collision tumor of the stomach: gastric adenocarcinoma intermixed with gastrointestinal stromal tumor. *Pathol Int* 2009; 59: 880-3.
- Jang KY, Moon WS, Lee H, Kim CY, Park HS. Gastric collision tumor of large cell neuroendocrine carcinoma and adenocarcinoma – a case report. *Pathol Res Pract* 2010; 206: 387-90.
- Chong VH, Idros A, Telisinghe PU. Triple synchronous gastrointestinal malignancies: a rare occurrence. *Singapore Med J* 2010; 51: e176-7.
- Wu J, He YJ, Tong SL. Gastric collision tumor (adenocarcinoma and gastrointestinal stromal tumor): report of a case. *Zhonghua Bing Li Xue Za Zhi* 2010; 39: 563-4.
- Yamashina M, Flinner RA. Concurrent occurrence of adenocarcinoma and carcinoid tumor in the stomach: a composite tumor or collision tumors? *Am J Clin Pathol* 1985; 83: 233-6.
- Chodankar CM, Pandit SP, Motiwale SS, Deodhar KP. Collision tumour of stomach. *Indian J Gastroenterol* 1989; 8: 297-8.
- Morishita Y, Tanaka T, Kato K, Kawamori T, Amano K, Funato T, Tarao M, Mori H. Gastric collision tumor (carcinoid and adenocar-

cinoma) with gastritis cystica profunda. *Arch Pathol Lab Med* 1991; 115: 1006-10.

- Corsi A, Bosman C. Adenocarcinoma and atypical carcinoid: morphological study of a gastric collision-type tumour in the carcinoma-carcinoid spectrum. *Ital J Gastroenterol* 1995; 27: 303-8.
- Kim EY, Park KC, Kwon JG. A case of double primary cancer: early gastric adenocarcinoma associated with adenocarcinoma and carcinoid. *Korean J Gastroenterol* 2003; 42: 533-8.
- Morishita Y, Sugitani M, Sheikh A, Nemoto N, Fujii M, Takayama T. Collision tumor of the stomach: a rare case of an adenocarcinoma and carcinoid tumor. *Arch Pathol Lab Med* 2005; 129: 407-9.
- Jayaraman A, Ramesh S, Jeyasingh R, Bagyalakshmi KR. Gastric collision tumour – a case report. *Indian J Pathol Microbiol* 2005; 48: 264-5.
- Mróz A, Kiedrowski M, Malinowska M, Sopyło R. Collision tumour of the stomach – adenocarcinoma and neuroendocrine carcinoma: case report and review of the literature. *Pol J Pathol* 2009; 60: 94-7.
- Lewin KJ, Appelman HD. Endocrine cell proliferation of the stomach. In: Rosai J (ed.). *Tumor of the Esophagus and Stomach. Atlas of Tumor Pathology. 3rd series, fascicle 18.* Armed Forces Institute of Pathology, Washington, DC 1996; 331-56.
- Graeme-Cook F. Neuroendocrine tumors of the GI tract and appendix. In: Odze RD, Goldblum JR, Crawford JM (eds.). *Surgical Pathology of the GI Tract, Liver, Biliary Tract, and Pancreas.* WB Saunders, Philadelphia 2004; 483-503.
- Gilligan CJ, Lawton GP, Tang LH, West AB, Modlin IM. Gastric carcinoid tumors: the biology and therapy of an enigmatic and controversial lesion. *Am J Gastroenterol* 1995; 90: 338-52.
- Soga J. Carcinoid tumors: a statistical analysis of a Japanese series of 3126 reported and 1180 autopsy cases. *Acta Med Biol* 1994; 42: 87-102.
- WHO Classification of Tumours of the Digestive System. 4th ed. Bosman FT, Hruban RH, Theise ND (eds.). IARC Press, Lyon 2010.
- American Joint Committee on Cancer Staging Manual. 7th ed. Edge SB, Byrd DR, Compton CC, et al. (eds.). Springer, New York 2010.
- Ozgun YM, Ergul E, Sisman IC, Kusdemir A. Gastric adenocarcinoma and GIST (collision tumors) of the stomach presenting with perforation; first report. *Bratisl Lek Listy* 2009; 110: 504-5.
- Camu as Mohinelo FA, Melgar Requena P, Martínez Zaragoza J, Estrada Caballero JL, Jiménez Torres MJ, Arroyo Guijarro A. Gastric collision tumor with osseous metaplasia. *Rev Esp Enferm Dig* 1997; 89: 317-3.

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