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Gastric Endocrine Cell Carcinoma with Long-Term Survival Developing Metachronous Remnant Cancer

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Key Words
Endocrine cell carcinoma · Stomach · Long-term survival · Metachronous tumour

Abstract
A rare case of primary gastric endocrine cell carcinoma in a 79-year-old man is reported. Upper gastrointestinal endoscopy showed a large Bormann's type 2 tumour located in the middle of the stomach. On computed tomography, the gastric wall was thickened by the large tumour, and there were no distant metastases. Distal gastrectomy, lymph node dissection, and partial resection of the transverse colon were performed because the tumour involved the transverse mesocolon. The final pathological diagnosis was endocrine cell carcinoma, with tumour infiltration up to the subserous layer. Adjuvant chemotherapy was given, but metachronous remnant gastric cancer developed 2 years after surgery. Endoscopic submucosal dissection was performed for the early 0-IIc type gastric cancer, and the surgical margin was preserved. The patient has survived for 5 years after the primary surgery, remaining disease-free so far.

Introduction

Neuroendocrine tumours (NETs) in the stomach, especially poorly differentiated ones, have a poor prognosis, since most cases are already in an advanced stage at the time of diagnosis. This type of NET must be treated like a normal gastric carcinoma, but three-quarters of patients die within 1 year of diagnosis due to extensive metastatic disease, and metachronous tumours develop in about 10% during follow-up. Age, tumour size, depth, and location are significant predictors of metastases. However, there is no established adjuvant therapy.

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Here, a case of gastric endocrine cell carcinoma with long-term survival due to the combination of curative surgery, adjuvant chemotherapy, and early treatment of metachronous remnant gastric cancer is reported.

Case Report

A 79-year-old man presented in June 2004 with epigastric pain, weight loss, and vomiting. He had no previous diseases and was on no medications. He was 167 cm tall and weighed 53 kg. Upper gastrointestinal endoscopy showed a large Bormann's type 2 tumour located in the middle body to the antrum of the stomach (fig. 1). Upper gastrointestinal radiographs showed that the gastric wall at the greater curvature from the body to the antrum was distorted irregularly by the tumour. On computed tomography, the gastric wall was thickened by the tumour (fig. 2). There were no metastatic lesions in the lungs, liver, or bones. Laboratory data included the following: white blood cell count 7,600/mm^3, haemoglobin 11.6 g/dl, platelets 315,000/mm^3, and carcinoembryonic antigen increased to 114 ng/ml. On laparotomy, distal gastrectomy and lymphadenectomy with partial resection of the transverse colon were undertaken because the tumour involved the transverse mesocolon. Operative time was 2 h 25 min, with blood loss of 250 ml. The specimen showed an ulcerating large tumour 11.0 × 5.5 cm in size. Microscopically, the tumour was composed of endocrine cells with dark round nuclei and scant cytoplasm stained with haematoxylin and eosin (fig. 3). Immunohistochemically, the tumour was positive for chromogranin and synaptophysin. The final pathological diagnosis was gastric endocrine cell carcinoma with microlymphovascular invasion.

Adjuvant chemotherapy consisting of S-1 and lentinan was given. Two years after surgery, upper gastrointestinal endoscopy showed an early type 0-IIC gastric cancer at the remnant stomach, and endoscopic submucosal dissection was performed. The pathological findings showed well-differentiated tubular adenocarcinoma. The tumour depth of the gastric wall was not beyond 500 μm, and the surgical margin was well preserved.

The patient has survived for 5 years after the surgery with adjuvant chemotherapy and successful resection of the metachronous early gastric cancer.

Discussion

Endocrine tumours of the gastrointestinal tract, first called carcinoids in 1907, are collectively termed NETs [1]. Primary gastric endocrine cell carcinoma is relatively rare and thought to account for 2–4% of all gastrointestinal NETs [2].

NETs in the stomach may be subdivided into different types. Some authors have divided them into three types: type 1 is associated with corpus-predominant atrophic gastritis, type 2 is associated with gastrinoma as part of MEN-1, and type 3 is the sporadic type of enterochromaffin-like cell carcinoid, as well as other types of neuroendocrine or mixed tumours with or without hormone production [3–5]. If the poorly differentiated NETs are added, four types of NETs can be distinguished [6, 7]. Type 1 accounts for approximately 70–80% of all cases, followed by type 3 as the next most frequent type, while type 2 and type 4 are rare [5].

The biologic behaviour and prognosis vary considerably by type. The prognosis of type 4 is frequently poor; the cumulative crude survival rate was only 33.3% at 5 years after diagnosis [8]. Some authors reported that the mean survival rates ranged from 6.5 to 14.9 months, and only about one-third of patients survived longer than 1 year [9, 10].

In general, there is no doubt that type 3 and type 4 should be treated aggressively with radical resection and lymph node dissection, because these types of tumours infiltrate

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beyond the submucosa more often than other types [8]. Even with curative surgery, liver metastases or lymph node recurrence occur frequently. The aggressive biological and clinical character of these types is similar to that of pulmonary small cell carcinoma, and some authors have proposed CDE chemotherapy (cisplatin, doxorubicin, and etoposide) or PE chemotherapy (cisplatin and etoposide) [11, 12]. Other treatment was based on adjuvant chemotherapy of the gastric cancer itself.

In our case, adjuvant chemotherapy with S-1 plus lentinan was given. Lentinan, a purified β-glucan, is a biological and immunological modifier that has been used as an anticancer drug in combination with 5-fluorouracil for gastric cancer in Japan. Oba et al. proposed that immunochemotherapy with lentinan has a synergistic effect, stimulating the immune system to reject and destroy tumours, especially advanced gastric cancer [13]. Though the efficacy of lentinan for gastric NETs is not established, we used it as adjuvant therapy, hoping for such a synergistic effect.

The main sites of recurrence are liver metastases or lymph node metastases, which are often impossible to resect surgically [8, 10]. In case of type 3 or type 4 NETs, more careful follow-up must be undertaken to provide early detection and treatment of recurrence and metachronous tumours. Metachronous tumours develop in about 10% of cases during follow-up, and they usually occur within 4 years of the original tumours. Most tumours are adenomatous colonic polyps (26%), followed by gastrointestinal carcinoma (21%), urinary tract malignancy (19%), and female reproductive organ malignancies (17%) [14].

Conclusion

The case of a patient with a gastric endocrine cell carcinoma treated by curative resection, in whom a subsequent annual medical check-up resulted in the early detection and treatment of metachronous gastric remnant carcinoma, is presented. In this case, the careful follow-up may have contributed to the patient's long-term survival for 5 years.

Disclosure Statement

The authors had no financial and personal relationships with other people or organizations that might inappropriately influence (bias) this work.

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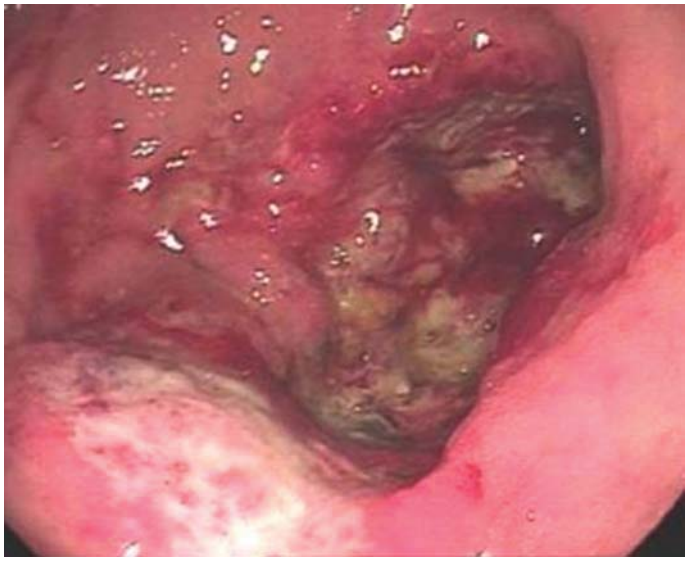

Fig. 1. Upper gastrointestinal endoscopy showing the massive Bormann's type 2 tumour located at the middle body of the stomach extending to the antrum.

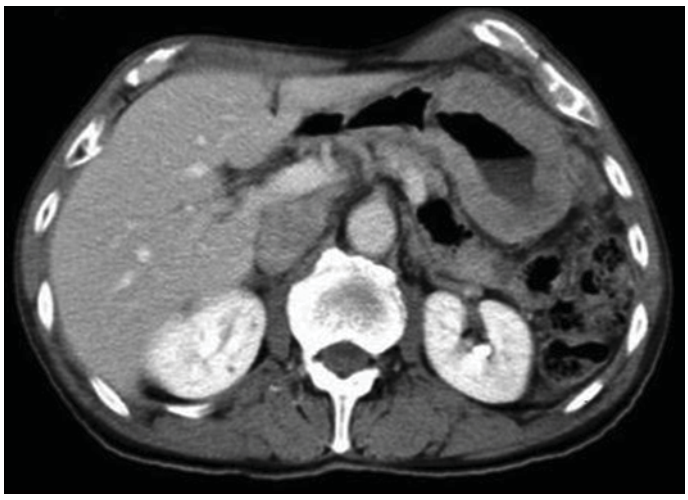

Fig. 2. Computed tomography showing that the tumour was detected as the thickness of the gastric wall.

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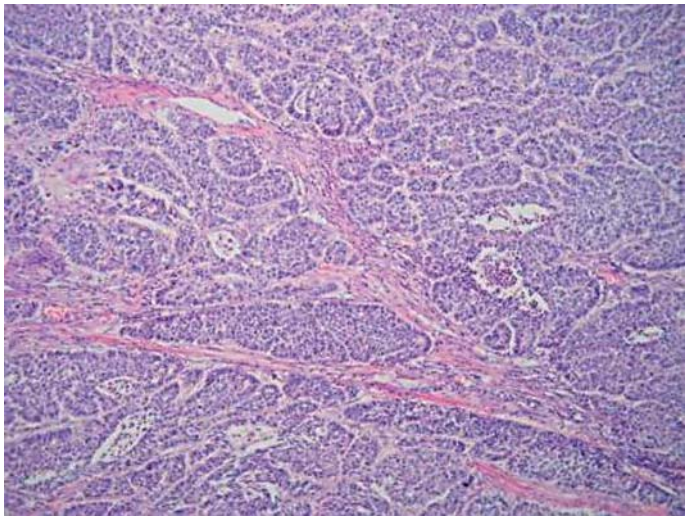

Fig. 3. The tumour was composed of endocrine cells with dark round nuclei and scant cytoplasm stained with haematoxylin and eosin (×200).

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Written informed consent was obtained from our 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.