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CASE REPORT

EDGE non-invasive radiosurgery for gastric neuroendocrine hepatic portal lymph node metastases: a case report

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Abstract

Treating metastatic gastric neuroendocrine neoplasms (gNENs) is challenging, especially for those with progressive disease during somatostatin analog processing. In this report, we present a case of a well-differentiated grade 2, type 3 gNEN with metastatic hepatic portal lymph nodes. EDGE non-invasive radiosurgery (800 cGy × 5 F) was performed to radiate the metastatic hepatic portal lymph nodes. Three months after the hyperfractionated radiotherapy, no signs of metastatic hepatic portal lymph nodes were observed using ^{8}Ga-dotatate positron emission tomography-computed tomography or magnetic resonance imaging. Therefore, EDGE non-invasive radiosurgery could be a potential option for treating local metastatic nodes.

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Key words: gastric neuroendocrine neoplasm (gNEN); hepatic portal lymph node metastases; EDGE non-invasive radiosurgery

Case presentation

History

A 46-year-old man with the complaint of stomach ache for two months underwent gastroscopy at the First People's Hospital of Jingzhou (China) on January 3, 2014. Gastroscopy showed an irregular ulcer lesion (3.0 cm × 0.8 cm) at the posterior wall adjacent to the greater curvature of the junction of the gastric sinus and body, as well as chronic non-atrophic gastritis. Pathological and immunohistochemical findings demonstrated the presence of a malignant gastric tumor, with suspected adenocarcinoma or neuroendocrine neoplasm (NEN). Preoperative examinations showed no distant metastases. The patient underwent radical resection of the distal gastric cancer on January 15, 2014 at Wuhan Union Hospital, China. Postoperative pathological examinations revealed the presence of NEN (G2) measuring 3 cm × 3 cm in size, with penetration of the entire gastric wall, perineural invasion, occasional vascular cancer embolus, and (4/16) lymph node metastases. The immunohistochemical results were as follows: PCK(+), CK8/18(+), Syn(+), CgA(+), CD56(+), and Ki67 (LI:8%). During the follow-up and monitoring, gastrin and serum CgA levels were stable in the normal range. There was no sign of recurrence until August 29, 2016, when single-photon emission computerized tomography suggested multiple liver metastases. Considering the low tumor burden and asymptomatic behavior, the patient chose to postpone treatment until 2 months later. Between November 2016 and April 2017, the patient received octreotide acetate treatment monthly. Liver magnetic resonance imaging (MRI) in May 2017 showed enlargement of liver metastases and emerging hepatic portal lymph node metastases. Biopsy of the liver lesion revealed NEN metastases (G2). The patient was treated with arterial embolization on May 11, 2017 and microwave ablation on May 22, 2017 and May 27, 2017 to control liver metastases. MRI on August 2017 showed that liver metastases had partially shrunk, and hepatic portal lymph nodes were of the same size as the anterior one, in contrast to the image taken in July 2017.

Personal and family medical history

A history of chronic viral hepatitis B; no other special

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records.

Examinations and diagnosis at admission

Physical examination

Physical examination showed stable vital signs, no palpable superficial lymph node throughout the body, no significant abnormalities by cardiopulmonary auscultation, soft abdomen without tenderness, no palpable liver or spleen below ribs, normal bowel sounds, and negative digital rectal examination findings.

Auxiliary examination

I. Laboratory tests: Results of routine blood test, blood biochemistry, coagulation functions, and tumor markers showed no obvious abnormality.

II. Gastroscopy: An irregular ulcer lesion (measuring 3.0 cm × 0.8 cm) at the posterior wall adjacent to the greater curvature of the junction of gastric sinus and body, and chronic non-atrophic gastritis.

III. Gastroscopic pathology: Presence of a gastric malignant tumor, with a suspicion of adenocarcinoma or NEN.

IV. Postoperative pathological examination: NEN (G2) measuring 3 cm × 3 cm in size, with penetration of the entire gastric wall, perineural invasion, occasional vascular cancer embolus, and (4/16) lymph node metastases. The immunohistochemical results were as follows: PCK(+), CK8/18(+), Syn(+), CgA(+), CD56(+), and Ki67 (LI:8%).

Diagnosis

I. Distal gastric well-differentiated NEN (G2), type III, with hepatic portal lymph node metastases.

II. Multiple liver metastases.

Process of treatment

In September 2017, the patient was treated with EDGE non-invasive radiosurgery, 800 cGy × 5F every other day, to treat hepatic portal lymph node metastases. Radiation target volume is shown in Fig. 1. The patient did not complain of any particular discomfort during the radiotherapy process.

Follow-up

MRI in October 2017 showed that liver metastases and hepatic portal lymph nodes were the same size as the anterior one, in contrast with the image taken August 2017. According to the Response Evaluation Criteria In Solid Tumors version 1.1 [1], the patient obtained a stable-disease response (i.e., no signs of tumors observed in other sites of the body except the liver and hepatic portal lymph nodes).

^{8}Ga-dotatate positron emission tomography-computed tomography taken in December 2017 revealed multiple liver nodules in low density without a high expression of somatostatin receptor; multiple peritoneal nodules, and with or without low expressions of somatostatin receptor, being inclined to metastases (Fig. 2).

MRI in April 2018 showed that liver metastases enlarged, in contrast with the image taken October 2017; no apparently enlarged hepatic portal lymph nodes were observed (Fig. 3).

Discussion

gNENs are a group of heterogeneous tumors arising from the endocrine cells of the stomach. gNENs have diverse clinical manifestations and extremely different outcomes that depend on the clinical subtype, pathological grade, tumor stage, and other factors [2]. Based on the WHO Classification of Tumors of the Digestive System, 4th edition [3], gNENs can be divided into well-differentiated NENs (including G1 and G2) and poorly differentiated neuroendocrine carcinoma (NEC, G3). Mixed adenoneuroendocrine carcinomas (MANECs) and hyperplastic and preneoplastic lesions are special groups.

In addition to pathological typing and tumor staging, the clinical typing of gNENs is very important. Clinically, gNENs are classified into four types, which demonstrate various clinicopathologic features. Each type calls for different treatment strategies.

Type 1 tumor appears as a small (< 1 cm), polypous, multifocal NEN in the gastric body in patients with autoimmune chronic atrophic gastritis. Type 2, which also develops multifocally, is associated with gastrinoma or a type 1 multiple endocrine neoplasm (MEN-1). Type 3 is a solitary sporadic NENd and has normal gastrin level and normal gastric acid secretion. Type 4 covers solitary sporadic NEC, including poorly differentiated gNEC and MANEC [4].

Type 3 gNENs account for 14%–25% of gNENS. Patients belonging to type 3 show no manifestation of atrophic gastritis, no elevated gastrin levels, no ECL cell proliferation, or gastrinoma/MEN-1. Tumors arise solitarily in polypoid or ulcered appearance, and in most cases, the lesions are > 2 cm in diameter, which can be observed in any part of the stomach. The histopathology corresponds to mostly NEN G2 or G3 and sometimes to NEN G1. More than 50% of patients with type 3 have metastasized at the time of diagnosis with a relatively poor prognosis compared to Type 1 and Type 2.

For Type 3 gNENs in the localized phase, the treatment strategy is similar to that for gastric adenocarcinoma. Partial or total gastrectomy plus lymph node dissection is recommended; if the tumor is ≤ 2 cm, endoscopic resection or wedge resection of the stomach may also be feasible. For patients with distant metastasis, somatostatin analog (SSA) is preferred [5–6]. Octreotide and lanreotide are most commonly used SSA in clinical practice and have relatively mild toxicities and good tolerance. Additionally, everolimus can be considered after SSA

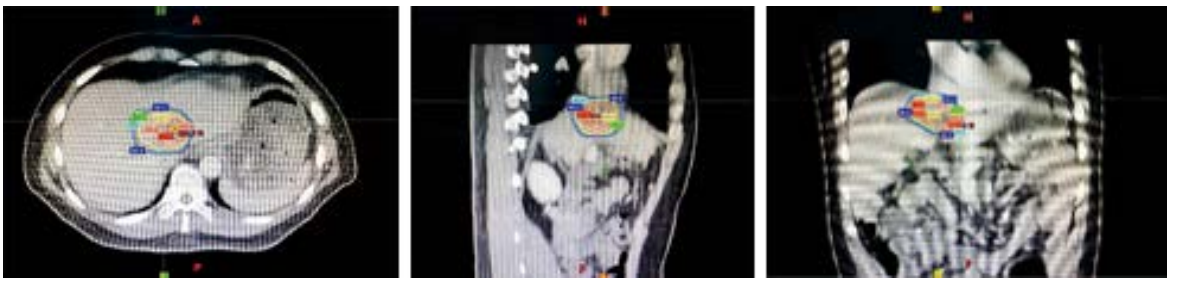

Fig. 1 Radiation target volume of EDGE non-invasive radiosurgery targeting metastatic hepatic portal lymph nodes

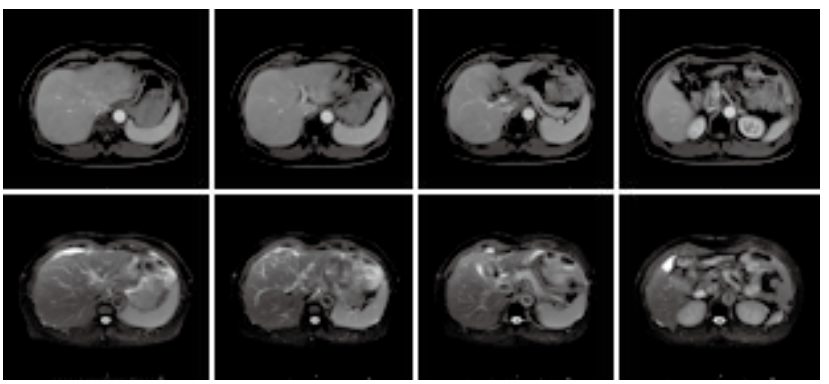

Fig. 3 MRI taken April 2018. No apparently enlarged hepatic portal lymph nodes were observed

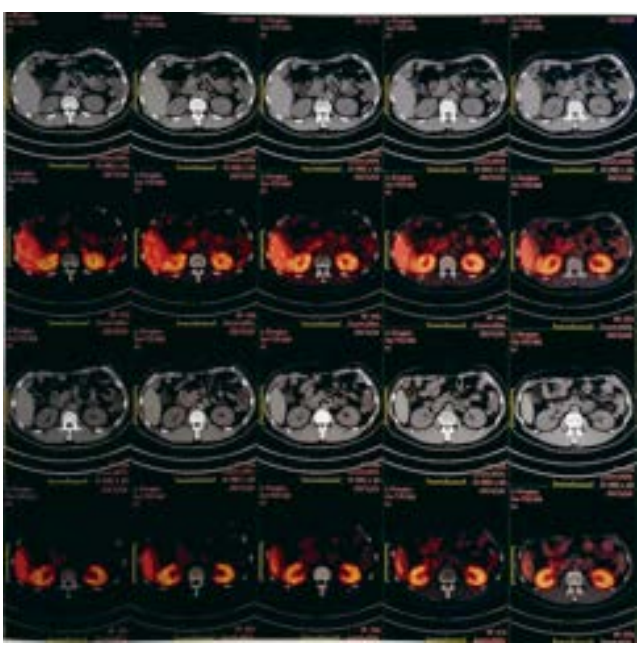

Fig. 2 ^{8}Ga-dotatate PET/CT taken December 2017. Multiple peritoneal nodules, with or without low expression of somatostatin receptor; no abnormal retroperitoneal lymph nodes with concentrated ^{8}Ga-dotatate intake

treatment failure. The RADIANT-4 study showed that everolimus lengthened progression-free survival of patients with advanced gastrointestinal and pulmonary NENs [7]. Cytotoxic chemotherapy may be applied if no other options are available, especially for patients with highly proliferative NEN (NEN G3) [8].

With respect to hepatic-predominant disease, locoregional interferences, such as arterial embolization, hepatic chemoembolization, hepatic radioembolization, or cytoreductive surgery/ablative, are also recommended [9–10]. However, for local lymph node metastasis, the locoregional therapy is hindered. It is well known that conventional radiotherapy is not widely performed for treating well-differentiated NENs owing to their radiation resistance. Therefore, we adopted hyperfractionated radiotherapy, EDGE non-invasive radiosurgery, for the treatment of well-differentiated NEN. As a result, the metastatic hepatic portal lymph nodes disappeared three months after the EDGE non-invasive radiosurgery, with no signs of recurrence seven months after EDGE non-invasive radiosurgery. Therefore, hyperfractionated radiotherapy might be an alternative treatment for local metastatic nodes.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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