



Case Series

Primary tumor resection of metastatic gastric cancer in a multimodal era: Two case reports



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ABSTRACT

INTRODUCTION: Although no consensus has been reached on the role of surgical treatment for metastatic gastric cancer, some reports suggest promising results on patients with a small disease volume upon presentation. We present two cases of metastatic disease with a favorable outcome following surgical treatment.

PRESENTATION OF CASES: The first case presented with an adenocarcinoma of the cardia, which was staged as oligometastatic due to a small liver nodule on segment III. Treatment consisted of neoadjuvant chemotherapy followed by laparoscopic esophagectomy and hepatectomy. The patient remains disease-free 62 months after surgery. Unlike the first case, the second case presented with a large number of liver nodules upon diagnosis, ruling out metastasectomy as a possible treatment. The tumor expressed HER2 receptors and responded favorably to chemotherapy plus trastuzumab for 34 months. At this point, disease progression was observed on the primary site, but the hepatic lesions remained stable. The patient underwent gastrectomy, resumed the chemotherapy regimen, and had a favorable outcome, with stability of the liver metastasis and no local recurrence following primary tumor resection.

DISCUSSION: We illustrate through these two cases the effectiveness of a combined approach featuring perioperative chemotherapy and radical surgery for selected cases of oligometastatic gastric cancer, which we hope will spur further research on the topic.

CONCLUSION: Systemic treatment in metastatic gastric cancer may represent a novel treatment approach that allows surgical resection of the primary tumor in select cases.

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1. Introduction

Historically, the presence of metastasis in gastric cancer signified ineligibility for surgical treatment and led to a marked decrease in overall survival [1,2]. Recent advancements in systemic therapies leading to better disease control have motivated a renewed discussion surrounding the role of surgical resection in metastatic gastric cancer [3]. The following two cases, which illustrate this

new paradigm, are reported in line with the SCARE criteria [4], and illustrate this new paradigm.

1.1. Case 1

A 68-year-old woman presented with dysphagia and unquantified weight loss. She had a history of smoking, mild asthma, and dyslipidemia.

Upper digestive tract endoscopy revealed an infiltrative lesion extending from the distal esophagus into the cardia that was diagnosed through biopsy as an adenocarcinoma. Positron emission tomography-computed tomography (PET-CT) revealed elevated metabolism in perigastric lymph nodes, as well as a small nodule on hepatic segment III (Fig. 1A–D). Endoscopic ultrasonography characterized the lesion as uT3 N+.

A decision was made for chemotherapy with neoadjuvant intent. The selected regimen comprised three cycles of capecitabine

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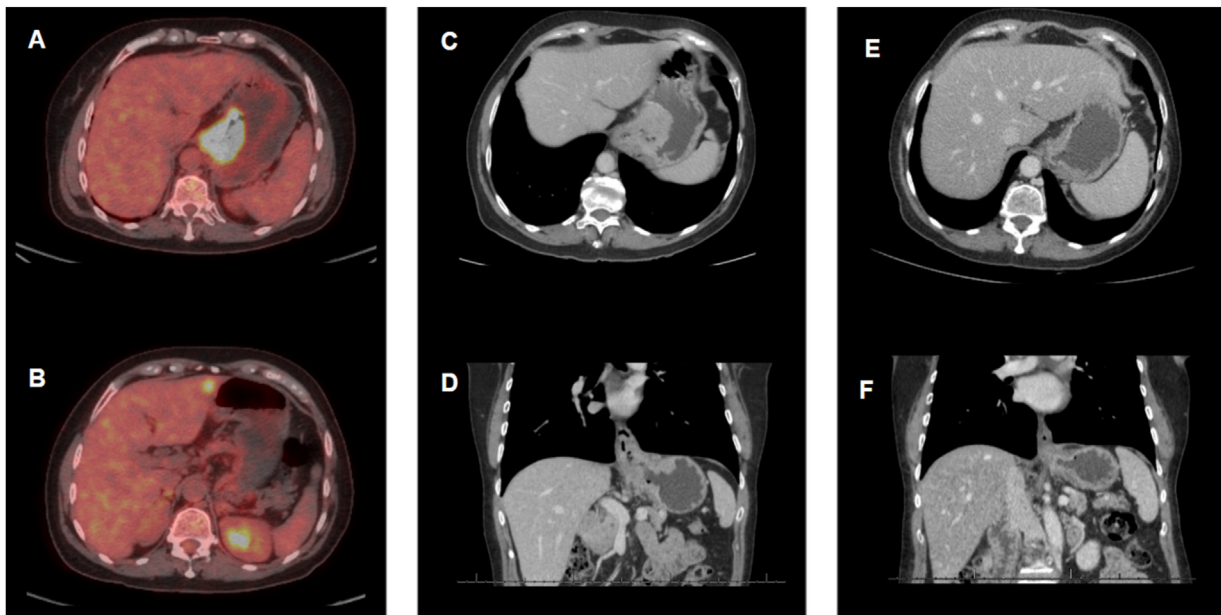


Fig. 1. (1A) PET–CT scan showing a hypermetabolic primary lesion. (1B) PET–CT scan showing a liver nodule on segment III. (1C) CT scan showing the primary lesion before neoadjuvant treatment. (1D) Coronal plane of the same study shown in 1C. (1E) CT scan showing the primary tumor after neoadjuvant chemotherapy. (1F) Same study as 1E showing the coronal plane.

(2000 mg/m²/d × 14) + cisplatin (70 mg/m² × 1). On re-staging, a remarkable decrease in volume of both the primary lesion and the secondary hepatic nodule were observed (Fig. 1E, F), motivating surgery with curative intent.

The patient underwent total gastrectomy and transhiatal esophagectomy, followed by wedge resection of the liver lesion on segment III. The postoperative period was uneventful, and the patient was discharged on the 13th postoperative day. Adjuvant chemotherapy was initiated 49 days after surgery, with two cycles of the same regimen administered preoperatively, which was interrupted by neutropenia.

Repeat imaging was performed every six months for the first two years, and once annually thereafter. As of the writing of this report, the patient has been followed for 56 months, throughout which the patient has remained disease-free. In regard to quality of life, the patient still presents symptoms of gastroesophageal reflux, but reports no other complaints. Furthermore, the patient is accepting oral intake with no restrictions and maintaining basal weight.

1.2. Case 2

A 75-year-old male presented with upper abdominal discomfort and a dry cough. He had a history of coronary heart disease and two previous stent angioplasties. Initial laboratory testing revealed anemia (Hb =9.0 mg/dL), and CT scanning of the chest was unremarkable other than multiple liver nodules. Abdominal magnetic resonance imaging (MRI) revealed gastric wall thickening in the smaller curvature with infiltration of the adjacent fat tissue measuring up to 8.2 cm, as well as the aforementioned multiple liver nodules (Fig. 2). Upper tract digestive endoscopy indicated a 6-cm infiltrative lesion on the anterior gastric wall and along the smaller curvature. Biopsy confirmed adenocarcinoma with HER2 expression. Serum CEA on diagnosis was 665.9 mg/dL.

The patient underwent nine cycles of FOLFOX associated with targeted therapy with trastuzumab. The response was favorable, with the size of the hepatic nodules decreasing significantly to 2.5 cm and with CEA dropping to 8.28, representing a 98.8 % decrease. The regimen was altered to 5-FU + trastuzumab and maintained for a total of 63 additional cycles over 34 months, with a satisfactory

response and hepatic nodules reaching a size of 1.3 cm. After this point, the gastric lesion showed growth despite stability of the liver nodules. In the face of localized disease progression, a decision was made for surgical resection.

The patient underwent partial gastrectomy with D2 lymphadenectomy and Roux-en-Y reconstruction. The surgical specimen was staged as ypT3 ypN1 (2/18). Chemotherapy was resumed postoperatively with the same regimen.

As of the writing of this article, the patient has been followed for 49 months since the beginning of the treatment, and 14 months since surgery. The patient remains under the same chemotherapy regimen, with minor toxicity-related symptoms (G1 neuropathy). The patient is reportedly content with the treatment approach, and no signs of disease progression have been observed on any site thus far.

2. Discussion

Metastatic disease is present on diagnosis in up to 32.6 % of all gastric cancer cases and represents a poor prognosis factor, with overall survival ranging from 4 to 5 months [1,2]. To date, there is no international consensus establishing the role of surgery in the metastatic scenario. Notably, Japanese studies generally issue a weak recommendation for hepatectomy in patients with a small number of metastases and no other incurable factors [5], while the ESMO guidelines recommend against metastasectomy on the grounds that it does not improve survival [6]. Nevertheless, several retrospective studies point towards a survival benefit associated with surgical therapies for metastatic disease [7–16], particularly when R0 resection can be achieved [17]. Additionally, the FLOT3 trial showed a survival benefit in patients subjected to surgical resection of metastatic lesions after neoadjuvant chemotherapy [18]. Ongoing studies are further investigating this treatment modality, such as the FLOT5 and the SURGIGAST trial.

The idea of oligometastatic disease as distinct from both localized and advanced disease was first proposed in 1995 and has since been used as a model to explain the prolonged disease-free survival observed in some patients who undergo metastasectomies. Multiple definitions have been proposed for oligometastasis, all of which

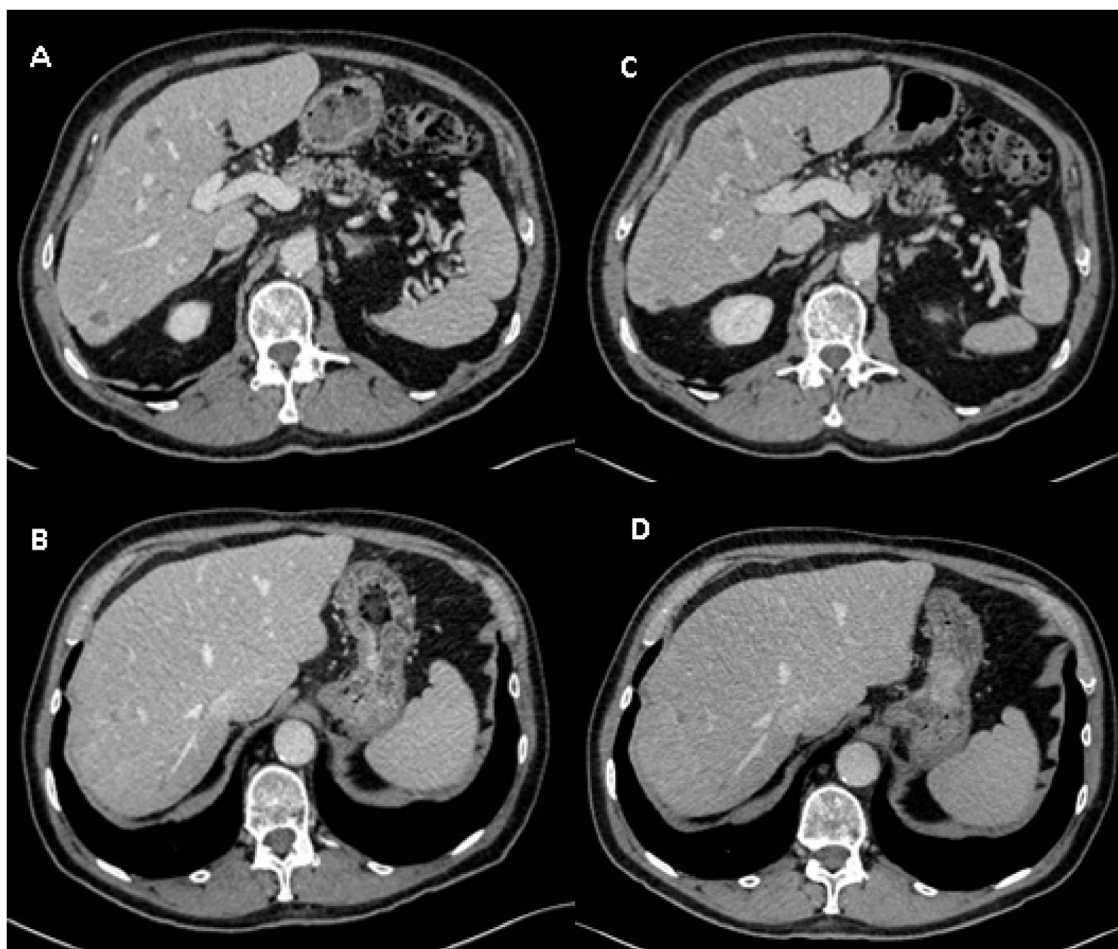


Fig. 2. (2A) CT scan showing liver metastases. (2B) Same CT scan showing the primary gastric lesion. (2C) Restaging CT scan showing stable liver metastases. (2D) Same CT scan showing progression of the disease in the primary gastric lesion.

center around a small number of metastases that are restricted to one or two sites. While definitive proof of the validity of such a concept remains to be reached, molecular findings suggest differing tumor biologies between multiple and oligometastatic cancers [19].

In the first case presented, the patient had metastatic disease on diagnosis, which was restricted to a single liver metastasis of a small diameter, in line with favorable prognosis factors described in the current literature [19]. A favorable response to neoadjuvant chemotherapy further reinforced that this case was a good candidate for resection. The results, as reflected by prolonged survival relative to what is usually expected for metastatic disease, support the current trends regarding the treatment of oligometastatic gastric cancer.

The second case illustrates a tailored approach to a heterogeneous tumoral response to systemic treatment. The patient presented with a large volume of disease in the liver that was considered unresectable on diagnosis. After an initially excellent response to chemotherapy associated with anti-HER2 therapy, there was disease progression restricted to the primary site, while liver disease was stable. Surgical approach proved effective, and the metastatic lesions remained responsive to systemic treatment after removal of the primary site.

Although gastrectomy in the context of metastatic disease has been discouraged since the results of the REGATTA trial [20], which showed no survival benefit for gastrectomy following chemotherapy relative to systemic treatment alone, this particular case benefitted from the approach, warranting further investiga-

tion of the possibility of heterogeneous response across multiple sites.

3. Conclusion

Although not reflected in current guidelines, oligometastatic gastric cancer appears to possess a distinct course and etiology in which surgical treatment could play a significant role. The cases presented serve as two examples of surgical intervention yielding survival times longer than would have been expected with systemic treatment exclusively.

As mentioned, the current literature houses a compelling repertoire of retrospective studies on this topic, but few controlled clinical trials. More studies of this type are needed to formulate practice guidelines. We expect the upcoming results of the FLOT5 and SURGIGAST trials to bring further advancements on this front.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

Ethical approval exemption was given for this study.

Consent

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Author's contribution

Flavio Roberto Takeda: Conceptualization, writing, formal analysis.

Rodrigo N Garcia: writing – review and editing.

Serli Kiyomi Nakao Ueda: writing – review and editing radiological images.

Renata D'alpino Peixoto: writing – review and editing.

Rubens Antonio Aissar Sallum: writing and Supervision.

Ivan Cecconello: Supervision.

Registration of research studies

Not applicable.

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