Case Reports in Oncology

Case Rep Oncol 2018;11:305–310

DOI: 10.1159/000488978
Published online: May 17, 2018

Case Report

Complete Response for More than 4 Years following Neoadjuvant FOLFOX and Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy for a Patient with Advanced Gastric Cancer with Extensive Peritoneal Carcinomatosis

Renata D'Alpino Peixoto[a] Tercia Tarciane de Sousa[b]
Pedro Alexandre Ismael Amaral Silva[b] Luciana Rodrigues de Meirelles[c]
Carlos Henrique Andrade Teixeira[b]

[a]Centro Oncológico Antônio Ermírio de Moraes, São Paulo, Brazil; [b]Hospital Alemão Oswaldo Cruz, São Paulo, Brazil; [c]Hospital Sírio Libanês, São Paulo, Brazil

Keywords

Gastric cancer · Cytoreductive surgery · Intraperitoneal chemotherapy

Abstract

Background: Peritoneal carcinomatosis is usually a terminal disease with short median survival in patients with gastric cancer. Systemic FOLFOX is one of the most used regimens in the first-line treatment of metastatic gastric cancer. However, there is scarce evidence that cytoreductive surgery (CRS) and intraperitoneal heated chemotherapy (HIPEC) improves oncological outcomes of patients with advanced gastric cancer. ***Methods:*** Herein we present a case of a young woman with advanced gastric cancer with omental and peritoneal metastases who achieved an excellent response after 6 months of FOLFOX followed by CRS and HIPEC. ***Results:*** A 53-

KARGER

Renata D'Alpino Peixoto
Hospital Alemao oswaldo Cruz
Rua Treze de Maio, 1815
São Paulo 01327-001 (Brazil)
E-Mail renatadalpino@gmail.com

Case Reports in Oncology

Case Rep Oncol 2018;11:305–310
DOI: 10.1159/000488978

year-old woman was diagnosed with advanced gastric carcinoma, with extensive omental caking and several peritoneal implants measuring 2 cm at the largest diameter. The patient received mFOLFOX6 for 6 months with excellent clinical and radiographic response. She was then submitted to a D2 total gastrectomy followed by CRS and HIPEC with mitomycin. The final pathology report showed a focal adenocarcinoma in the stomach measuring 0.4 mm with no residual tumor in the peritoneum (ypT1ypN0). The patient has been well and disease free for more than 4 years. ***Conclusion:*** While still controversial, CRS followed by HIPEC may be a curative therapeutic option for highly selected patients.

Introduction

Gastric cancer is one of the most common cancers worldwide, being responsible for several thousands of deaths every year [1]. Most patients either present with advanced disease or develop recurrence after a curative-intent treatment [2]. Despite improvement of systemic therapy in the recent era, long-term survival rates for patients with advanced gastric cancer remains poor [3].

The peritoneal surface is the major failure site for patients with gastric cancer and has been associated with female gender, advanced T-stage, distal lesions, and diffuse-type tumors [4, 5]. Indeed, intraperitoneal spread of tumor cells has been observed in more than 50% of patients who die of recurrence following surgery in gastric cancer [6]. The physiopathology of peritoneal carcinomatosis involves exfoliation of the cancer cells from the serosal surface of the stomach into the peritoneal cavity, which confers an even shorter survival in patients with advanced gastric cancer. Traditionally, treatment options for gastric cancer patients with peritoneal deposits include systemic chemotherapy, supportive care, and palliative surgery for those who develop obstruction.

During the more recent years, novel techniques have been under development and allowed aggressive surgery to gain a definitive role among selected patients with peritoneal carcinomatosis. This strategy consists of complete cytoreductive surgery (CRS) of peritoneal lesions followed by administration of hyperthermic intraperitoneal chemotherapy (HIPEC). The aim of CRS is to eradicate all macroscopic disease, while intraperitoneal perfusion of a heated solution containing antineoplastic drugs tries to eliminate remaining viable tumor cells in the peritoneal cavity [7]. Since the extent of peritoneal deposits, as measured by the peritoneal cancer index, is essential to a favorable outcome, prognostic indicators are used to select patients for treatment [8]. Although long-term survivors have been described with CRS and HIPEC [9, 10], both complexity and toxicity associated with the procedure have prevented them from gaining widespread acceptance.

Here we present the case of a patient with advanced gastric cancer who achieved a near-complete clinical response to neoadjuvant FOLFOX and underwent CRS and HIPEC, being now cancer free for more than 3 years.

Case Description

A previously healthy 53-year-old woman presented in May 2013 with increased abdominal volume. An ultrasound revealed ascites and peritoneal deposits. This was followed by computed tomography on May 24, 2013, which demonstrated omental caking and several peritoneal implants measuring 2 cm at the maximum diameter (Fig. 1). There was no evidence

of visceral metastasis. An endoscopy was requested and revealed a 5.0-cm ulcerated lesion at the greater curvature. Biopsy confirmed a signet-ring cell carcinoma of the stomach, HER2 negative (Fig. 2). The patient was started on systemic 5-fluorouracil and oxaliplatin (FOLFOX) and achieved an excellent clinical response, as demonstrated by a computed tomography scan of August 1, 2013 (Fig. 3). It showed a marked reduction of the ascites, omental and peritoneal lesions. After 12 cycles of FOLFOX, she underwent total gastrectomy, D2 lymphadenectomy, and CRS with HIPEC (mitomycin C) on January 2, 2014. The final pathology report demonstrated only a focal adenocarcinoma in the stomach measuring 0.4 mm with no residual tumor in the peritoneum (ypT1 ypN0) (Fig. 4, Fig. 5). Since then, the patient has been well and disease free for more than 4 years.

Discussion

With limited available data from the literature, CRS with HIPEC seems to provide survival benefits to selected patients with advanced gastric cancer due to peritoneal carcinomatosis. However, the results of HIPEC with conventional drugs such as oxaliplatin, mitomycin C, and 5-fluorouracil in peritoneal carcinomatosis of gastric origin have been disappointing when compared to pseudomyxoma peritonei or colorectal cancer [9]. In a retrospective French study including 159 gastric cancer patients with peritoneal disease as the only site of metastatic involvement, CRS plus HIPEC yielded a 5-year overall survival (OS) rate of 13% and a median OS of only 9.2 months [10]. Moreover, complete cytoreduction increased the 5-year OS to 23% [10]. Later, the beneficial effect of HIPEC in the treatment of gastric carcinoma with peritoneal carcinomatosis was demonstrated in a small phase III trial with 68 patients who were randomized between complete CRS alone or complete CRS followed by HIPEC [11]. Macroscopic complete cytoreduction was achieved in approximately 60% of the patients in each arm. In this study, intraperitoneal chemotherapy involved cisplatin 120 mg and mitomycin C 30 mg each in 6,000 mL of normal saline at 43°C over 60–90 min. At a median follow-up of 32 months, there was only 1 patient alive (2.9%) in the CRS group, while there were 5 (14.7%) long-term survivors in the CRS plus HIPEC group. Median OS was significantly increased in the HIPEC group (11 vs. 6.5 months, $p = 0.046$). A multivariate analysis revealed that complete CRS plus HIPEC, synchronous peritoneal carcinomatosis, completeness of surgery, systemic chemotherapy ≥6 cycles, and no serious adverse events were independent predictors for better OS [11].

More recently, a small trial with 17 gastric cancer patients randomized them to CRS plus HIPEC and systemic 5-fluorouracil, oxaliplatin, and irinotecan (FOLFOXIRI) or systemic FOLFOXIRI alone [12]. Median OS was 11.3 months in the more aggressive arm compared to only 4.3 months in the chemotherapy alone group. In addition, the authors reported 2 long-term survivors in the surgery plus systemic chemotherapy group (one of them for more than 4 years). All 4 patients surviving beyond 12 months achieved complete cytoreduction and had an initial peritoneal cancer index of ≤15 [12].

However, CRC with HIPEC has been considered a highly morbid approach. In the aforementioned retrospective French study, postoperative mortality was 6.5% with an estimated grade 3–4 morbidity of 28.8% [10]. In addition, the phase III trial comparing CRS with or without HIPEC reported serious adverse events in 14.7% of the combined strategy group, including wound infection, sepsis, respiratory failure, gastrointestinal bleeding, severe bone marrow suppression, and intestinal obstruction [11]. Those serious adverse events had a marked negative impact on OS.

The fact that our patient has been cancer free for more than 4 years highlights the importance of considering CRS plus HIPEC in selected patients. The optimal clinical response to neoadjuvant FOLFOX was crucial to determine the choice of this aggressive strategy, allowing the patient to achieve complete cytoreduction. This is a very unique case since patients with upfront large peritoneal involvement are usually denied surgery and have a dismal prognosis. However, this patient achieved an almost complete response with FOLFOX and was then submitted to CRS with HIPEC, offering her a disease-free interval of more than 4 years now.

In conclusion, maximal CRS combined with HIPEC and systemic chemotherapy in well-selected patients with gastric carcinomatosis and limited disease burden may achieve prolonged OS. Patient selection should be carried out by a multidisciplinary team of specialists, including experienced surgeons, anesthesiologists, clinicians, and oncologists.

Statement of Ethics

The patient has approved this case report.

Disclosure Statement

The authors have nothing to disclose.

Funding Sources

There were no funding sources.

References

1 Botterweck AA, Schouten LJ, Volovics A, Dorant E, van Den Brandt PA. Trends in incidence of adenocarcinoma of the oesophagus and gastric cardia in ten European countries. Int J Epidemiol. 2000 Aug;29(4):645–54.
2 Glehen O, Mohamed F, Gilly FN. Peritoneal carcinomatosis from digestive tract cancer: new management by cytoreductive surgery and intraperitoneal chemohyperthermia. Lancet Oncol. 2004 Apr;5(4):219–28.
3 Wagner AD, Unverzagt S, Grothe W, Kleber G, Grothey A, Haerting J et al. Chemotherapy for advanced gastric cancer. Cochrane Database Syst Rev. 2010 Mar;(3):CD004064.
4 Maehara Y, Hasuda S, Koga T, Tokunaga E, Kakeji Y, Sugimachi K. Postoperative outcome and sites of recurrence in patients following curative resection of gastric cancer. Br J Surg. 2000 Mar;87(3):353–7.
5 D'Angelica M, Gonen M, Brennan MF, Turnbull AD, Bains M, Karpeh MS. Patterns of initial recurrence in completely resected gastric adenocarcinoma. Ann Surg. 2004 Nov;240(5):808–16.
6 Fujimoto S, Takahashi M, Mutou T, Kobayashi K, Toyosawa T. Successful intraperitoneal hyperthermic chemoperfusion for the prevention of postoperative peritoneal recurrence in patients with advanced gastric carcinoma. Cancer. 1999 Feb;85(3):529–34.
7 Brücher BL, Piso P, Verwaal V, Esquivel J, Derraco M, Yonemura Y et al. Peritoneal carcinomatosis: cytoreductive surgery and HIPEC—overview and basics. Cancer Invest. 2012 Mar;30(3):209–24.
8 Sugarbaker PH. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the management of gastrointestinal cancers with peritoneal metastases: progress toward a new standard of care. Cancer Treat Rev. 2016 Jul;48:42–9.
9 Glehen O, Gilly FN, Boutitie F, Bereder JM, Quenet F, Sideris L et al.; French Surgical Association. Toward curative treatment of peritoneal carcinomatosis from nonovarian origin by cytoreductive surgery combined with perioperative intraperitoneal chemotherapy: a multi-institutional study of 1,290 patients. Cancer. 2010 Dec;116(24):5608–18.

10 Glehen O, Gilly FN, Arvieux C, Cotte E, Boutitie F, Mansvelt B et al.; Association Française de Chirurgie. Peritoneal carcinomatosis from gastric cancer: a multi-institutional study of 159 patients treated by cytoreductive surgery combined with perioperative intraperitoneal chemotherapy. Ann Surg Oncol. 2010 Sep;17(9):2370–7.
11 Yang XJ, Huang CQ, Suo T, Mei LJ, Yang GL, Cheng FL et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from gastric cancer: final results of a phase III randomized clinical trial. Ann Surg Oncol. 2011 Jun;18(6):1575–81.
12 Rudloff U, Langan RC, Mullinax JE, Beane JD, Steinberg SM, Beresnev T et al. Impact of maximal cytoreductive surgery plus regional heated intraperitoneal chemotherapy (HIPEC) on outcome of patients with peritoneal carcinomatosis of gastric origin: results of the GYMSSA trial. J Surg Oncol. 2014 Sep;110(3):275–84.

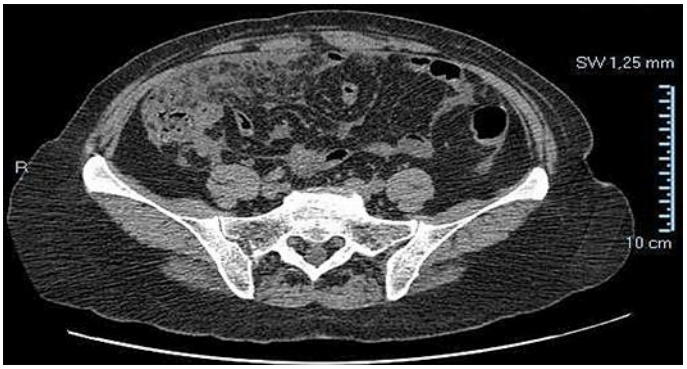

Fig. 1. CT scan showing omental caking and several peritoneal implants measuring 2 cm in the maximum diameter.

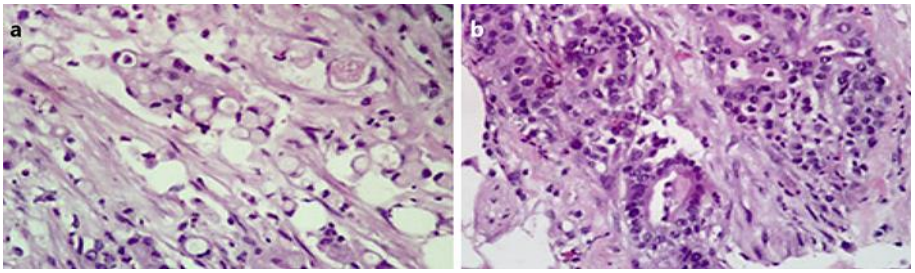

Fig. 2. **a**, **b** Poorly differentiated adenocarcinoma infiltrating the epiplon with signet-ring cells (HE).

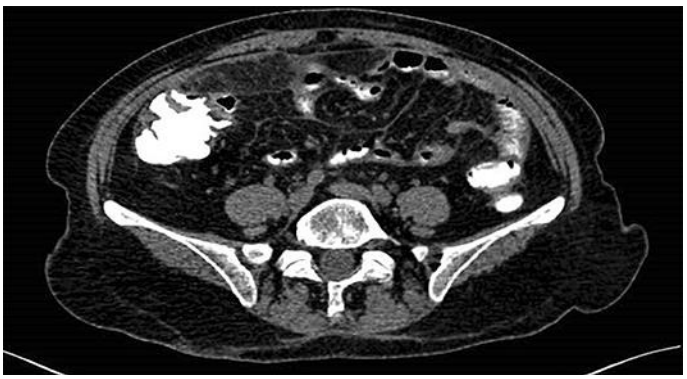

Fig. 3. CT scan showing marked reduction of the ascites, omental and peritoneal lesions.

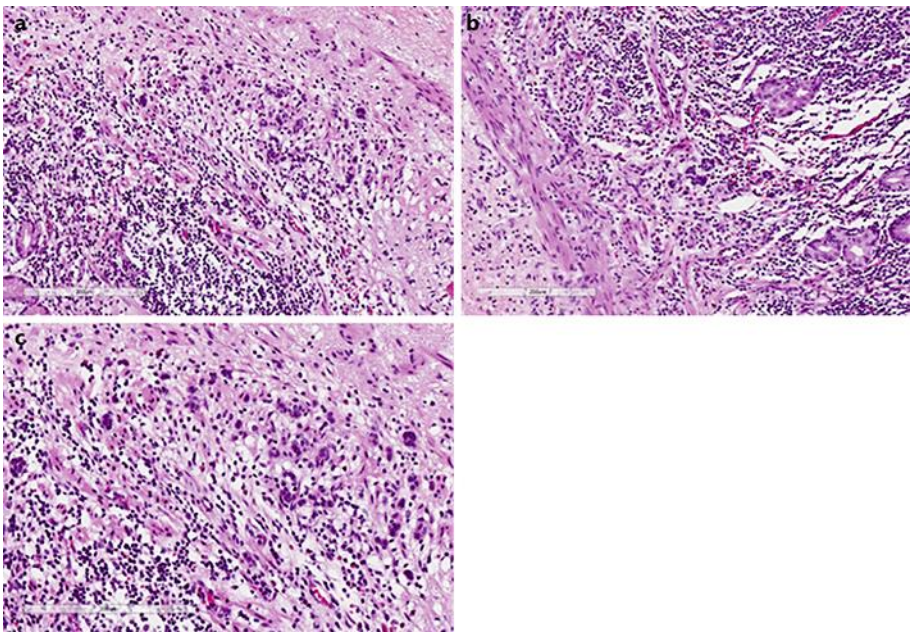

Fig. 4. **a–c** Sparse clusters of residual neoplastic cells infiltrating the muscular layer of the mucosa. The largest focus measures 0.4 mm.

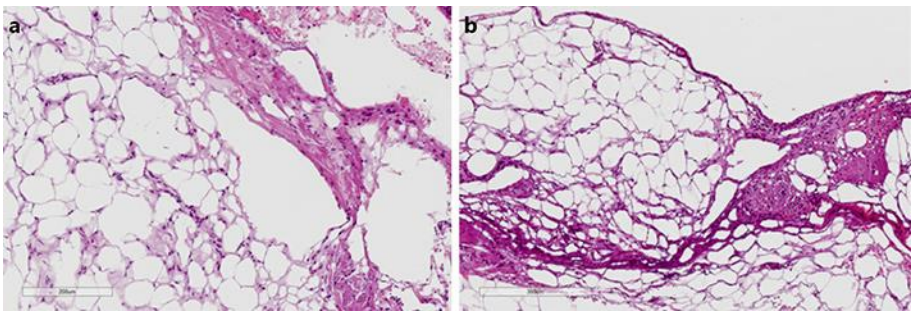

Fig. 5. **a**, **b** Peritoneum (HE, ×200). Areas of peritoneal fibrosis. Absence of residual neoplasia.