Annals of Medicine and Surgery 22 (2017) 7–11

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.annalsjournal.com

Peritoneal metastases of rare carcinomas treated with cytoreductive surgery and HIPEC – A single center case series

Andreas Brandl*, Christina Barbara Zielinski, Wieland Raue, Johann Pratschke, Beate Rau

Department of General, Visceral and Transplantation Surgery and Department of General, Visceral, Vascular and Thoracic Surgery, Campus Virchow and Mitte, Charité, Universitätsmedizin Berlin, Berlin, Germany

HIGHLIGHTS

- The difficulties in deciding of whether to perform CRS and HIPEC for PSM arising from unusual malignancies are remaining.
- Perioperative morbidity for extensive surgical treatment and HIPEC is acceptable in specialized PSM centers.
- The prospective registration in tumor registries could help to better define the indications for CRS and HIPEC in rare PSM.

ARTICLE INFO

Article history:
Received 22 May 2017
Received in revised form
3 August 2017
Accepted 3 August 2017

Keywords:
Peritoneal surface malignancies
Rare diseases
Cytoreductive surgery
HIPEC

ABSTRACT

Introduction: In selected cases, cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is an established treatment for patients suffering from peritoneal metastases from colorectal, ovarian, gastric or appendiceal origin. The effectiveness of this extensive has not been elucidated within other rare diseases by now.

Methods: We conducted a retrospective analysis of patients treated with CRS for peritoneal carcinomatosis during the period between July 2010 and September 2015. Exclusion criteria were adenocarcinomas of the stomach, colon, neoplasms of the appendix, mesothelioma and ovarian cancers. Aim of this study was to examine the feasibility, complication rate and survival of patients with rare diseases.

Results: A total of 14 Patients were included: Four rare gynecological tumors, three adenocarcinomas of the small intestine, three retroperitoneal sarcomas, one cholangiocellular carcinoma, one neuroendocrine gastric tumor, one malignant peripheral nerve sheath tumor and one cancer of unknown primary syndrome. In 12 of 14 patients a macroscopically complete tumorresection could be achieved. No patient died during hospitalization. Seven of 14 patients experienced general complication of grade III according to NCI CTCAE V4.0, while two experienced complications of grade IV. Median follow-up and one year overall survival were 15.5 months and 46.8%, respectively.

Conclusion: For patients with rare tumors, CRS and HIPEC is feasible with an acceptable perioperative morbidity and mortality. To improve knowledge in patient selection and outcome, rare tumors treated with CRS and HIPEC should be documented in central databases (as for example BIG RENAPE, Pierre-Benite, France).

1. Introduction

The key factor for improving of survival in patients with peritoneal surface malignancies (PSM) was the development of cytoreductive surgery (CRS) and intraperitoneal (IPC) or hyperthermic intraperitoneal chemotherapy (HIPEC) in recent decades. It is the gold standard for curative treatment of primary peritoneal malignancies, low-grade appendiceal mucinous neoplasm (LAMN), peritoneal mesothelioma and PSM from colorectal origin [1–6]. The indication for CRS and HIPEC in patients with PSM from ovarian or gastric carcinoma, or neuroendocrine sarcoma remains contended [7]. There are several ongoing studies, which aim to answer this question and many excellence centers do not recommend HIPEC for these indications outside of clinical trials. The treatment for PSM

* Corresponding author. Department of General, Visceral and Transplantation Surgery and Department of General, Visceral, Vascular and Thoracic Surgery, Campus Virchow and Mitte, Charité, Universitätsmedizin Berlin, Charitéplatz 1, 10117, Berlin, Germany.
E-mail address: Andreas.Brandl@charite.de (A. Brandl).

http://dx.doi.org/10.1016/j.amsu.2017.08.009

arising from other origins is even more exceptional and lacks data in the literature, which exceeds clinical case reports. While these exceptional cases of PSM of non-gastrointestinal origin are often presented with diffuse extraperitoneal dissemination, only a few of these cases can be considered for complete cytoreduction and HIPEC. The decision for this procedure has to be taken in an individual approach.

The aim of this study was to analyze morbidity, mortality of CRS and HIPEC as well as long-term results in patients with PSM of unusual origin.

2. Material and methods

This retrospective study included all consecutive patients who were treated with CRS and HIPEC between July 2010 and September 2015 at Campus Mitte, Charité, Universitätsmedizin-Berlin, Germany. Patients with gastric, colorectal, ovarian and appendiceal cancer were excluded as patients with LAMN or mesothelioma.

Routine preoperative examination was performed in every patient; CT scans of the chest, abdomen, and pelvis and tumor markers (CEA, CA19-9, and CA 125) were obtained. The surgical procedure was recommended for all patients without evidence of extraperitoneal metastases if complete cytoreduction (CC) was deemed feasible by the operating surgeon. Each therapeutic decision was preoperatively discussed in the multidisciplinary tumor board, including oncologist, radiologist, radiotherapist, and visceral surgeon. The extent of peritoneal involvement was assessed through the Peritoneal Cancer Index (PCI) [8]. The assessment took place directly after explorative laparotomy and just before cytoreductive procedures and was performed by B.R. for every patient. B.R. performed more than 300 CRS and HIPEC procedures and is an experienced surgeon in the field PSM. The PCI score was simultaneously recorded and calculated by an assistant.

Definitive CRS was carried out to achieve complete cytoreduction using, but not limited to, the following procedures: exploratory laparotomy, abdominal wall resection, abdominal and pelvic lymphadenectomy, appendectomy, cholecystectomy, bilateral adnexectomy with hysterectomy, cytoreductive surgery and biopsy of peritoneal implants, enterolysis, and ureterolysis. The peritonectomy procedures included diaphragmatic, parietal, and pelvic peritonectomy and omentectomy. Resection of hollow viscus and/or organs was performed if they could not be cleared of disease or were affected by the primary cancer. Every effort was made to avoid extensive small bowel resection and/or ostomy formation to preserve quality of life. Complete cytoreduction was defined as nodules less than 2.5 mm in size (CC = 1) or the absence of visible tumor nodules (CC = 0). Cytoreduction was followed by immediate HIPEC. HIPEC protocols differed according to different tumor entities. HIPEC was delivered for 60 min in most of the cases (83.3%) and in a closed abdomen technique in 71.4% of the patients. An open circulation system was used for the remaining 28.6% of patients. Complications were retrospectively classified regarding to Dindo/Clavien [9]. Grade $\geq$ 2b complications were considered severe. Medical complications were classified by National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI CTCAE V4.0).

Clinical data were collected during follow-up visits and no patient was lost to follow-up. The study was approved by the ethics committee of the Charité, Universitätsmedizin – Berlin, Germany (EA1/009/16). The study was registered in accordance with the Declaration of Helsinki 2013 (UIN: researchregistry1938). The case series is reported in line with the PROCESS criteria [10]. All statistical analyses were performed using either SPSS 23.0 (International Business Machines Corporation, Armonk, NY) or Prism 6.0 (Graphpad Software, Inc., La Jolla, CA). Continuous descriptive data are given as mean and standard deviation. Categorical data are given as frequencies and proportions. Univariate analysis of time to event data was performed using Log-Rank tests to compare several groups. Univariate results were visualized by Kaplan-Meier curves. A p-value below 0.05 was considered significant.

3. Results

Between July 2010 and September 2015, 14 patients underwent CRS and HIPEC of unusual origin, representing 5.7% of all patients treated with HIPEC during the same period. There were 7 female (50%) and 7 male (50%) patients, with a mean age of 52 years (±12.8). Seven unusual histologic origins of PSM were included. The patient demographics are stated in Table 1. The mean time from diagnosis to CRS and HIPEC was 17.4 months (±35.6) whilst 8 patients (57%) were treated with systemic chemotherapy preoperatively. In all 14 patients PSM was the only metastatic side. The mean intraoperative peritoneal cancer index was 12.2 (±4.8). A complete tumorresection without macroscopic visible remnants could be achieved in 12 patients (86%). The mean operation time was 6.5 (±1.9) hours. HIPEC was performed in 10 (71%) patients in a closed abdomen technique and in 3 (21%) patients using the open coliseum approach. In one patient HIPEC was not performed. The duration of circulation was in 12 patients (79%) 60 min and in one patient 30 min. The mean temperature of the chemoperfusion was 40.9 °C (±0.8). Eight (57%) patients were treated with a postoperative systemic chemotherapy after recovery of the surgical procedure. Postoperative morbidity was 50%. Surgical complications $\geq$2b occurred in one patient developing fascial dehiscence treated with operation. Non-surgical complications were found in 8 patients (1 cardiac, 3 gastrointestinal, 4 infectious, 5 respiratory disorders and 2 other complications). No patient died postoperatively. The median hospital stay was 13 (range: 8–34) days. The median follow-up was 16 months, whilst 8 (57%) patients died and 6 (43%) patients were alive. Every still living patient developed a peritoneal tumor recurrence or tumor progression. Patient's

Table 1
Patient demographics, comorbidities and ASA = physical status classification system of the American Society of Anesthesiologists.

Descriptive	
Patient	
female [%]	50 (7/14)
age [years]	50.9 ± 13.0
PCI	14.0 ± 7.8
Primary malignancy [%]	
adenocarcinoma small bowel	21.4 (3/14)
sarcoma	21.4 (3/14)
gynecologic tumor	28.6 (4/14)
cholangiocellular carcinoma	7.1 (1/14)
Gastric neuroendocrine tumor	7.1 (1/14)
CuP-syndrome	7.1 (1/14)
malignant peripheral nerve sheath tumor	7.1 (1/14)
Comorbidities [%]*	
None	42.9 (6/14)
Pulmonary	28.6 (4/14)
Cardiac	21.4 (3/14)
Renal	7.1 (1/14)
Metabolic	7.1 (1/14)
Artheriosclerosis	0 (0/14)
Hepatic	0 (0/14)
Orthopaedic	0 (0/14)
ASA [%]	
I	0 (0/14)
II	64.3 (9/14)
III	35.7 (5/14)
IV	0 (0/14)