

Case Report

From HIPEC to End-of-Life Care in Patients with Advanced Cancer: Getting to “NO”

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Background: Radical debulking with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) has been shown to potentially increase disease-free survival in highly-selected patients with certain advanced malignancies, such as pseudomyxoma peritonei, primary peritoneal mesothelioma, ovarian, gastric, and colorectal cancer; and soft tissue sarcoma with peritoneal dissemination. The goal of cytoreductive surgery is to remove all gross disease, at which point HIPEC is administered [1]. However, given the advanced state of disease and the extent of operations required to achieve optimal cyto reduction, the natural history of disease, procedure-related toxicity, anticipated meaningful recovery times, and expected symptom- and disease-free survival must be particularly considered.

Prior literature evaluating overall survival (OS) following CRS and HIPEC ranges from 19.4 to 24 months in ovarian cancer, 32.4 to 34.7 months in colorectal cancer with peritoneal spread, and 45.2 to 53 months in primary peritoneal mesothelioma and median 11.9 months for gastric cancer. Case series have demonstrated 53.4 to 86% five-year OS in pseudomyxoma peritonei [5-7,10]. Median OS for peritoneal sarcomatosis following CRS and HIPEC is 12 months [11]. Completeness of cytoreduction is associated with survival following CRS and HIPEC [10,11]. Patients who undergo initial debulking and HIPEC with good functional recovery who subsequently develop disease recurrence may undergo repeat attempts at CRS and HIPEC. However, as disease recurrence or other sequelae of those operations manifest, further operative intervention is frequently associated with diminished benefit [1]. With recurrent disease, the best opportunity for disease cure has passed, and goals of treatment may need to shift from operation with curative intent for control of disease to palliative intent to improve symptoms [2,3]. In appropriately selected patients, improved quality of life may be achieved with palliative operations while minimizing treatment toxicity [4].

Surgical palliation of cancer is defined as procedures performed explicitly with non-curative intent to improve quality of life, decrease pain, and mitigate symptoms of advanced disease [2,3]. The palliative triangle has been defined as the process of communication and shared decision-making among the patient, patient family, and surgeon in order to develop a successful therapeutic relationship and optimize patient selection and outcomes. By focusing on patient-driven goals such as symptom relief and quality of life, rather than traditional outcome measures such as morbidity and mortality at thirty days, patient satisfaction is improved following palliative operation. Our group has demonstrated high patient-reported symptom relief (90.7%) while also minimizing thirty-day morbidity (20.1%) and mortality (3.9%) when utilizing the palliative triangle in counseling patients and their families [3,8]. Frequent reassessment of patients' goals of care within the framework of the palliative triangle aids in reorienting patient counseling over the spectrum of disease [9].

Aim: To illustrate the complexity of end-of-life care in patients with advanced cancer, specifically patients who undergo maximally invasive surgery such as HIPEC, and the changing goals of care associated with disease progression, which is facilitated by utilizing the palliative triangle.

Methodology: Retrospective review of prospectively-maintained Rhode Island Hospital palliative surgery and HIPEC databases was performed, from 2008 to 2015. A case series of patient cases that illustrate the breadth and complexity of palliative surgical decision-making are provided.

CASE SERIES

Case 1

A 56 year-old man who was found to have a 12.5 cm high-grade dedifferentiated retroperitoneal liposarcoma underwent primary resection. His first recurrence was three years after initial operation, at which time he had radical debulking of all gross peritoneal metastatic sarcoma and HIPEC. In the year that followed, the patient underwent palliative resections of large, painful soft tissue metastases of both thighs. Despite several regimens of systemic chemotherapy over the next two years, the patient demonstrated disease progression with local intra-abdominal disease recurrence and distant metastases to the right shoulder and left gluteal region. The patient presented with

rectal bleeding associated with a recurrence in the descending colon that progressed to a malignant bowel obstruction with evidence of pneumatosis intestinalis. The patient was evaluated for operation but due to the patient's extent of disease and associated prognosis, metabolic and hematologic derangements, low likelihood for successful symptom palliation with surgery, and patient preference, it was decided to not proceed with operation. After extensive discussion with the patient and family, the patient transferred to inpatient hospice.

Case 2

The next patient is a 59 year-old man who presented with painful abdominal distention caused by primary peritoneal mesothelioma and underwent CRS and HIPEC. After making an

excellent recovery, he remained disease- and symptom-free for two years. However, at that point he was diagnosed with disease recurrence, amenable to repeat CRS and HIPEC. Six months later, peritoneal, pulmonary and hepatic metastases were identified. Due to his tumor biology and extent of disease, operation was not recommended and the agreement among patient, family, and surgeon was to pursue a palliative approach to his care by maximizing symptom management and quality of life. Within one month of starting palliative chemotherapy, the pelvic, pulmonary, and hepatic lesions completely regressed. He has done well for over eighteen months and has remained symptom-free with no evidence of disease progression.

Case 3

After initially presenting with colon cancer and metastatic peritoneal implants, this 72 year-old man was referred for resection of his primary disease, tumor debulking and HIPEC after having an excellent response to FOLFOX. He had a complete pathologic response and no residual tumor was identified. He did well for three years but then presented with evidence of ischemic bowel associated with a malignant bowel obstruction. He was found to have a single metastatic recurrence and underwent small bowel resection. Four months after an unremarkable recovery, he was readmitted with another malignant bowel obstruction and evidence of multiple obstructing recurrences. After initial successful symptom improvement with steroids and octreotide, the patient's symptoms progressed and he was transitioned to inpatient hospice.

Case 4

This 48 year old man initially presented with advanced pseudomyxoma year-old by severe malnutrition that required preoperative parenteral nutrition (PN) support. He underwent radical debulking of over twenty liters of gross disease and was treated with HIPEC. His pathology was consistent with high-grade malignancy. Following recovery from surgery, the patient received adjuvant chemotherapy. He remained disease-free for one year prior to his first recurrence, which presented as a malignant bowel obstruction. Imaging showed diffuse involvement of intra-abdominal structures. The patient was taken for repeat debulking, requiring total abdominal proctocolectomy and end ileostomy, and HIPEC. Although the patient has shown no evidence of recurrent disease for over two years, he has had several office and emergency room visits for abdominal pain, metabolic abnormalities, and other issues including non-occlusive superior mesenteric vein thrombosis, all of which have been managed non-operatively. Because of his anticipated disease prognosis and extent of prior surgery, it was decided that active symptom management with non-operative interventions would be utilized going forward. He continues to report an excellent quality of life and enjoys raising his young children.

Case 5

The final patient is a 53 year-old woman who was diagnosed with high-grade appendiceal cancer. She underwent a right hemicolectomy at an outside hospital followed by adjuvant chemotherapy. The pathology from her initial operation revealed poorly-differentiated adeno carcinoma of the appendix with

signet ring features. Two years later, the patient was found to have disease recurrence, and at that time she received radical debulking of all gross disease and HIPEC. Three months later, the patient presented to the emergency department with a complete small bowel obstruction. She was found to have ischemic bowel associated with an obstruction caused by a single adhesive band managed operatively with exploratory laparotomy and small bowel resection. An incidental small bowel metastasis was also resected. One year later, she continues to have no evidence of disease on serial imaging and enjoys an excellent, symptom-free quality of life.

DISCUSSION

Patients with peritoneal surface malignancy represent a diverse array of tumor biology. Many patients have the potential for long-term disease-free survival following radical cytoreductive surgery and HIPEC, while others will develop disease recurrence relatively soon after initial operation. Peritoneal cancers are considered to be advanced malignancy, and as such the ideal outcome of disease cure is tempered by the real possibility of disease progression. When the opportunity for cure is lost, shifting the goal of treatment from curative to palliative intent coincides with the transition of treating the disease itself to focusing on treating the symptoms associated with the disease. The palliative triangle provides the framework within which such a transition is facilitated, by involving the patient, patient family, and surgeon.

Palliation of disease recurrence following CRS and HIPEC takes many forms. In the case summaries presented here, patients underwent a variety of subsequent operations with palliative intent, from bowel resection or soft tissue excision for metastatic lesions to operation for benign disease processes that are well-described in the literature [12 -14]. The selected cases represent a wide range of primary tumor types and clinical courses following CRS and HIPEC. The commonality that links these five cases together is that over the course of their care, the patients went from maximal surgical treatment involving radical tumor debulking followed by HIPEC, to subsequent palliative operation(s), to the shared decision to pursue no further operative management of their disease. This progressive and continual reevaluation of treatment goals exemplifies the range of decision-making required to care for the patient with advanced peritoneal surface malignancy. The tendency for operations in this patient population to be initially performed with curative intent but after three or more operative interventions be performed exclusively for symptom management with palliative intent has been describe previously. As the duration of the symptom-free interval decreases with each subsequent operation [1], there is an inflection point at which the burden of therapy (operative risk, recovery, cost, ect.) overwhelms the potential benefits. Similarly, just as highly-selected patients will benefit from a palliative operation, other patients derive more benefit from alternative palliative treatments such as radiation or chemotherapy.

Optimal surgical palliative care often requires the surgeon to recommend non-surgical therapy Previous literature has shown that approximately 50% of palliative surgical consultations do not lead to operations. Optimal care of patients such as these is greatly enhanced- and to a large part requires- and long-

term and effective relationships among patient, family, and surgeon [3]. In this case series, as patients' conditions and active symptoms changed, initial plans of care including extensive and complex operations were replaced with decisions to not proceed with additional invasive procedures. In this case series, as patients' conditions and active symptoms changed, initial plans of care including significant disease- and symptom-free state that would potentially have been diminished by recovery from further operative intervention. In all of these cases, an established and effective patient-provider relationship over the course of treatment complemented the shared decision-making process and eventually enhanced end-of-life care in a meaningful and culturally appropriate way for patients and their families. The ongoing counseling process among surgical oncologists and patients and their families allows for the appropriate determination of treatment plans that match goals of care, including the decision to arrange for hospice care, for patients with advanced malignancy.

CONCLUSION

A continuum of care exists in the care of the advanced cancer patient. Providers must be well-versed in the tumor biology while being actively involved in overall cancer treatment plans in order to best effect optimal care even after cure is no longer possible. Effective use of the palliative triangle fosters open dialogue among patient, family, and surgeon to best assess treatment goals and pursue appropriate management over the spectrum of disease.

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