

CASE REPORTS

An Invasive Treatment of Pseudomyxoma Peritonei with Intrathoracic Involvement

Rami ABABNEH^a; Pompiliu PISO^b; Hans-Stefan HOFMANN^b;
Anca DUMITROVICI^a; Rares BUIGA^a; Gabriel SAMASCA^c; Claudia BURZ^{a,b}

^a “Prof. Dr. Ion Chiricuta” Institute of Oncology, Cluj-Napoca, Romania

^b Barmherzige Brueder Hospital Regensburg, Germany

^c Department of Immunology; “Iuliu Hatieganu” University of Medicine and Pharmacy Cluj-Napoca, Romania

ABSTRACT

Pseudomyxoma peritonei (PP) is a rare disease characterized by the presence of mucinous ascites and low and progressive accumulation of peritoneal implants. We report the case of a 44-year-old man presented with ascites, imaging evaluations suggesting the diagnosis of gelatinous peritoneal carcinomatosis. The patient underwent laparoscopy with extensive cytoreductive surgery combined with hyperthermic intraoperative peritoneal chemotherapy (HIPEC). Microscopic features confirmed the diagnosis of low-grade PP. Nine months later the patients developed left pleural effusion and cytological examination releaved the intrathoracic extension of PP. The treatment consisted in extensive intrathoracic cytoreductive surgery in combination with hyperthermic intrathoracic chemotherapy perfusion (HITOC). Further surgery was required due to intra-abdominal recurrence and finally, the patient developed hepatic and pulmonary metastases treated by systemic chemotherapy, with good tolerability and complete response.

Keywords: pseudomyxoma peeritonei, cytoreductive surgery, hyperthermic intraoperative, peritoneal chemotherapy, hyperthermic intrathoracic chemotherapy perfusion

INTRODUCTION

Pseudomyxoma peritonei (PP) is characterized by intra-abdominal gelatinous collections and progressive accumulation of peritoneal implants. It is accepted that PP arises from the neoplastic mucin-secreting cells derived from the appendix. Intrathoracic extension of PP is unusual that explain the lack of informations about morphologic features of thoracic involve-

ment (1). The optimal treatment of PP remains poorly defined, aggressive cytoreduction combined with hyperthermic intraperitoneal chemotherapy (HIPEC) have demonstrated prolonged survival but with high morbidity (2). Regarding the treatment of intrathoracic extension of PP there is not a standard recomandation, systemic palliative chemotherapy remains a usual option, intrathoracic cytoreduction combined with chemotherapy (HITOC) being performed only in specialized centers. PP rare-

Address for correspondence:

Gabriel Samasca, Department of Immunology, 19-21 Croitorilor Street, “Iuliu Hatieganu” University of Medicine and Pharmacy, Cluj-Napoca, Romania.

E-mail: Gabriel.Samasca@umfcluj.ro

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ly spreads through the lymphatic or blood system so the efficacy of systemic chemotherapy in metastatic setting is unclear.

We report a case of a 44-year-old man with PP and intrathoracic involvement by PP who underwent multiple extensive cytoreductive surgeries in combination with intraoperative hyperthermic chemotherapy followed by systemic chemotherapy for systemic disease with a good tolerability and complete response. □

CASE REPORT

A 44-year-old man from an urban area, with no past medical or surgical history, was admitted complaining of one week history of progressive lower abdominal pain and continuous vomiting. Physical examination showed a distended abdomen with mild lower abdominal tenderness. Complete blood analysis were within normal level, carcinoembryonic antigen level (CEA) was high (86 ng/ml). Computed tomography (CT) showed significant ascites and suspicion of peritoneal carcinomatosis (Figure 1). The patient underwent exploratory laparoscopy, which revealed massive gelatinous ascites, peritoneal metastases, and a tumor with mucoid content in contact with the cecal appendix. The patient underwent extensive cytoreductive surgery with parietal and visceral peritonectomy, total parietal peritonectomy, omentectomy, hepatic Glisson's capsule and caudate lobe resection, right hemicolectomy, proctectomy, splenectomy, gastrectomy including lymphadenectomy. The histopathology examination revealed PP with predominant low-grade appendiceal mucinous neoplasm. Treatment was completed by HIPEC with Oxaliplatin, 5FU, Leucovorin. Postoperative course was complicated by leakage of the ileo-transverse anastomosis and further re-do surgery was performed.

Imaging evaluation nine months after surgery revealed left pleural effusion with no signs of abdominal recurrence. Cytological examination of the pleural effusion was positive for mucinous adenocarcinoma and the levels of CEA was high (100.85 ng/ml). A thoracotomy was performed. The operation revealed pleural effusion (nearly 500 ml) and myxomatous tumor on the visceral and parietal pleura. Cytoreductive surgery included total pleurectomy, subtotal pericardiectomy and total resection of the left diaphragm. Pericardium as well as dia-

phragm were reconstructed with bovine pericardium. HIPEC with 150 mg/m² cisplatin was performed for one hour during surgery. Nine months after the second surgery increased levels of tumor marker CEA were registered. Abdominal ultrasound and CT showed intraabdominal tumour relapse. Third surgical intervention was performed consisting in resection of the bladder dome, abdominal wall and reconstruction of abdominal wall by a prosthetic mesh. The histopathology examinations revealed this time high grade neoplasm, more aggressive than in the previous examinations.

A CT scan two months later showed hepatic and pulmonary metastases. Palliative chemotherapy was recommended. The patient subsequently underwent eight cycles of chemotherapy with FOLFOX regimen (oxaliplatin, leucovorin, 5-FU), with complete response after 8 cycles of treatment (Figure 2). □

DISCUSSION

PP is attributable to a ruptured mucinous appendicular cystadenocarcinoma. Unlike most cancers, this disease rarely spreads through the lymphatic system or through the

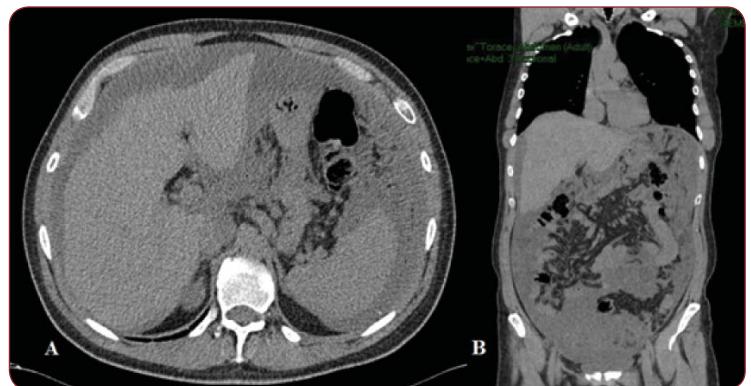


FIGURE 1. Abdominal CT scan showing significant ascites.



FIGURE 2. Abdominal CT scan after surgery showing no evidence of tumor formation.

bloodstream. Current treatment strategies range from watchful waiting to cytoreductive surgery with HIPEC or early postoperative intraperitoneal chemotherapy (3). Even if the complete cytoreduction is attempted, the major organ resection is rarely performed due to high rate of morbidity. Our patient underwent aggressive surgery including splenectomy, right colectomy, gastrectomy, proctectomy, despite peritoneal cancer index above 20 justified by the good performance status and young age. The patient received HIPEC with Oxaliplatin, 5FU and Leucovorin. HIPEC enhances the cytotoxicity of chemotherapeutic agents and increases tissue penetration by chemotherapy in cancerous tissue as compared to normal tissue. Nine months after the first surgery, the patient developed intrathoracic extension of PP. Rarely described, the thoracic involvement by the PP has been documented as pleural effusions or pulmonary metastasis but little is known about the morphological features of intrathoracic tumor spread. The interval between the diagnosis of PP and the discovery of intrathoracic disease range from less than 1 years to 15 years. Several mechanisms for explaining the invasion of tumor cells from the peritoneal cavity to pleural space have been proposed as iatrogenic damage of the diaphragm during peritonectomy, the presence of a congenital or acquired pleuroperitoneal communication or directly pass via lymphovascular spaces or direct invasion with intact diaphragm. Sometimes, the mechanisms remains idiopathic (4).

Rarely, in patients whose primary appendiceal neoplasm was low-grade the malignant cells had been found during a pleural fluid examination. Intrathoracic cytoreductive surgery is rarely performed and only in specialised centers which explain the lack of information regarding the morphological features of intrathoracic tumors or outcomes of such aggressive treatment. There is not standard treatment in these cases, usually the palliative chemotherapy being the single option. Our patient underwent cytoreductive surgery included total pleurectomy, subtotal pericardiectomy and total resection of the left diaphragm with surgery reconstructed followed by HITHOC with cisplatin. The histopathology examinations revealed this time high grade neoplasm, more aggressive than in the previous examinations.

Because of the rarity of disease there are insufficient data regarding the role of adjuvant

chemotherapy. Systemic chemotherapy is reserved for patients with unresectable or recurrent PP. Several regimens were used, the majority including Fluorouracil (5 FU). Palliative regimens as FOLFIRI, FOLFOX, Cisplatin plus Paclitaxel or Mitomycin, Doxorubicin, and Irinotecan, Cisplatin plus Pemetrexed have showed objective response between 20% -50%, a median progression-free survival 7.6 months and a median overall survival 55 months (5). When our patient developed hepatic and pulmonary metastasis, FOLFOX4 regimen was recommended. After eight cycles of FOLFOX chemotherapy, with a mild neurotoxicity our patient was achieved complete response.

Regarding the follow-up, there is a paucity information on the utility of serum tumor markers in appendiceal malignancies. Baseline elevated tumour markers CEA, CA 19.9 and CA 125 may indicate an increased risk of recurrent disease in patients with gastrointestinal tract tumors. Even if there are no recommendation for using tumor markers in surveillance after curative intent surgery for appendiceal carcinomas, the extrapolation of data from colorectal cancer should be applied in this setting when tumor markers are initially elevated. CT controls in the follow-up (first 3 months postoperatively, then every 6 months) will facilitate detection of recurrence or surveillance of progressive disease. □

CONCLUSION

This case report emphasizes individual and complex treatment of a metastatic PP disease including aggressive cytoreductive surgery, HIPEC, HITHOC and systemic chemotherapy. Radical resection of the tumour and short-time follow up with adequate treatment on recurrence may result in good quality of life and long time survival. Cytoreduction of intrathoracic disease revealed the tumour transformation in a more aggressive phenotype from low-grade to high grade malignancy. There is a paucity of information about the features of intrathoracic spread of PP. Data from literature showed that improved survival is associated with complete cytoreduction and low grade mucinous adenocarcinomas. Tumour high grade transformation was associated in our case with systemic disease, rarely observed in the literature. In metastatic setting, the complete response of tumour

at systemic chemotherapy represents another particularity of this case.

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