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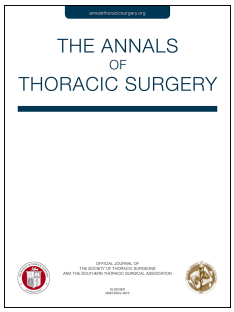

Cytoreductive Surgery and Hyperthermic Chemotherapy for Intrathoracic Pseudomyxoma Peritonei

Yo Kawaguchi, MD, Jun Hanaoka, MD, PhD

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Cytoreductive Surgery and Hyperthermic Chemotherapy for Intrathoracic Pseudomyxoma Peritonei

Running head: Cytoreductive surgery for PMP

Yo Kawaguchi, MD[1, 2] and Jun Hanaoka, MD, PhD[1]

[1]Division of General Thoracic Surgery, Department of Surgery, Shiga University of Medical Science, Shiga, Japan

[2]Division of General Thoracic Surgery, Kusatsu General Hospital, Shiga, Japan

Correspondence:

Yo Kawaguchi, MD

Division of General Thoracic Surgery, Department of Surgery

Shiga University of Medical Science

Tsukinowacho, Seta, Otsu, Shiga, 502-2192, Japan

E-mail: kawaguchi1228@yahoo.co.jp

Abstract

Dissemination of pseudomyxoma peritonei into the thoracic cavity is rare and carries a poor prognosis. Optimal treatment has not been defined. In our institution, patients had received cytoreductive surgery with hyperthermic intrathoracic chemotherapy, which demonstrated good prognosis. A 51-year-old woman was referred to our hospital with right intrathoracic dissemination of pseudomyxoma peritonei. We performed parietal and mediastinal pleurectomy and simple resection of all visible tumors on the diaphragm and visceral pleura, followed by hyperthermic intrathoracic chemotherapy with 20 mg mitomycin at 42–43ºC. The patient had no evidence of disease progression in the thoracic cavity 1 year after surgery.

Pseudomyxoma peritonei (PMP) is a rare disease, with an estimated incidence of two cases per million people per year[1]. PMP is caused by the dissemination of a mucin-producing tumor, characterized by the accumulation of mucinous ascites in the peritoneal cavity. Although the optimal treatment for PMP has not been adequately defined, aggressive cytoreductive surgery with intraperitoneal chemotherapy (HIPEC) has demonstrated prolonged survival or even a complete cure[2]. Extension of PMP into the thoracic cavity is extremely rare and carries a poor prognosis[1]. Although systemic palliative chemotherapy remains the usual treatment option, only one report has demonstrated that cytoreductive surgery with hyperthermic intrathoracic chemotherapy (HITHOC) prolonged the 5-year survival rate by 46.1% in patients with intrathoracic PMP[3].

Because intrathoracic dissemination of PMP is extremely rare and cytoreductive surgery with HITHOC may be performed in our institution only, and sixteen patients received the treatment between January 2010 and December 2019, we introduced the method for the first time.

Technique

Institutional review board approval was obtained for this study (Approval Number: 2018-0704-10).

We had previously reported surgical outcome of intrathoracic PMP in patients received

treatment between January 2010 and June 2018[3]. After we had reported, we continued cytoreductive surgery with hyperthermic intrathoracic chemotherapy for patients with intrathoracic dissemination of PMP. We showed a typical case of our treatment with a figure and video, which performed after the report. A 51-year-old asymptomatic woman was referred to our hospital because of a suspected right intrathoracic dissemination of PMP based on an imaging test. Computed tomography revealed diffuse masses along with pleura (Fig 1A), and magnetic resonance imaging reveals high intensity T2 masses (Fig 1B). The patient had undergone cytoreductive surgery and HIPEC for peritoneal dissemination of PMP 3 years ago, and there had been no evidence of recurrences in the abdominal cavity. Thoracoscope under local anesthesia revealed multiple masses on the parietal and visceral pleura (Fig 2A), and biopsy confirmed diagnosis of intrathoracic PMP.

Under general anesthesia, ventilation was provided to the left lung using a double-lumen endotracheal tube. The patient was placed in a left lateral position on the operating table. We performed cytoreductive surgery and macroscopic complete resection of all intrathoracic tumors. A posterolateral incision of approximately 25 cm was made and the 7^{th} intercostal muscle was resected. Between the 7^{th} intercostal space, parietal pleura was detached from the chest wall using the surgeon's finger; the mediastinal pleura was also detached. The parietal and mediastinal pleura with tumors were thus removed from the thoracic cavity. Visible tumors on

the diaphragm were resected with electrocauterization and the diaphragm was partially resected with tumors. Visible tumors on the visceral pleura were cut off with scissors, and if the tumor adhered strongly to the lung, we performed partial resection of the lung using an Endo GIA tri-stapler (Covidien). Damaged visceral pleurae were repaired with 4-0 PDS* Ⅱ (Ethicon) and damaged diaphragm with 3-0 PDS* Ⅱ (Ethicon). We confirmed no air leaks with a sealing test, performed under bilateral ventilation at 15 cmH_2O of maximum intrabronchial pressure. Following complete cytoreductive surgery (Fig 2B), the patient was administered HITHOC. Saline and anticancer therapy with 20 mg mitomycin at 42–43ºC were administered. We positioned two intrathoracic drains; one inflow from the midaxillary line at the 7^{th} intercostal space to the apical portion, and one outflow from the posterior axillary line at the 9^{th} intercostal space to the supradiaphragmatic portion. The medications were then circulated for one hour.

Patients were discharged from our hospital on postoperative day 11 without complications and had no evidence of disease progression in the thoracic cavity 1 year after surgery.

Comment

PMP has been regarded as an incurable disease for a long time and, if untreated, is usually fatal. There was no evidence of the efficacy of systemic chemotherapy or radiation therapy for PMP. Recently, some reports have shown that cytoreductive surgery, macroscopic complete resection

of visible peritoneal lesions, and HIPEC provided the possibility of a cure or at least an increased survival time[4].

Extension of PMP to the thoracic cavity through the diaphragm is extremely rare (5.4%)[1]. Thoracic dissemination will cause restrictive ventilatory impairment due to accumulation of mucinous fluid in the thoracic cavity. In such cases, early treatment is needed for patients. In contrast, most patients with intrathoracic disseminations received only palliative care because 1) lack of studies has been a major challenge in the management of this extremely rare disease, 2) treatments are thought to be associated with high morbidity and mortality, and 3) these patients are expected to have a poor prognosis. However, we believed that cytoreductive surgery and HITOC might contribute to a better prognosis, such as in abdominal PMP. We previously reported that long-term patient survival can be expected, with a 5-year survival rate of 46.1%, with intrathoracic cytoreductive surgery followed by HITHOC for disseminated PMP with feasible complications[3]. It is essential for us to communicate the method used to treat this rare disease to other institutions.

The goal of cytoreductive surgery was complete macroscopic resection of the tumors. To achieve this goal, we first performed parietal and mediastinal pleurectomies because most tumors adhered to the parietal and mediastinal pleurae. Next, we performed simple resection of all visible tumors on the diaphragm and visceral pleura. During simple resection, sufficient

margin between tumors and adjacent organs is not necessary because following HITHOC microscopic, residual tumors are expected to be eliminated. Yonemura, et al reported that anticancer drugs penetrate 2 mm into the adjacent tissues by HITHOC[5].

If possible, we should set a goal of microscopic complete resection by extrapleural pneumonectomy or pleurectomy decortication. However, microscopic complete resection of PMP is challenging because it is easy for mucus, which includes tumor cells, to drop into the thoracic cavity during surgery, facilitating the development of local recurrences. Furthermore, extrapleural pneumonectomy or pleurectomy decortication are more invasive than our cytoreductive surgery. Patients who had received abdominal cytoreductive surgery or systemic chemotherapy often have poor physical capacities and thus we should avoid invasive surgery. Therefore, cytoreductive surgery following HITHOC may be a feasible treatment for managing this disease.

In conclusion, the cytoreductive surgery and HITHOC approach described here might constitute an optimized method to treat intrathoracic dissemination of PMP. We hope that, in the future, patients with this condition in various institutions can receive the survival benefits offered by this method.

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Figure legends

Fig 1. (A) Computed tomography shows diffuse masses along the pleura. (B) Magnetic resonance imaging reveals high intensity T2 masses.

Fig 2. (A) Thoracoscope under local anesthesia shows multiple masses on the parietal and visceral pleura. (B) Visible tumors in the thoracic cavity completely resected by cytoreductive surgery.