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SHORT COMMUNICATION

Hyperthermic intrathoracic chemotherapy (HITHOC) in ovarian carcinoma - a propos of a case

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Summary

A female patient aged 42, started chemotherapy for advanced ovarian carcinoma in June 2016. Considering intraoperative findings, cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) were performed, followed by adjuvant chemotherapy. In March 2018, computed tomography (CT) examination showed disease progression in the form of pleural carcinomatosis with increased levels of tumor markers. In April 2018, total parietal pleurectomy, partial visceral pleurectomy, and then hyperthermic intrathoracic chemotherapy (HITHOC) with cisplatin were performed. The procedure was uneventful, as was the postoperative course. The patient was discharged on the 13th postoperative day with no major postoperative complications. Three months after surgery, CT showed no signs of disease relapse. Since this is a relatively new method of treating pleural carcinomatosis, real results are to be expected with larger series of patients and longer postoperative follow-up.

Key words: *carcinomatosis, chemotherapy, HITHOC, intrathoracic, hyperthermic*

Introduction

Hyperthermic intrathoracic chemotherapy (HITHOC) is based on the known principle that by increasing the concentration of cytotoxic agents the rate of tumor cell destruction is also increased. This method is based on the synergistic effect of increased temperature and high cytotoxic concentration on tumor cells. Filling the thoracic cavity with cytotoxic agents results in increased drug exposure of tumor cells as opposed to systemic administration of cytotoxics, where reduction of toxic level occurs due to often limited absorption [1,2].

Prerequisite for performing HITHOC is absence of tumor outside the thoracic cavity. The efficiency of the method consists of surgical removal of all macroscopically visible intrathoracic metastatic lesions because penetration after the application of the drugs to the microscopic residual deposits is limited to a few millimeters [3-5].

HITHOC as relatively new method has gained application in treating pleural mesothelioma, thymoma and also in advanced malignancies of abdominal and pelvic cavity origin.

Cisplatin is the most commonly used cytotoxic for HITHOC, either alone or in combination with other drugs. Contact with residual tumor cells is achieved through free diffusion [6-9].

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Case presentation

In June 2016 a female patient was admitted to the Clinic for Oncological Surgery of the Institute of Oncology and Radiology of Serbia (IORS) with abdominal pain. Diagnostic work-up revealed free fluid in the abdomen and small pelvis, cystically altered left ovary and peritoneal carcinomatosis. Intraoperative exploration confirmed advanced ovarian cancer, fine-grained changes in the peritoneum of the small pelvis, on the greater omentum, and on the peritoneum of both hemidiaphragms. Considering theses findings, cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) were performed. The operation consisted of total hysterectomy with bilateral adnexectomy, total omentectomy, small pelvis peritonectomy and of both hemidiaphragms, partial resection of the right diaphragm, pleural biopsy on the right and then HIPEC with 80 mg cisplatin for 45 min. Definitive histopathological examination confirmed the existence of adenocarcinoma of ovarian origin (FIGO IV) with metastases in the small pelvis peritoneum, metastases in the omentum, metastases in the peritoneum of both hemidiaphragms, metastases in the muscular part of the right hemidiaphragm, and metastases in the pleura. The postoperative course was uneventful. After that, the treatment was continued with 6 cycles of adjuvant chemotherapy with paclitaxel 175 mg/m^2 and carboplatin area under the curve (AUC) 5. The patient was put on follow-up but in February 2017 she was re-admitted to IORS after CT scan showed areas compatible with tumor lesions of the right diaphragm. A definitive histopathological finding has confirmed the existence of metastases of ovarian adenocarcinoma in the preparation of the right hemidiaphragm. The postoperative course went well and the patient was regularly followed-up according to our protocols in use.

According to the examination in March 2018, a CT confirmed progression of disease on the pleura in the form of carcinoma and increase in the level of tumor markers CEA and CA125.

By examining the condition of the patient and by a detailed examination of the medical documentation, the patient was proposed surgical treatment of changes in the pleura plus HITHOC.

After the patient's consent and detailed diagnostic procedures with the fulfillment of all necessary examinations for the purpose of preoperative preparation and preparation of the surgical and anesthetic team, in April 2018, in IORS, total right parietal pleurectomy, partial visceral pleurectomy of the right medial lobe, and then HITHOC with cisplatin 160 mg were performed.

The operation included right posterolateral thoracotomy through the seventh intercostal space, and then removal of the complete parietal pleura. Several segments of the visceral pleura from the right lung, as well as changes from the right hemidiaphragm, were removed. The operational field was then prepared for HITHOC in a standard manner after which a procedure was performed using a solution of 160 mg of cisplatin, dissolved in 1000 ml of 5% glucose, heated to 42 °C for an hour. The central temperature of the organism was monitored by a probe placed in the esophagus, and the cooling was conducted by the solutions through the central venous catheter. During the perfusion, the temperature in the esophagus did not exceed 38 °C. There were no metabolic or haemodynamic disorders. After completion, the complete content of the dissolved cisplatin was removed. After placement of the operative drains, the chest was closed in a standard way. The procedure went properly, as did the postoperative course.

On the second postoperative day there was a decrease in the level of hemoglobin due to cisplatin which finally led to a fall in the complete blood count and a consequent fall in blood pressure of the patient. The patient received the required dose of concentrated erythrocytes. Other reactions such as nausea, vomiting and neuropathy did not occur. There was no renal function disorder.

Discussion

In our case we have described the use of cytoreduction and HITHOC treatment modalities of advanced ovarian cancer with metastases on the pleura.

HITHOC as a relatively new treatment modality has gained the widest use in the treatment of pleural mesothelioma and advanced thymoma with very satisfactory results, whereas its use to metastatic disease of ovarian cancer is rarely described. After HITHOC administration in thymoma, no relapse of disease was observed after 18 months, whereas in mesothelioma this period was twice as long as in the use of conventional protocols [10-14].

In our case the dose of cisplatin was 160mg. In the literature, cisplatin doses vary between 80 and 250 mg/m^2. There is no consensus on how much the optimal dose should be [14,15]. Richards et al. indicate that higher doses of cisplatin (175-225 mg/m^2) have a better effect on survival compared to lower doses [16].

Any increase in the cisplatin dose may lead to systemic absorption of the drug and consequent depression of the hematopoietic system, renal im-

pairment, gastrointestinal toxicity, which did not happen in our case [17].

Conclusion

At the check up 3 months after surgery, CT showed no signs of disease relapse. Since this is a relatively new method of treating pleural carcinomatosis, real results are to be expected with larger series of patients and longer postoperative follow-up.

Conflict of interests

The authors declare no conflict of interests.

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