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EDITORIAL

New approach to peritoneal surface malignancies

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Abstract

Peritoneal surface malignancies (PSM) are a clinical entity with an unfavourable prognosis. They comprise peritoneal carcinomatosis, pseudomyxoma peritonei, and primitive tumors of the peritoneum. Because the treatment of PSM presents unique and challenging problems to the cancer clinician, many new approaches have been attempted in recent years. In the current and next issues of *World Journal of Gastrointestinal Oncology*, some international groups of researchers discuss the most important and innovative aspects of PSM treatment, with particular accuracy for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. In conclusion, because this new approach to PSM has a reputation for being based more on common sense than on experimental data, I hope that highlighting this topic can make a contribution to the treatment of this group of diseases.

Key words: Peritoneal surface malignancy; Peritoneal carcinomatosis; Pseudomyxoma peritonei; Peritoneal mesothelioma; Gastric cancer; Colorectal cancer; Ovarian cancer; Cytoreductive surgery; Hyperthermic intraperitoneal chemotherapy; HIPEC

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EDITORIAL

Peritoneal surface malignancies (PSM) are a clinical entity with an unfavourable prognosis. They comprise, peritoneal carcinomatosis (PC), that is the progression of neoplastic diseases from abdominal, pelvic or extra-abdominal organs[1-3], pseudomyxoma peritonei (PMP), an uncommon "borderline malignancy" generally arising from a perforated appendiceal epithelial tumour; primitive tumors of peritoneum, such as diffuse malignant peritoneal mesothelioma (DMPM).

Generally, PC has been treated similarly to metastatic cancers, but is associated with worse outcomes when compared to other sites of metastatic disease from the same primary tumor site. With supportive care alone, the median survival in patients with PC is 3-6 mo[4]. The long-term survival in most patients with PMP, submitted to usual treatments, remains poor, with reported 5 and 10 years survival rates of 50% and 10%-30%, respectively[5]. DMPM is an uncommon tumor which is rapidly fatal if treated with conventional therapies.

Because the treatment of PSM presents unique and challenging problems to the cancer clinician[6], in the recent years, many new approaches have been attempted. Cytoreductive surgery (CRS) followed by hyperthermic intraperitoneal chemotherapy (HIPEC) and/or early postoperative intraperitoneal chemotherapy (EPIC) is now advocated as the standard treatment in PSM.

In the current and next issues of *World Journal of Gastrointestinal Oncology*, some international groups of researchers will discuss the following topic: Pathophysiology and biology of PC; Rationale and technique of HIPEC; Selection of patients and staging of PSM; Postoperative management; PMP; Peritoneal mesothelioma; Gastric, colorectal and ovarian cancer. Here, I introduce briefly the major authors of this group of articles.

Shigeki Kusamura, researcher at National Cancer Institute of Milan, Milan, Italy, affirms that the pathogenesis

of PC "could be partly explained by 3 major molecular pathways: (1) Dissemination from the primary tumor; (2) Primary tumor of peritoneum; and (3) Independent origin from the primary tumor and peritoneal implants. They are not mutually exclusive and combinations of different mechanisms could succeed inside a single case"[7].

Paul H Sugarbaker, director of the Program in Peritoneal Surface Malignancy at The Washington Cancer Institute, Washington, United States, attests that "Chemotherapy agents are selected to be administered by the intraperitoneal or intravenous route based on their pharmacologic properties. A peritoneal-plasma barrier which retards the clearance of high molecular weight chemotherapy from the peritoneal cavity results in a large exposure of small cancer nodules on abdominal and pelvic surfaces. Tissue penetration of the intraperitoneal chemotherapy is facilitated by moderate hyperthermia (41-42℃)… Timing of the hyperthermic chemotherapy as a scheduled part of the surgical procedure to uniformly expose all peritoneal surfaces is crucial to success"[8].

François-Noël Gilly and Olivier Glehen, respectively chief and senior general surgeon in the Department of Surgical Oncology at University Hospital of Lyon Sud, Lyon, France, writes that "Because of its important but acceptable morbidity and mortality and high cost, this comprehensive management plan requires knowledgeable patient selection… Indications for treatment of PC with cytoreduction and HIPEC are now validated for several diseases: peritoneal mesothelioma, pseudomyxoma peritonei, PC from appendix and colorectal cancer. Indications are still discussed for gastric and ovarian carcinomatosis. Computed tomography is the best radiologic exam to assess staging disease. Extent of peritoneal carcinomatosis is however difficult to evaluate preoperatively, and precise evaluation is most often performed by the surgical exploration. Cytoreductive surgery associated with HIPEC for the treatment of peritoneal carcinomatosis should be performed for young patient with limited and resectable carcinomatosis, into specialized institutions involved in the management of PSM"[9].

Dario Baratti, attending surgeon at National Cancer Institute of Milan, Milan, Italy, suggests that it is important that "Early recognition and appropriate management of the most common adverse events are addressed, in order to minimize the impact of treatment-related morbidity on survival and quality of life results"[10].

Brendan J Moran, director of the Pseudomyxoma Peritonei Centre at North Hampshire Hospital, Basingstoke, Hampshire, United Kingdom, comments that "Optimal treatment involves a combination of cytoreductive surgery with heated intraperitoneal chemotherapy… Following CRS with HIPEC, 5-year survival ranges from 62.5% to 100% for low grade, and 0%-65% for high grade disease… Surgery and HIPEC are the optimal treatment for PMP which is at best a borderline peritoneal malignancy"[11].

Santiago González-Moreno, surgical oncologist at Centro Oncológico MD Anderson International in Madrid, Spain, supports the suggestion that "The combination of complete cytoreductive surgery and perioperative intraperitoneal chemotherapy provides the only chance for long-term survival to selected patients diagnosed with a variety of peritoneal neoplasms… HIPEC combines the pharmacokinetic advantage inherent to the intracavitary delivery of certain cytotoxic drugs, which results in regional dose intensification, with the direct cytotoxic effect of hyperthermia. Hyperthermia exhibits a selective cell-killing effect in malignant cells by itself, potentiates the cytotoxic effect of certain chemotherapy agents and enhances the tissue penetration of the administered drug… Delivery of HIPEC requires an apparatus that heats and circulates the chemotherapeutic solution… An open abdomen (Coliseum) or closed abdomen technique may be used… Future trials to ascertain the ideal HIPEC regimen in different diseases and to evaluate the efficacy of new drugs or drug combinations in this context are warranted"[12].

Marcello Deraco, responsible for Peritoneal Surface Malignancies Program at National Cancer Institute of Milan, Milan, Italy, says that for DMPM "Therapeutic option have been traditionally limited and ineffective… In recent years, an innovative treatment approach involving aggressive cytoreductive surgery and perioperative intraperitoneal chemotherapy has reportedly resulted in improved outcome, as compared to historical controls"[13].

Yutaka Yonemura, chief of Gastric Cancer Division, and Peritoneal Carcinomatosis Division at Shizuoka Cancer Center, Osaka, Japan, comments that "No standard treatment for PC from gastric cancer has been proposed… Neoadjuvant intraperitoneal-systemic chemotherapy protocol and complete cyotreduction are the essential treatment modalities for the improvement of survival of patients with PC from gastric cancer"[14].

Our group of the University of Messina, Messina, Italy, supports the idea that "Peritoneal carcinomatosis is, after liver metastases, the second most frequent cause of death in colorectal cancer patients… Also if CRS plus HIPEC allow to obtain better results than standard therapies, we suggest, that a large prospective randomised control trial is needed to compare long-term and progression-free survival under the best available systemic therapy with or without cytoreductive surgery and hyperthermic intraperitoneal chemotherapy"[15].

Giovanni Scambia, chief of Division of Gynecologic Oncology, Catholic University of the Sacred Heart, Rome - Italy, writes that "Epithelial ovarian cancer (EOC) is the second most common genital malignancy in females and is the most lethal gynecological malignancy with an estimated 5 years survival rate of 39%… Comprehensive management using surgical cytoreduction to decrease the tumor load to a minimum and intraperitoneal chemotherapy to eliminate microscopic disease on peritoneal surface has the potential to greatly improve quality of life and have an impact on survival in ovarian cancer patients… Given the poor outcome of women with advanced EOC, it is imperative to continue to explore novel therapies"[16].

In conclusion, because of, as stated by Bartlett[6], the field of PSM (HIPEC in particular) has a reputation for

being based more on common sense than on experimental data, I hope that highlighting this topic can make a contribution to the treatment of PSM.

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