PART BODY HYPERTHERMIA PLUS RADIO-CHEMOTHERAPY IN THE PALLIATIVE TREATMENT OF LIVER METASTASES FROM COLORECTAL CANCER

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Introduction. Colorectal cancer represents a very important cause of cancer death in Europe and USA. More than 15% of patients in advanced stages develop synchronous liver metastases (15-20% after surgery and adjuvant chemotherapy and 50% during the natural evolution of the disease); only a small number (10-20%) of these lesions are radically resectable.
In chemonaive patients with metastatic colorectal cancer, the use of 5-Fluorouracil (5-FU) plus Folinic Acid improves the median survival to 12 months, giving an objective response of about 20-25%, while in previously chemo-treated patients 5-FU does not significantly improve the overall survival. Furthermore, in patients with 5FU-resistant metastatic colorectal cancer, the use of Irinotecan and Oxaliplatin yields further toxicity without a significant improvement in overall survival.
Radiofrequency Ablation (RA) with percutaneous technique is frequently used in the treatment of liver metastases. The results of RA are comparable with those of surgery, but a prospective randomized trial is still needed to demonstrate the efficacy of this invasive approach. An important limitation of this technique is represented by the size of the metastases, which determines the diameter of the coagulation necrotic volume that can be produced by a single RA session. Furthermore, the majority of patients show multiple lesions with too large diameters to be treated by RA, so that an alternative heating technique should be proposed.
Materials and Methods. From 2001 to 2006, we delivered a combined chemo- or radio-hyperthermia treatment in 16 patients who were heavily affected by liver-metastatic colorectal cancer and who had not responded to a conventional first-line chemotherapy. All patients were previously treated with a first-line chemotherapy (FOLFOX or FOLFIRI) as adjuvant therapy. Chemotherapy consisted of 5-FU 300 mg/mq per 7 days in bolus. Exceptionally, in one patient who refused intravenous 5-FU, an oral fluoropyrimidine (Capecitabine) was preferred. In 5 patients with very poor general conditions, a conventional hypofractionated irradiation with palliative intent was preferred. In all cases, hyperthermia was combined with radio- or chemotherapy. Hyperthermia was delivered as Part-Body hyperthermia (PBHT), using a BSD 2000 radiofrequency equipment, with a sigma 60 annular phase array applicator®, and a total output of 400 W; the treatment was performed once weekly, for 4-6 weeks. In order to avoid the sequelae of invasive techniques, a dedicated treatment planning has been used for the measurement of the intratumoral temperature distribution in collaboration with a team from the University of Padua (IPERCHEM Project). Hyperthermia was combined with a second-line chemotherapy (5-FU via bolus or continuous infusion; Capecitabine in one patient). In 5 patients hyperthermia was combined with radiotherapy alone; in 3 patients with a good compliance to the combined treatment, more than 6 fractions (range 9-20 fractions) were delivered with concomitant chemotherapy in order to maintain a prolonged response.
Results. At follow-up (range 4-24 months), 13/16 patients died, 12 due to metastases progression and one due to bowel injury probably because of irradiation. One patient was lost at follow-up. The remaining 2/16 patients (12.5%) had a median overall survival of 11 months from the beginning of the combined treatment; this data are comparable to the ones published in the work of Hager[1] . No severe complications referred to hyperthermia or combined treatment have been reported.
Conclusions. In patients affected by liver metastases, hyperthermia combined with radio- or chemotherapy is feasible and well tolerated. Hyperthermia seems to improve the efficacy of chemotherapy also in previously chemo-refractory tumors. Some technical aspects as the applied frequencies, the time of exposure, the optimal temperature level, the number of sessions, and the interval between radiochemotherapy and hyperthermia, have not been defined yet. In patients with metastatic colorectal cancer, Capecitabine showed a better overall response compared with 5-FU as first-line treatment . In order to allow a concomitant chemotherapy-hyperthermia treatment, Capecitabine could be a reasonable choice.

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[1] Hager ED, Dziambor H, Hohmann D et al. Deep hyperthermia with radiofrequencies in patients with liver metastases from colorectal cancer. Anticancer Res 1999; 19: 3403-3408