

Treatment of advanced cervical cancer with complex chemoradio - hyperthermia

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Abstract

This single arm, retrospective, single institution study investigated intention to treat patients (n=72) with advanced cancer of cervix of uterus. The study was performed in 2001-2010; providing 331 sessions. All patients had radiotherapies as fractional radiotherapy and intracavitary brachytherapy. Some patients (n=34) received chemotherapy (Cisplatin 40 mg/m²/week; concomitantly with tele-radiotherapy) as well. Complementary to the tele-radiotherapy, oncothermia was used two times a week, targeting the pelvis. Applied energy dose was 45 W, 60 min. Oncothermia was applied immediately just after the infusion, when chemotherapy was also administered. Complete & partial remission were achieved in trimodal therapies for 73.5% of the patients, while we could stabilize the disease for 14.7% of the patients.

Introduction

Carcinoma of the cervix of uterus is the second deadly female malignancy after mammary carcinomas. Cervical cancer incident in Hungary, 21 incidences per 100,000 females (higher than the rate in Eastern Europe), and the mortality rate is 9.6 / 100,000 women /year, which is more than 500 deaths of women a year, [1].

Hyperthermia treatments are popular for gynecological applications [2], [3]. These focus on radiotherapy combinations [4], showing highly significant benefit of hyperthermia in overall survival, disease-free survival and local-relapse-free survival made by a randomized trial [4]. A large randomized controlled clinical trial of the radiohyperthermia was published in the Lancet [5], with great success. The results were very promising [5], but the control study [6] was disappointing. The explanation may be simple: a reference point was missing [7]. The chemotherapy combination (Cisplatin + hyperthermia for previously radiated cases) also shows feasibility [8] as well as the trimodal applications for cervix [9], [10], [11]. There are large debates in the topic [12], with counterpoints [13], and contras [14]. Our objective is to treat advanced cervical tumors with a new kind of hyperthermia (oncothermia) and add new results for the professional discussions.

Our department accepts patients from the three neighboring counties (Veszprem, Zala and Vas) for preoperative, postoperative, definitive and palliative treatments. In addition to the applied standard professional protocols since 2001 we have the possibility to apply complementary oncothermia treatments.

Method

A single arm, retrospective, single institution study investigated intention to treat patients (n=72) with advanced cancer of cervix of uterus. The study was performed from 2001 till 2010; involving 331 oncothermia treatment sessions.

After a complete medical check-up upon the decision of the conference of professionals (OncoTeam), the treatment protocol was prescribed and the patients were hospitalized. Patients with solid diagnostic proofs of advanced cervix carcinoma were involved in the study. The chemoradio-therapy was administered according to the standard protocol, and in the appropriate indications complementary oncothermia was used. All patients had radiotherapy. The CT based radiation with 3D conformity, targeting the pelvic regional lymph-nodes up to 30 Gy; it was followed by field-concentration in 1-2 steps until 50 Gy, in fractional solution by 2 Gy doses. Intracavitary brachytherapy was applied complementary to teletherapy. After-loading technique was used once a week and three times altogether, providing 6-7 Gy/treatment. Additional chemotherapy was applied for n=34 patients, (Cisplatin 40 mg/m²/week; concomitantly with tele-radiotherapy). Complementary to the teleradiotherapy, oncothermia was used two times a week, targeting the pelvis. Two types of treatment devices were in use –'EHY 2000' and 'EHY 3000' (Oncotherm GmbH, Germany). Applied energy dose was 45 W, for 60 min. (In days of chemotherapy it was applied just after the infusion.) (The electrode positioning is shown on Figure 1.)

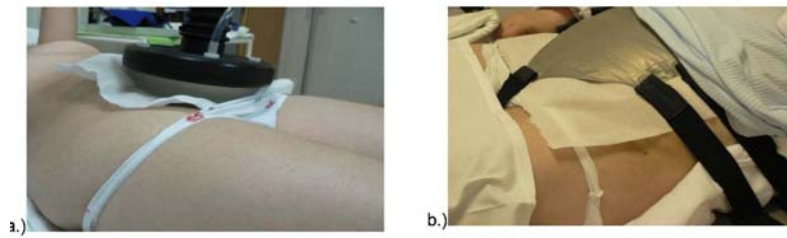


Figure 1. Arrangement of the treatment electrodes of oncothermia EHY2000 (a) and EHY3000 (b) type devices

The most important aspect of the treatment was the time schedule. The precise timing between chemo-, radio- and brachytherapy treatments was organized with high care, and oncothermia was applied immediately after chemo- or brachytherapy treatments, and at max 20 min before EBRT, and delivered during the whole course of the treatment schedule. The effectiveness was measured within confines of the oncological care. Imaging procedures as well as gynecological check-ups used to keep track of the development of the patients' status.

Note, this complementary treatment is currently not financed by the social insurance, therefore, patients had to pay privately for the oncothermia treatments. Unfortunately, this problem may affect the therapeutic plan in numerous cases, when the patient is unable to finance their own complementary treatment modality, even when the treatment is justified by professional aspects. In case of private cofinancing, the treatment plan of the commentary application is carefully designed to achieve the best available results.

Results

We first show a case report. The anamnesis of the 54 years-old female patient was G2,P2, with comorbidity hypertonia for 15 years. She had a stroke at the age of 54. She had vaginal bleeding symptom at the first diagnosis: Neopl.cerv.ut.std IIIB-IV; Fig. 2. Histology: carcinoma planocellulare. She received the first external irradiation 2 Gy/day fractions, with 50 Gy complete dose. Additionally, afterloading brachytherapy was applied: 8 Gy, 5 Gy and 4.5 Gy, subsequently for three times.

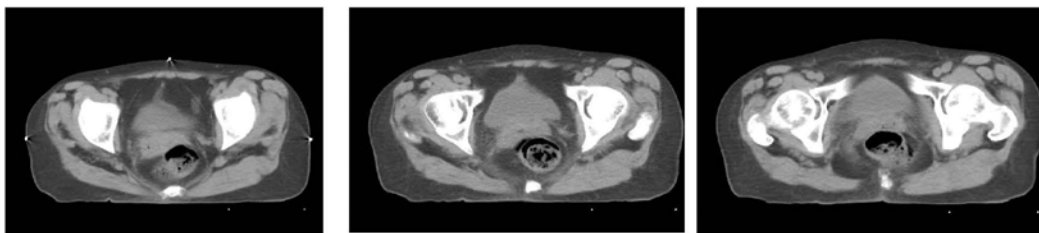


Figure 2. The diagnosis and the planning of the radiation and oncothermia complementary

Chemotherapy Cisplatin 40 mg/m²/week complementary to external radiation was performed, and oncothermia was given to her in 10 sessions. The result was a complete remission. With permanent checkup no evidence of disease (NED) can be found. The last control (four years after the finishing of the oncothermia) was NED again, Figure 3.

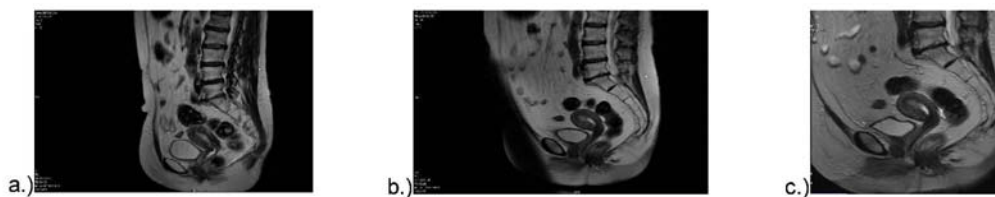


Figure 3. Control MRI of the patient: 1 months after oncothermia (a), one year after oncothermia (b), four years after oncothermia (c)

Patients had various number of treatments, Figure 4. in average 4.7 sessions were applied.

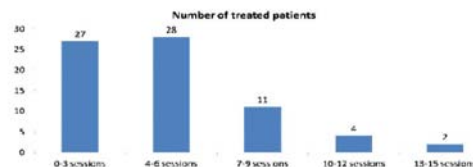


Figure 4. Distribution of the number of treatments for the patients (n=72)

The clinical response was measured in cases of trimodal applications (radiotherapy, chemotherapy and oncothermia, n=34). Results are promising: 73.5% (25/34) complete and partial remissions, 14.7% (5/34) stable disease and 11.8% (4/34) progressive disease, Figure 5.



Figure 5. Efficacy of radio-chemo-thermotherapy half year after finishing of the treatment

Our experience has shown that the addition of oncothermia had increased the effectiveness of conventional modalities, measured in the quality of life and survival elongation.

Conclusions

With a therapeutic plan prepared with due care and implemented precisely—especially the time between treatments and appropriate setting of treatment parameters—oncothermia can effectively complement the conventional oncotherapies. We will present our results in a case study, in which a patient's treatment was started only with palliative intent but at the end complete remission was available.

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