Preoperative brachytherapy in endometrial cancer - proposal of a new clinical protocol

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Summary

High-dose rate brachytherapy preoperative treatment has been described. The proposal of a protocol contains an outline of patient qualifications for this kind of treatment, as well as necessary laboratory and diagnostic imaging examinations. Methods of brachytherapy (low-dose rate and high-dose rate), methods of surgery and postoperative management of patients with endometrial cancer are discussed.

Key words: Brachytherapy; Endometrial cancer.

Introduction

Due to growing clinical experience many changes have developed in the oncologist's way of thinking. During the last decades tactics of cancer treatment have been changing. As a basis of these changes lay at least two trends. Firstly – treatment should be more effective – because of this, new methods and doses in radiotherapy, chemotherapy, surgical procedures have taken place in clinical investigations and practice. Secondly – a more important factor continuously becomes achievement of a better, optimal quality of life for patients after successful therapy.

Traditional and contemporarily used treatment in women with endometrial cancer is surgery followed by brachytherapy and, in many cases, teleradiotherapy [1-3]. Brachytherapy depending on the dose delivered in a unit of time may be HDR (high-dose rate) or MDR/LDR (medium/low-dose rate). Often hormonotherapy and sometimes chemotherapy are indicated. All these methods are curative but are not free of undesirable and long-term side-effects.

If possible and safe - omitting one or more parts of the curative procedure in these patients may be very valuable. Optimization of planned therapy, thus minimizing the adverse effects as much as reasonably achievable, has been discussed in previous articles [4, 5].

On the basis of the experience of other oncological centers [6-9] and our own, we prepared a modified scheme of treatment of endometrial carcinoma. This protocol is a preliminary proposal, and may need some changes after discussion with collaborating operative gynecology institutions. Since 1999 we have been using this treatment in clinical practice. This protocol came about as an analogy of very satisfying results in preoperative curietherapy in cervical cancer. The method has been successful due to the excellent collaboration of other gynecology institutions (Polish Mother's Memorial Hospital - Research Institute, Lodz; Gynaecology and Obstetrics Institute of Medical University in Lodz; Jordan's Memorial Hospital in Lodz) in our region.

Patients

For treatment with preoperative brachytherapy (PB) qualified patients must be:

1. in good performance status (without general contraindications to radiotherapy and radical surgical treatment);
2. in clinical Stage I or II of endometrial cancer (preoperatively assessed with adequate FIGO scale);
3. with a pathological diagnosis of *adenocarcinoma* from material obtained after D&C.

After preliminary qualification at outpatient services, the patient is admitted to a gynaecological radiotherapy department.

In all cases the following diagnostics are performed:

– general physical examination with assessment of performance status by Karnofsky or Zubrod scale;
– gynaecological, bimanual examination (measurement of uterine cavity length is necessary), rectal palpation;
– EKG;
– X-ray chest examination;
– abdominal and pelvic sonography (assessment of paraaortic lymph nodes, uterine shape and size in 3D, length and width of uterine cavity, thickness of endometrium and myometrium); both abdominal and transvaginal examination is recommended;
– magnetic resonance imaging with assessment of uterine size, thickness of muscle layer of uterine wall, deepness of neoplasmatic myometrial infiltration;
– hysteroscopy (recommended);
– laboratory tests: blood-type, Rh factor, blood count with amount of platelets, serum levels of creatinine, blood proteins, glycemia, hepatic tests, coagulogram, CRP, hepatoglobulin, ceruloplasmin, alpha-2 macroglobulins, immunoglobulin A, M and G serum levels.

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Methods

If during the diagnostic procedures adnexal masses, uterine myomas or other evident pathologies are found the patient is excluded from the PB schedule and undergoes operative treatment as a primary step. After completion of all the diagnostic tests, considering the collected data on stage of disease [10], uterine size, shape, precise localisation of cancer tissue, level of deepest layer of infiltration, performance status of patients [11] - choice of radiation technique (high- or low-dose rate) and kind of applicators are selected:

– in Stage IA and II (uterine length < 8.0 cm) a Rotte type applicator is preferred;

– in Stage IB and II (uterine length > 8.0 cm) the Heymann insertion technique is a better choice.

Irradiation in HDR conditions with Rotte or Heyman's applicator is performed five times, once weekly, for five consecutive weeks. A dose of 7.5 Gy per fraction is delivered at the reference line, which is a contour of the uterus. A routine imaging, computerized and individual planning procedure is obviously done in each patient. The total physical dose is 38.5 Gy/reference line and depending on the radiation source strength one application lasts several minutes.

LDR (or MDR) irradiation uses only special, caesium-adapted Rotte type applicators. Applications take place three times, once a week, over three consecutive weeks. The dose delivered on the reference line lying on a contour of uterus is 17.0 Gy per fraction; physical total dose is 51 Gy/reference line.

Each patient (except those with strong contraindications) contemporarily undergoes long-term hormonotherapy:

– medroxyprogesterone acetate orally or intramuscularly is as follows: 500 mg daily for 14 days, then 500 mg twice weekly for three months and later 500 mg once weekly for one to two years, according to individual indications and presence of adverse effects,

or

– megestrol acetate, orally 160 mg twice daily for six to 12 months.

After about six to eight weeks, when the acute irradiation effect disappears from the critical organs and genital tract, patients are admitted to the operative gynecology department.

After reassessment of operability of cancer, the patient undergoes the TAH & BSO Wertheim-Meig's method. It is of critical importance to remove the uterus, adnexa, half the length of the vagina, and as many as technically possible pelvic lymph nodes. Intraoperative findings of metastatic changes in the abdominal cavity exceeding the genital organs should be the end of a radical operation making laparotomy only an explorative procedure. Furthermore surgical discovery of infiltration of the parametrial region which was not seen earlier makes it imperative to discontinue any radical surgery. As soon as possible radiotherapy or radiochemotherapy must be started.

Results

Postoperative pathologic examination of removed organs and tissues is a sign post for further clinical steps with patients. It is very important that the pathological diagnosis contain: a detailed macroscopic description of removed specimens and microscopic assessment of each part or operated organ. Of great value is information about the number and histological structure of the lymph nodes. Microscopic evaluation must give information about the depth of myometrial infiltration and maturity index (obviously if cancer is present). If microscopic pictures are unclear we additionally ask experienced pathologists at the Oncology Department of Tumour Pathology, Medical University of Lodz to reevaluate them. If in all removed tissues the pathologist has not found any live cancer cells the patient is referred only for observation and continuation of hormonotherapy as an outpatient. She does not need further pelvic teleradiotherapy. If cancer cells are seen in the uterus, parametria and/or iliac or obturatory lymph nodes the patient must be irradiated with external fields on the pelvis minor with external fields at routinely prescribed doses. The used technique is the same as in radiotherapy, being the only treatment. Irradiation is performed in megavoltage therapy with gamma rays of ^{60}Co, 4 - 15 MeV photons with two opposite fields. Irradiated pelvic fields are limited up to the horizontal line lying between L_4 and L_5, the lower border is a level of half of the *foramen obturatum,* and side borders are 1/3 the width of the corpus of the iliac bone. The described field must get a dose of 44.0 Gy/t in 22 daily fractions at 2.0 Gy per fraction, for four to five weeks. In case metastatic nodes are found in the adnexal and/or paraoartic region fields covering nodes along the aorta must be irradiated. These external fields are limited from up to Th_{12} and from both sides with transversal apophyses of the vertebra. The dose for this field routinely is 40.0 Gy/t in 20 fractions at 2.0 Gy, for four weeks.

The patient is most often irradiated in an ambulatory mode. It depends on where she lives and the tolerability of treatment. In cases of disseminated abdominal disease the patient may be referred to a form of salvage therapy which is chemotherapy.

The statistical data and results of using this protocol is a topic of another paper but already now it may be stated that due to PB about 80.0% of the patients with endometrial cancer can avoid teleradiotherapy.

Discussion

The described protocol may be a topic for further discussion. It has many followers and many antagonists. All treatments of uterine cancer undergo evolution, more or less rapid changes in treatment strategy conceptions. For us it is obvious that due to this modality of treatment many well diagnosed, perfectly operated women could be disqualified from external therapy and not have the many complaints and side-effects of radiation. Omitting teleradiotherapy, in well selected patients, is not of negligible importance from an economic point of view.

There are plenty of possibilities to improve diagnostic and treatment methods in the future [12-14].

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