

Evaluation of treatment results and toxicity in cases of repeated radiation therapy of spinal metastasis

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The study evaluates retrospective results and toxicity in repeated radiation therapy in patients with recurrent pain caused by backbone metastasis, having undergone previous radiotherapy in the same body region. Fifty-seven patients were analyzed: 24 women and 33 men, aged 45–74 years (median = 59 years). They underwent a second radiation therapy treatment of the spinal column, between March 2002 and May 2004, performed due to recurrent pain in the previously irradiated region. The radiation used cobalt isotope 60 (^{60}Co), to include the metastatically changed vertebrae and the margin of the adjoining healthy upper and lower vertebra. The radiated skin area measured 84–104 cm². Patients were divided into 3 groups depending on their treatment schemas:

- 12 patients – first course of radiotherapy 4 Gy x 5, second 4 Gy x 5;
- 16 patients – first course of radiotherapy 4 Gy x 5, second 8 Gy x 1;
- 29 patients – first course of radiotherapy 8 Gy x 1, second 8 Gy x 1.

The time delay between the first and the second radiation therapies was between 11 and 766 days (median = 135 days).

An analgesic effect was achieved with most treated patients – 41/57 (71.9%) with the use of second radiotherapy and with an insignificant percentage of complications, unimportant from the clinical point of view. No serious complications such as paralysis, paresis, spinal cord necrosis, neurological dysfunction of urethral or sigmoidorectal sphincters were noted in any of the treated patients.

Based on our experience, this retrospective analysis shows usefulness of the second radiotherapy treatment as a safe method of palliative treatment in cases of painful bone metastasis appearing after a previous radiation therapy.

Key words: re-irradiation, spinal cord, metastases, toxicity

Re-irradiation of neoplastic lesions is an important and difficult clinical issue, especially in cases with a tumor regrowth or a second primary tumor appearing in the previously irradiated region. Need for the second radiation of metastatic backbone lesions, where the spinal cord is an organ at risk, appears in case of recurrence of pain not responding to other medical treatment [5, 9, 10].

Indication of such treatment should be undertaken with care, taking into account poor prognosis and a certain percentage of varying late complications, such as spinal cord inflammation, cervical nerves paresis or osteonecrosis [3, 6].

Factors that should be taken into consideration for a decision of the second radiation therapy are [7, 14]:

1) the previously irradiated region (how much will the second radiation field overlap the primary irradiated field) and the plan of fractionation doses;

2) which critical tissues or organs are endangered; and
3) how much time has passed since the first radiation therapy.

This work presents a retrospective analysis of treatment results and toxicity after the second radiation therapy of metastatic lesions in the spinal column.

Patients and methods

Fifty-seven patients comprising 24 women and 33 men aged between 45 and 74 years (median = 59 years) were analyzed retrospectively. They underwent a second radiation therapy of the spinal column, between March 2002 and May 2004, performed due to recurrent pain in the previously irradiated region.

Neoplastic disease was confirmed in all patients, using

histological and cytological examinations. Metastatic lesions in bones were diagnosed using plain radiograms. The general health condition of patients who underwent the second radiation therapy 0, 1 or 2 was assessed by the Eastern Cooperative Oncology Group Scale. The hematological parameters were within normal limits in all patients. No pathological fracture or symptoms of spinal cord compression were found.

Nine patients were diagnosed with metastatic lesions in the cervical, 25 patients in the thoracic, and 23 patients in the lumbar spinal column. The primary tumor sites were breast 21, prostate 16, rectum 9, lung 11.

Patients characteristics are presented in Table 1.

Table 1. Patients characteristics (n=57).

| | |
|--------------------------|------------------|
| Male/Female | 33/24 |
| Performance status 0/1/2 | 6/27/24 |
| Median age (range) | 59 years (45–74) |
| Cervical metastases | 9 |
| Thoracic metastases | 25 |
| Lumbar metastases | 23 |

Standard technique was used for all patients: radiation with cobalt isotope ^{60}Co , with 1 field involving the metastatically changed vertebra and the margin of the adjusting healthy upper and lower vertebra.

Patients were divided into 3 groups depending on their treatment scheme:

Group A – 12 patients, 1st course of radiotherapy (RTH) = 4 Gy x 5, 2nd = 4 Gy x 5; the time between the first and the second RTH range 17 to 125 days (median = 32 days).

Group B – 16 patients, 1st course of RTH = 4 Gy x 5, 2nd = of 8 Gy x 1; the time between the first and the second RTH range 54 to 646 days (median = 340 days).

Group C – 29 patients, 1st course of RTH = 8 Gy x 1, 2nd also = 8 Gy x 1; the time between the first and the second RTH range 11 to 766 days (median = 154 days).

The RTH scheme 4 Gy x 5 was applied for the patients who had no presence of metastatic disease beyond the spinal column.

The RTH scheme 8 Gy x 1 was used for the patients who had dissemination of the disease in other organs.

Assessment criteria. Assessment of the clinical effect of radiation therapy involved the evaluation of the bone pain 1 to 3 months after the radiation. Because the Visual Analogue Scale (VAS) of pain intensity, used as an auxiliary test in clinical practice, is subjective, we tried to use a more objective method of pain assessment – the 3-grade analgetic scale of World Health Organization [16, 17].

In this study, the positive analgetic effect was defined as a state in which the patient needed drugs from a lower analgetic scale after the radiation therapy.

The lack of positive effects meant a state in which the patient needed the same drugs as before or drugs from the upper analgetic scale. The toxicity assessment involved: abnormal-

ities in the neurological examination (normally done about 1 month after the re-irradiation), hematological complications, general symptoms: fatigue, nausea/vomiting, skin erythema, diarrhea, and fever.

Results

Positive analgetic effect defined as a decrease in the analgetic scale degree of the used drugs was observed in 41 out of 57 patients (71.9%). No correlation was found between the analgetic effect and the radiation dose. Toxicity evaluation of the second radiation therapy was analyzed retrospectively based on treatment documentation dating up to 6 months after the radiation.

In group A we found nausea to be the most frequent symptom, appearing during radiotherapy in 6 out of 12 patients (50%). It disappeared after administering standard symptomatic drugs. One patient showed Lermitt's symptoms 2 months after the second radiation therapy.

In group B, skin erythema was the most common symptom (in 10 patients (62.5%)), followed by pain increase in the 1st week after the second radiation therapy in 1 patient (6.25%).

In group C, skin erythema was also the most common symptom, observed in 9 patients (47.4%). Some hematologic changes were noted as well: granulocytopenia in 5 patients with the lowest values of leucocytes of 2.8 g/l, drop of hemoglobin level til 9.5 g/dl in 6 patients. No patient with leucopenia required antibiotics. No serious complications such as paralysis, paresis, spinal cord necrosis, neurological dysfunction of urethral or sigmoidorectal sphincters were noted in any of the treated patients. For detailed data, see Table 2.

Table 2. Re-irradiation toxicity – all patients (n=57).

| | Group A (n=12) | Group B (n=16) | Group C (n=29) |
|------------------|----------------|----------------|----------------|
| Nausea/Vomiting | 6/1 | 2/0 | 1/1 |
| Erythema of skin | 4 | 10 | 9 |
| Diarrhea | 0 | 0 | 1 |
| Fever | 1 | 1 | 2 |
| Fatigue | 3 | 4 | 7 |
| Granulocytopenia | 1 | 2 | 2 |
| Erythrocytopenia | 2 | 1 | 3 |
| Lhermitte's sign | 1 | 0 | 0 |

Discussion

Medical treatment used to maintain life comfort of patients with neoplastic pain caused by bone metastasis implies a risk of side effects and cannot always be considered as an effective therapeutic method. Radiation therapy is an approved palliative method of treatment of painful bone metastasis [3, 8]. Recurrence of pain in patients previously irradiated is a clinical problem for many oncologists. The decision to use

the second radiation therapy is difficult, taking into account the possibility of serious complications, like: paralysis, paresis or sphincter dysfunctions, and reduced quality of life.

In the literature re-irradiation of the spinal cord with a total dose being greater than a tolerated dose has been reported [1, 11, 13]. The authors mention a good regeneration process of the spinal cord after the radiation therapy, but an important parameter is a delay time between two courses of radiation.

Active reparation processes in the spinal cord cells correcting post-radiation damage depends on the time allowed for reparation, on the total dose and its fractionation [6, 7, 15].

The data shows a certain safety margin for spinal cord toleration of radiotherapy. JEREMIC et al [4] confirmed the efficacy of the third RTH dose of 4 Gy, applied as a single fraction in patients with painful bone metastasis who had previously had two single doses of radiation therapy (4 Gy, 6 Gy or 8 Gy + 4 Gy). No early or late toxicity of such treatment has been observed.

Complications appearing after the second radiation therapy and presented in this study do not differ from those observed after palliative radiation [2, 12].

In most of our treated patients, an analgesic effect was obtained after the second radiotherapy, with a minimal percentage of insignificant complications. Serious complications were not observed.

Based on our experience, the presented retrospective analysis shows usefulness of the second radiotherapy as a safe method of palliative treatment in cases of painful bone metastasis appearing after the previous radiation therapy.

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