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Brachytherapy ■ (2015) ■

BRACHYTHERAPY

Is there a place for brachytherapy in the salvage treatment of cervical lymph node metastases of head and neck cancers?

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ABSTRACT

PURPOSE: Therapeutic options are limited for unresectable isolated cervical lymph node recurrences. The purpose of the study was to evaluate the feasibility, safety, and efficacy of high-dose-rate (HDR) and pulsed-dose-rate (PDR) brachytherapy (BT) in such cases.

METHODS AND MATERIALS: Sixty patients have been analyzed. All them had previously been treated with radical radiotherapy or chemoradiotherapy with or without surgery. PDR-BT and HDR-BT were used in 49 and 11 patients, respectively. In PDR-BT, a dose per pulse of 0.6−0.8 Gy (median 0.7 Gy) was given up to a median total dose of 20 Gy (range, 20−40 Gy). HDR-BT delivered a median total dose of 24 Gy (range, 7−60 Gy) in 3−10 fractions at 3−6 Gy per fraction.

RESULTS: The overall survival and lymph node control rates at 1 and 2 years were estimated for 31.7% and 19%, and 41.4% and 27.3%, respectively. Serious late side effects (soft tissue necrosis) were observed in 11.7% of patients. Adverse events occurred statistically more often in patients >59 years ($p = 0.02$).

CONCLUSIONS: HDR-BT and PDR-BT are feasible in previously irradiated patients with isolated regional lymph node metastases of head and neck cancers. The techniques should be considered if surgery is contraindicated. They provide acceptable toxicity and better tumor control than chemotherapy alone.

Keywords: PDR brachytherapy; HDR brachytherapy; Neck recurrence; Head and neck cancers; Salvage treatment

Introduction

Isolated cervical lymph node recurrences occur in approximately 10% of patients after radical irradiation of squamous cell carcinoma of the head and neck. Although surgical salvage is the preferable treatment for this population, it is not feasible in at least one-third of cases (1). For patients with unresectable nodal tumor, the current standard treatment is concurrent chemoirradiation (2). However, chemotherapy is of limited benefit when administered as a single modality and provides median survival of only 6 months (3). On the other hand, because of considerable toxicity, full-dose reirradiation cannot be implemented in most previously irradiated patients. Is there a place for brachytherapy (BT) in such cases?

In the literature, minimal data exist regarding the treatment of regional neck metastases with the interstitial BT. Moreover, most of them are presenting results of low-dose-rate (LDR) techniques which have been replaced by more adaptable and safer modalities (4, 5).

The aim of our study was to evaluate the feasibility, safety, and efficacy of interstitial high-dose-rate (HDR) and pulsed-dose-rate (PDR) BT in the salvage treatment of isolated cervical lymph node relapses.

Received 8 May 2015; received in revised form 19 June 2015; accepted 9 July 2015.

Conflict of interest: None.

Funding: None.

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1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2015.07.003

Methods and materials

Patients

Sixty patients with squamous cell carcinoma neck metastases amenable for salvage surgery treated with interstitial BT have been included into the analysis. Surgery was abandoned due to the infiltration of internal carotid artery or prevertebral fascia in 50 and 4 patients, respectively, while was contraindicated because of anesthetic reasons in six cases. There was no evidence of local recurrence in the primary tumor site nor distant metastatic spread. All patients completed full-dose external beam radiotherapy (EBRT) or chemoradiotherapy more than 6 months before BT. The median time from the end of prior radiotherapy to cervical lymph node relapse was 32 months (range, 7−48 months).

The median age of patients was 59 (range, 36−81 years). In the study group, there were 56 men and 4 women. Primary tumor sites were as follows: larynx and hypopharynx (31 of 60; 51.7%), oropharynx (16 of 60; 53.3%), floor of the mouth/tongue (7 of 60; 11.7%), nasopharynx (1 of 60; 1.7%), and unknown in 5 of 61 (8.2%) patients. Most of the nodal recurrences were localized at the Level II (30 of 60; 50%), whereas the remaining at the Level II and III (25 of 60; 41.7%), Level III (3 of 60; 5%) and Level IV (2 of 60; 3.3%). They were classified as N1, N2a, N2b, N2c, and N3 in 8, 13, 19, 9, and 11 cases, respectively. Patients' characteristics, including previous neck treatment modalities details, are described in Table 1.

Table 1
Patients' characteristics—age, gender, primary tumor site and histopathology, primary treatment, recurrence nodal status

	Number (percent of patients)
Age (y)	Mean—59 years
<59	31 (51.7)
>59	29 (48.3)
Gender	
Male	56 (93.3)
Female	4 (6.7)
Primary tumor site	
Larynx and hypopharynx	31 (51.7)
Oropharynx	16 (53.3)
Floor of the mouth/tongue	7 (11.7)
Unknown primary	5 (8.2)
Nasopharynx	1 (1.7)
Primary tumor histopathology	
Squamous cell carcinoma	60 (100)
Primary treatment	
Surgery and radiotherapy	41 (68.4)
Radiotherapy	11 (18.3)
Radiotherapy and chemotherapy	5 (8.3)
Surgery, radiotherapy, and chemotherapy	3 (5)
Recurrence nodal status	
N1	8 (13.33)
N2	41 (68.33)
N3	11 (18.33)

Methods

The treatment was interstitial BT alone in all cases. Simultaneous chemotherapy had not been administered—due to the limited availability of that form of therapy, the patients' general condition, and their lack of consent for such a modality. PDR-BT and HDR-BT were used in 49 (81.7%) and 11 (18.3%) patients, respectively. There were no specific criteria for eligibility for PDR or HDR technique. The choice was conditioned by general patient state (long-term immobilization during PDR-BT, need for hospitalization in PDR-BT). Catheters (Flexible implant tube 6F, 30 cm, Single-leader, Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) were implanted in the Department of Otolaryngology—under general (36 patients) or local (24 patients) anesthesia, after defining the critical structures and the description of the target volume (clinical examination, CT scans/MRI, intraoperative ultrasonography), in a parallel alignment, with a constant distance of 10−15 mm. An average of 4 (range, 2−6) afterloading catheters were inserted. The proper treatment was introduced in the Department of Brachytherapy 1−2 days after catheters placement. Dose distribution was prepared individually for clinical target volume region using IPSA (Inverse Planning Simulated Anealing) optimization algorithm. Examples of treatment plan are presented on Figs. 1 and 2. The following equipment (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden): IBU (Integrated Brachytherapy Unit), PLATO planning system, and microselectrons PDR and HDR (Nucletron) with ^{192}Ir sources were used for treatment delivery. In PDR-BT group, a dose per pulse of 0.6−0.8 Gy (median 0.7 Gy) was given up to a median total dose of 20 Gy (range, 20−40 Gy). The pulses were delivered in 20−24 hours with a interval of 1 hour between the pulses. HDR-BT was applied twice a day with intervals of at least 6 hours. Median total dose was 24 Gy (range, 7−60 Gy) given in three−10 fractions (median 5) at 3−6 Gy (median: 5 Gy) per fraction for 2−5 days.

Followup ranged from 1 to 48 months (median: 12 months). Patients were evaluated 1 month after finishing the treatment and then at 3-month intervals. Lymph node control (LNC) was assessed by the clinical examination and imaging techniques if required. Treatment assessment was based on tumor volume response and defined according to the modified WHO response criteria for solid tumors. Four-grade scale was used to describe local status: (*1*) complete remission (CR), (*2*) partial remission (PR), (*3*) stable disease (SD), (*4*) progressive disease. LNC was based on the number of months between the first day of treatment to the date of locoregional progression after CR, PR, or SD. For censored patients, the last date of progression-free followup was used in the survival estimates. Overall survival (OS) was based on the number of months between the first day of BT to the date of death or the last date of followup for censored patients. Acute and late toxicities were scored using the Common Terminology Criteria for Adverse Events v3.0.