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Local control in advanced cancer of the nasopharynx: Is a boost dose by endocavitary brachytherapy of prognostic significance?

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ABSTRACT

PURPOSE: To analyze whether local tumor control in advanced nasopharyngeal cancer (NPC) can be optimized by boosting the primary dose by endocavitary brachytherapy (EBT).

METHODS AND MATERIALS: To study the role of EBT, three data sets on NPC, that is, the ''Vienna'', ''Rotterdam,'' and ''Amsterdam'' series, with a total number of 411 advanced NPC patients, were available. The Rotterdam series consisted of 72 patients (34 T1,2N+ and 38 T3,4N0,+) and were treated with neoadjuvant chemotherapy followed by external beam radiotherapy (dose 70/2 Gy). After 70/2 Gy, a boost was applied by EBT (in case of T1,2N+) or stereotactic radiation (in case of T3,4 tumors). The Amsterdam (Antoni van Leeuwenhoek Hospital/The Netherlands Cancer Institute) series consisted of 76 patients (40 T1,2N+ and 36 T3,4N0,+) and were irradiated to a dose of 70/2 Gy with concomitant chemotherapy. No second boost by EBT was applied.

RESULTS: In the case of T1,2N+ tumors, the local relapse rate (LRR) was significantly smaller if a boost was applied, that is, 0% (0/34, EBT boost) vs. 14% (14/102, no EBT boost) ($p = 0.023$). For the T3,4 tumors, an LRR of 10% (4/38, EBT or stereotactic radiation boost) vs. 15% (17/111, no boost) was found ($p = 0.463$).

CONCLUSIONS: In the case of advanced NPC (T1,2N+ vs. T3,4N+,0), for early T-stages (T1,2N+), an EBT boost seems an excellent way to deliver highly conformal high doses of radiation to the nasopharynx, with high local control rates. For advanced T-stages (T3,4N+,0), the reduction in LRR (10% vs. 15%) was not significant ($p = 0.463$).

Keywords: Head and neck cancer; Nasopharynx; Boost irradiation; Brachytherapy; Endocavitary; Prognostic factor

Introduction

Nasopharyngeal cancer (NPC) is highly prevalent in provinces of Southern China (e.g., Hong Kong), with an incidence rate of up to 20 per 100,000 inhabitants (1). In contrast, it is a relatively rare disease entity in the Netherlands, with an incidence of close to 1 per 100,000. Some of the countries of the Mediterranean Basin report an incidence rate in between 1 and 5 per 100,000 (2). The nasopharynx is a midline-located cuboidal-shaped cavity, anatomically located posteriorly to the nasal cavity and cranial posteriorly bordered by the base of skull. It is heavily infested with lymphoid tissue and surrounded by a network of critical structures. Laterally, a close anatomic relationship exists with the parapharyngeal space, containing critical structures such as the cranial nerves IX–XII. By traversing the foramen lacerum, the nasopharynx interconnects directly or by lymphatics with the middle cranial fossa. Consequentially, this anatomic route can cause NPC cells to destruct critical structures of the parasellar region, such as the cranial nerves I–VIII, inner ear, and carotid arteries. Approximately 80% of patients develop lymphadenopathy and/or have

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lymph nodes at the time of initial diagnosis (3), with frequently a typical involvement of the lymphnodes in Level V. Moreover, staging of NPC reveals that most patients have advanced disease, that is, either T1,2N+ or T3,4N0,+, Stage III/IV disease. Frequently, however, nodal disease in NPC can be cured by a combination of chemotherapy (CHT) and radiation therapy (RT) (mostly given in a ''concomitant'' fashion currently). One of the single most important prognostic factors is the extent of the primary lesion at the time of clinical presentation (4, 5). The purpose of the present report is to analyze whether, when using the Rotterdam nasopharyngeal applicator (RNA; see also Fig. 1), a boost of 11 Gy by endocavitary brachytherapy (EBT) is of significance in obtaining high local control rates in advanced (T1,2N+) NPC (6).

Methods and materials

Advanced NPC can be subdivided into T1,2N+ and T3,4N0,+ patients. Three databases of advanced NPC patients (''Vienna'', ''Rotterdam'', and ''Amsterdam'' series) have been analyzed to investigate whether local tumor control in NPC can be increased with the application of a highly focused, second boost dose of radiation. The radiation was applied either by EBT (in case of T1,2 tumors) or stereotactic radiation (in case of T3,4 tumors) (7, 8). With regard to the Vienna (67 T1,2N+ and 65 T3,4N0,+), Rotterdam (34 T1,2N+ and 38 T3,4N0,+), and Amsterdam series (40 T1,2N+ and 36 T3,4N0,+), the RT guidelines for the techniques to be used were quite similar for the first part of the treatment, that is, 46/2 Gy by external beam RT to the primary tumor site and bilateral neck, to be followed by a booster dose of 24/2 Gy to the primary tumor and lymphnodal disease. The gross tumor volume of the primary tumor was delineated with the use of magnetic resonance imaging (matching). Patients were treated in supine position with a head fixation mask. Dose is prescribed according to the International Commission on Radiation Units and Measurements guidelines.

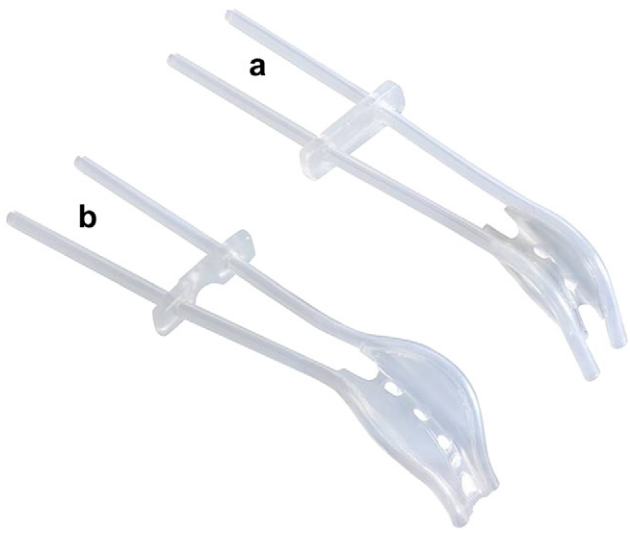

Fig. 1. (a) ''Old'' type Rotterdam nasopharyngeal applicator (RNA) and (b) ''new'' type RNA. Over time, the RNA was slightly modified. Flanges of both catheters were tilted more sideways; thus, the dose will be ''pushed'' more laterally toward/in parapharyngeal space.

All advanced NPC patients received CHT. The ''Vienna protocol'' patients were treated by neoadjuvant and concomitant combined CHT, the ''Rotterdam protocol'' patients by neoadjuvant CHT, and the ''Amsterdam protocol'' by concomitant CHT. To deliver the fractionated EBT boost dose of 11 Gy on an outpatient basis, an institutionally designed and currently commercially available, silicone afterloading device (RNA; Fig. 1) was used in the Vienna and Rotterdam protocols. For applying EBT, RNA was connected to a microSelectron high dose rate (HDR), a remote-controlled afterloading device containing an ^{192}Ir point source (37 MBq). No second boost was given in the Amsterdam series.

Results

Local control

Table 1 denotes a summary for the ''Rotterdam,'' ''Amsterdam,'' and the ''Vienna'' series, stratified for the T1,2N+ and T3,4N0,+ cancers (advanced NPC), number of patients, number of local relapses (LRs), and percentage of patients developing distant metastasis (M+). For the ease of interpreting the data, a letter code was assigned to the different treatment protocol groups (see Table 1). For T1,2N+ tumors, no LRs (0%; 0/34) were found for Group B (Rotterdam series), in contrast to Group C (Amsterdam series) (10%; 4/40) ($p = 0.058$). In the T3,4N0,+ category, brachytherapy (BT) does not impact the LR rate (LRR), that is, an LRR of 11% (4/38) for Group B vs. 11% (4/36) for Group C ($p = 0.935$). With respect to the Vienna protocol series, an LRR for T1,2N+ tumors of 12% (8/67) for Groups C + B (i.e., plus EBT boost) vs. 16% (10/62) for Groups C − B (i.e., no EBT boost) was observed ($p = 0.492$). Same was true for the advanced T-stage categories (T3,4N+,0): An LR of 26% (17/65) vs. 19% (13/69) for the Groups (C + B) vs. (C − B), respectively, was seen. Finally, because there was an overlap and similarity for the Groups C and (C − B), we compared the LRR of the group of patients denoted as C_{total} (=C + [C − B]) for T1,2N+ and T3,4N0,+ cases. For Group C_{total} T1,2N+ cancers, an LR of 14% (14/102) vs. 0% (0/34) was observed for the Group B ($p = 0.023$). For Group C_{total} T3,4N0,+ tumors, an LR of 15% (17/111) vs. 11% (4/38) for the Group B was seen ($p = 0.463$). The regional relapse rate for small tumors was 0%, for advanced tumors depending on the tumor stage variable from 7% (T1,2N+, T3,4N0,+, and Rotterdam series) to 15% (T1,2N+, T3,4N0,+, and Vienna series without boost) and 16% (T1,2N+, T3,4N0,+, and Vienna + Boost).

Seventeen of 72 $N_{0,1,2,3}$ (24%) patients, treated by the Rotterdam protocol, developed M+ at some point in time;