ELSEVIER

Brachytherapy 13 (2014) 178–186

BRACHYTHERAPY

Perioperative image-adapted brachytherapy for the treatment of paranasal sinus and nasal cavity malignancies

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ABSTRACT

PURPOSE: Sinonasal malignancies are a rare group of cancers often associated with late presentation and poor prognosis. In the past, there was little progress regarding survival rate, and often, multimodal treatment regimens are required. The aim of this study was to evaluate the clinical outcome of perioperative image-adapted brachytherapy (IABT) as part of a multidisciplinary treatment regimen for the therapy of sinonasal cancer.

METHODS AND MATERIALS: Since 2006, patients with sinonasal cancer at the University Hospital of Schleswig-Holstein Campus Luebeck, Germany, were offered a multimodal treatment concept including head and neck surgery, perioperative IABT with or without external beam radiation therapy, and chemotherapy. In a retrospective study, such patients were analyzed for survival rate, tumor control, and toxicity of the interdisciplinary treatment.

RESULTS: Thirty-five consecutive patients were analyzed. The majority of patients (63%) were treated for a primary tumor and 62% presented with tumor Stages III–IV. The mean follow-up time with IABT was 28 months. Overall survival estimate was 72% after 3 years. Disease-specific survival, disease-free survival, and local control rates were 83%, 63%, and 67%, respectively. On univariate analysis, a significant better disease-free survival rate was found in patients treated for primary, but not recurrent, sinonasal cancer ($p = 0.006$). The overall treatment toxicities were mainly classified Grade I.

CONCLUSIONS: Interdisciplinary perioperative IABT is associated with excellent locoregional control and survival rates. IABT is well tolerated and shows low toxicity. Furthermore, visual acuity can be preserved in advanced cases. The implementation of perioperative IABT into multimodal treatment regimens improves the oncologic outcome.

Keywords: Paranasal sinus cancer; Nasal cavity cancer; Brachytherapy; Brachytherapy tube; Multimodal treatment; Survival; Toxicity

Introduction

Malignancies of the paranasal sinuses and nasal cavity are a rare group of cancer often associated with late presentation and poor prognosis. In the past, there was little progress regarding survival rate, and often, multimodal treatment regimens are required (1, 2). The paranasal sinuses consist of four paired air-filled spaces that surround the nasal cavity. They are named after the bone they are located in (maxillary sinuses, frontal sinuses, ethmoidal sinuses, and sphenoidal sinuses). All sinuses are connected to the nasal cavity via small openings in the bone and mucosa. The nasal cavity itself starts anteriorly at each nostril and ends posteriorly in the nasopharynx. It is divided by the nasal septum. In larger tumor volumes, the origin of the tumor, nasal cavity, or paranasal sinuses is often not possible

Received 23 May 2013; received in revised form 4 October 2013; accepted 16 October 2013.

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1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2013.10.009

to be distinguished. Because of its localization, asymptomatic growth is common, and patients often present with advanced disease at the time of their histologic diagnosis. Nasal congestion, bloody discharge, and double vision because of orbital displacement or tumor invasion are some of the typical symptoms for which the patient seeks medical care. Sinonasal malignancies approximately account for 3% of all head and neck cancers only (3). Depending on the tumor entity, standard treatment regimen for the previously mentioned malignancies usually consists of radical surgery combined with radiation therapy. Even with recent progress in surgical techniques, such as endoscopic-guided power tools, a complete tumor removal can be limited by its proximity to the optical system or central structures. Furthermore, radical surgical treatment can result in loss of visual acuity. However, external surgical approaches via lateral rhinotomy, medial maxillectomy, or craniofacial resection, combined with midfacial degloving, are still reasonable for the need of better visualization and complete tumor removal.

Because of the previously mentioned limitations, postoperative external beam radiation therapy (EBRT) is often indicated and improves local tumor control (2, 4). Still, structures such as the orbital system, brainstem, or cranial nerves can be harmed by EBRT, leading to visual and nerve toxicity. In the past, nonmaximal radiation of the target volume often had to be tolerated to spare severe treatment-related toxicity. By the use of three-dimensional conformal radiotherapy or intensity-modulated radiation therapy (IMRT), both acute and late toxicities of radiation were reduced, and no radiotherapy-induced blindness or normal tissue necrosis was seen (5–7). The use of protons/heavy ions in EBRT is reserved to a few special institutions worldwide. Conformal proton radiation lowers the treatment toxicity on the surrounding normal tissues and allows local dose-escalation protocols (8). Because of the physical properties, proton therapy is more suitable for deeper tumor lesions, whereas electron therapy is more applicable for superficial tumors. Furthermore, electrons deliver higher dose to the skin than other beam qualities, and conformation of the beams to the given anatomy is not accurate. Photon therapy in form of IMRT lies in between (9, 10).

Recently, perioperative image-adapted brachytherapy (IABT) gained more attention for the treatment of sinonasal cancer. IABT allows the application of high local radiation doses to the target region while avoiding severe adverse events in the surrounding healthy tissues. This is possible by postoperative and fractionated positioning the radiation source (mostly ^{192}Ir) guided through previously intraoperative implanted plastic tubes directly into the target area (tumor bed). Even in patients already treated with EBRT, additional dose escalation within the region of recurrence is possible because of the very conformal dose delivery. By combination of perioperative IABT and function preservation (partly debulking) surgery in first- and second-line treatment strategies, an improvement of prognosis and quality of life was anticipated for the patients.

The aim of the present study was to evaluate the clinical outcome of perioperative IABT after less aggressive surgery as part of a multidisciplinary treatment regimen for the therapy of sinonasal cancer.

Methods and materials

At the University Hospital Schleswig-Holstein Campus Luebeck, Germany, 184 patients suffering from head and neck cancer were treated between January 2006 and January 2013 by a multidisciplinary approach including surgery and IABT with or without EBRT and chemotherapy. The aim of the multidisciplinary treatment was to achieve increased tumor control, better survival rates, and less radiation toxicity by the addition of IABT.

In a retrospective study of this cohort, 35 patients treated for paranasal and nasal cavity malignancies, hereafter referred to as sinonasal cancer, could be identified. All patients were staged, and the tumor stages were classified using the actual tumor-nodes-metastasis and Union for International Cancer Control (UICC) classification (11). Patients with recurrent disease treated elsewhere by primary EBRT or surgery were also included in the study. All patient characteristics are presented in Table 1.

The cohort was analyzed for overall survival (OS), disease-specific survival (DSS), and disease-free survival (DFS) rates. Data for local control (LC), regional control (RC), and distant control (DC) rates were collected. All treatment regimens were reviewed for acute and late toxicities of IABT. The intention to treat was curative. The retrospective study was approved by the ethics committee of the University of Luebek, Germany (11-065A).

Pretreatment and treatment planning

For all patients, complete medical history, physical examination, and routine blood counts including liver and renal function tests were taken. The clinical tumor stage was defined by CT and/or MRI of the head and neck regions, CT or X-ray of the chest, and CT or ultrasound scan of the upper abdomen. Biopsy of the tumor was performed either with local anesthesia as an outpatient procedure or via microscopic/endoscopic sinus surgery under general anesthesia.

All patient data were presented to an interdisciplinary tumor board consisting of a radiotherapist, brachytherapy expert, oncologist, and head and neck surgeon for further treatment planning. Before therapy was started, preoperative interdisciplinary treatment planning was performed on CT and/or MRI examinations. The aim was the maximal tumor resection with function preservation of surrounding structures at risk (e.g., eyes, optic nerve) and optimal intraoperative placement of brachytherapy tubes for postoperative IABT.