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Scientific Article

Risk of carotid blowout after reirradiation with particle therapy

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Abstract

Purpose: Carotid blowout (CB) is a serious complication in retreatment of neoplasms in the head and neck (H&N) region. Rates seem to increase in hypofractionated or accelerated hyperfractionated regimens. In this study, we investigate the CB rate and the cumulative doses received by the carotid artery (CA) in a cohort of patients who were reirradiated at CNAO with particle therapy in the H&N region.

Methods and materials: The dosimetric information, medical records, and tumor characteristics of 96 patients were analyzed. For 49 of these patients, the quality of dosimetric information was sufficient to calculate the cumulative doses to the CA. The corresponding biological equivalent dose in 2 Gy fractions (EQD2) was calculated with an α/β-ratios of 3.

Results: In the final reirradiation at CNAO, 17 patients (18%) had been treated with protons and 79 (82%) with carbon ions. Two patients experienced profuse oronasal bleeding, of which one case was confirmed to be caused by CB. If attributing both cases to CB, we found an actuarial CB rate of 2.7%. Interestingly, there were no CB cases in the carbon ion group even though this was the large majority of patients and they generally were treated more aggressively in terms of larger fraction doses and higher cumulative EQD2.

Conclusions: The current practice of particle reirradiation at CNAO for recurrent neoplasms in the H&N region results in acceptable rates of CB.

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Introduction

Carotid blowout (CB), defined as a sudden rupture of the carotid artery (CA) or one of its main branches, is a feared complication in the treatment of neoplasms in the head and neck (H&N) region. CB results from pathologic alterations in or loss of the soft tissues surrounding the CA and from alterations in the vessel wall itself. Risk factors include ulceration, radiation to lymph nodes, dose to the neck >70 Gy, reirradiation, radical neck surgery, nutritional status (body mass index <22.5 kg/m^2), osteonecrosis, and the degree to which the CA is involved in the tumor.[1-4]

The properties of radiation therapy (RT) also seem to affect the risk of CB because rates as high as 8.4% to 15% are observed in reirradiation with hypofractionated stereotactic body RT (SBRT)[4-6] in contrast to >4% with more conventional fractionated photon regimens.[2,7]

Particle therapy, because of its physical advantages in dose distribution, is a suitable treatment modality for recurrent neoplasms in the H&N region. For carbon ion RT (CIRT) in particular, there are even biological advantages that could be harnessed through the use of hypofractionated schedules.[8,9] In a report on CIRT reirradiation of 52 patients with recurrent adenoid cystic carcinoma, 2 patients (3.8%) developed CB after nasopharyngeal necrosis.[10] The patients received reirradiation doses of 36 Gy (relative biological effectiveness [RBE]) to 74 Gy (RBE) in a moderately hypofractionated regimen of 3 Gy (RBE) per fraction.

At the National Center of Oncological Hadrontherapy (CNAO) in Pavia, Italy, patients with recurrent neoplasms in the H&N region are treated under protocols for reirradiation using protons or carbon ions with fraction doses ranging from 2 Gy (RBE) to 5 Gy (RBE). This prompted us to investigate the outcome of these patients with regard to CB with a special focus on the cumulative doses received by the CA.

Methods and materials

Reirradiation at CNAO

All patients were treated under prospective protocols that were approved by the regional ethics committee. A signed consent was required for participation. Proton RT was used as a first option, with conventional fractionation of 2 Gy (RBE) per fraction. A fixed RBE value of 1.1 was employed. CIRT was used for histologies with a poor response to low linear energy transfer (LET) radiation (eg, sarcoma, melanoma, and salivary gland tumors), in cases of early in-field recurrence after photon RT (assuming selection of a radio-resistant clone), or in cases in which the sharper lateral penumbra of CIRT resulted in significantly better sparing of organs at risk (OARs). Dose per fraction ranged from 2 Gy (RBE) to 5 Gy (RBE). RBE was calculated with the local effect model version 1[11] using the *syngo* RT Planning (Siemens Healthcare, Erlangen, Germany) treatment planning system (TPS).

To avoid long-term toxicity to OARs that were previously irradiated, an estimate of the cumulative biological equivalent dose (EQD2) from the prior and planned reirradiation was performed using a conservative α/β-ratio of 2 Gy for all OARs. When using an active scanning technique, it is feasible to selectively restrain the dose to the CA while retaining a high dose to most of the target (Fig 1b). The current practice at CNAO is to avoid cumulative EQD2 to the CA that exceeds 120 Gy (RBE) by using this method.

Patient population

A total of 128 patients were reirradiated at CNAO with either protons or carbon ions from September 2012 to March 2016. Four patients were excluded from the study because there were no records on the doses given in the previous RT, and 27 patients were excluded because they did not receive doses to their CA in the primary RT or the reirradiation or because these doses did not overlap in their CA. One patient, a foreign citizen, never appeared for follow-up and was also excluded.

A total of 96 patients were available for analysis with regard to the rate of CB (Fig 2; pink boxes). General details on past and present RT, patient and disease characteristics, and prior surgery were collected. In addition, the following information was also gathered:

1) tumor involvement grade: *(a)* no involvement, *(b)* <1/3 of CA circumference, *(c)* 1/3 to 2/3 of CA circumference, or *(d)* >2/3 of CA circumference
2) segment of CA that received the highest dose: *(a)* neck, *(b)* skull base, *(c)* sinus cavernosus, or *(d)* intracranial
3) whether surgery had been performed in the immediate vicinity of the high-dose segment of the CA, thus potentially making the CA more vulnerable.

Because tumor involvement grade and surgery near the CA have been suggested as factors that decrease the integrity of the CA wall and thereby increase the risk of CB,[1,2,7] we defined 2 potential high-risk features to assess their impact on CB rate in our material:

1) tumor involvement grade that is >2/3 of the CA circumference
2) prior surgery in the immediate vicinity of the segment of the CA that received the highest cumulative dose

Calculation of cumulative dose statistics to carotid arteries

For 49 of the 96 patients, there was sufficient documentation on prior RT to calculate cumulative doses to