

Local Recurrence of Cavum Cancer: Experience of the Radiotherapy Department of the University Hospital of Marrakech

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Abstract

Original Research Article

Local recurrence of cavum cancer has a poor prognosis and poses a management problem. Re-irradiation remains the only effective therapeutic option to ensure a good local control rate, but it is limited by the doses previously received by the organs at risk in series. We retrospectively studied 8 patients re-irradiated for isolated local relapse of nasopharyngeal carcinoma, collected in the onco-hematology hospital of Marrakech between 2012 and 2022. The mean time to local relapse was 48 months (range: 10 months-12 years). The diagnosis was confirmed by biopsy in five cases and was based on MRI radiological evidence in three cases. Recurrence was classified rT1N0M0 in two cases, rT2N0M0 in three cases, rT3N0M0 in one case, and rT4N0M0 in two cases. Three patients first received chemotherapy combining taxotere, cisplatin, and 5-fluorouracil (TPF), followed by radiotherapy. Five patients received chemoradiotherapy, one of whom also received first-line chemotherapy. In our series we obtained a satisfactory rate of complete remission but at the cost of significant toxicity. Local therapeutic failures in the cavum constitute an unfavorable event. Salvage treatment involves radiotherapy associated in some cases with chemotherapy.

Keywords: Local recurrence, cavum cancer, re-irradiation.

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INTRODUCTION

Local recurrence of cavum cancers has a poor prognosis and poses a management problem. Re-irradiation remains the only effective therapeutic option to ensure a good local control rate, but it is limited by the doses previously received by organs at risk in series.

OBJECTIVE

- Management and efficacy of re-irradiation of local relapses of nasopharyngeal carcinoma.

MATERIAL AND METHOD

This was a retrospective study, including 8 patients re-irradiated for isolated local relapse of nasopharyngeal carcinoma, collected in the hospital of onco-hematology of Marrakech between 2012 and 2022.

RESULTS

Among 420 irradiated patients, eight patients had isolated local recurrence. The mean age was 48 years. The tumor was initially classified T2N0M0 in three cases. Initial treatment was based on concomitant

chemoradiotherapy for all patients, one of whom had first-line chemotherapy. Radiation therapy was conventional for all patients. The doses delivered were between 70 and 74 Gy, at a rate of 2 Gy per session. All patients were in complete remission. The mean time to local relapse was 48 months (range: 10 months-12 years). The diagnosis was confirmed by biopsy in five cases and was based on MRI radiological evidence in three cases. Recurrence was classified rT1N0M0 in two cases, rT2N0M0 in three cases, rT3N0M0 in one case, and rT4N0M0 in two cases. Three patients first received chemotherapy combining taxotere, cisplatin, and 5-fluorouracil (TPF), followed by radiotherapy. Five patients received chemoradiotherapy, one of whom also received first-line chemotherapy. The dose of radiotherapy was 60 Gy, at a rate of 2 Gy per session. Radiation therapy was three-dimensional in all cases. The macroscopic tumor volume was defined on imaging. The predictive target volume was created by an automatic margin of 5 mm from the macroscopic tumor volume. Dosimetry was validated by accepting a mean dose of 3 Gy to the brainstem. After a mean follow-up of 19 months (range 9-34 months), six patients were in complete remission and two died of

disease after a mean follow-up of 10 months. The late toxicity of re-irradiation was mandibular radionecrosis in one patient, trismus in two and cervical fibrosis in two.

DISCUSSION

The rate of local and/or locoregional recurrence varies between series ranging from 18 to 35% [1, 2, 9, 11, 12]. These rates generally do not exceed 10% in the case of IMRT [3-6]. In our series, the local recurrence rate was 10%. The majority of local recurrences occur within the first two to three years after the initial treatment [3, 12]. However, some relapses occur later [3]. Lee *et al.*, noted a median time to local relapse of 1.9 years, with 52% of relapses occurring within two years of treatment, 39% between two and five years, and 9% at more than five years.

In our series, 74% of local and/or locoregional relapses occurred within 3 years of the end of treatment. When treating the primary tumor, large tumor extension, low radiation doses and well-differentiated histological type correlate with a high relapse rate and are an important prognostic factor for local control [2]. The diagnosis of local recurrence is often made late; with locally advanced tumors classified as rT3 or rT4 in 44-50% of cases in published series [12]. In our series, 43.8% of the tumors were classified as rT3-rT4. An aggressive therapeutic attitude is justified because the absence of salvage treatment has a negative impact on survival [2]. The analysis of the results of the different series in the literature is ambiguous because of the heterogeneity of the therapeutic methods used. Reirradiation of the nasopharynx is the reference treatment. It can be exclusive or combined with another therapeutic modality, such as chemotherapy.

Cavum surgery is not widely used in the treatment of local recurrences. Its place is not clearly established and it is not without risks [2]. In our institution, we do not use this treatment modality. Lymph node surgery is recommended in case of associated lymph node relapse. Adenectomy or lymph node dissection is often proposed in the absence of contraindication. External reirradiation is indicated for locally advanced tumors, whereas exclusive brachytherapy is the treatment of choice for small local recurrences confined to the cavum.

In the first published series, external radiotherapy was classical, in two dimensions and sometimes associated with a brachytherapy boost. The results were poor, with 5-year local control rates not exceeding 60% and a high incidence of late toxicity. The 5-year overall survival rates ranged from 6% to 40% [2, 12].

Toxicity, mostly late, is the main limiting factor for re-irradiation of previously irradiated areas, which may affect the quality of life of patients. The

incidence of complications after re-irradiation of cavum cancer is between 6 and 45% [2]. It increases with the radiation dose [20] and for the interval between the two irradiations; a delay of less than 18 months or even one year seems to be unfavorable. In the series of Lee *et al.*, 24% of patients suffered from late toxicity, the most common being trismus (17%), and 5.5% suffered from neurological toxicity [9]. The occurrence of complications was not influenced by the dose levels received. In the series of Leung *et al.*, 57% of patients suffered a major complication [12]. Temporal lobe necrosis was observed in 27% of cases. Statistical analysis showed the influence of the treatment modality (external radiotherapy or brachytherapy) and the rT stage on the occurrence of complications. Hemorrhage is the most serious complication in cases of nasopharyngeal re-irradiation. Its rate varies between 2% and 7% [21-24]. Some hemorrhages were massive, despite the use of modern re-irradiation techniques, resulting in death. Vascular ruptures are usually due to cervical re-irradiation in case of associated lymph node relapse. Chua *et al.*, reported 5% bleeding with unfractionated stereotactic radiotherapy versus 2% with multiple fractions [25]. Seo *et al.*, reported three cases of hemorrhage, two of which were in the carotid artery and resulted in death.

The incidence of late sequelae should decrease with the advent of innovative radiotherapy techniques. IMRT has become the therapeutic standard for tumors of the ENT sphere. It can be adapted to concave shapes of target volumes and allows to spare adjacent organs at risk. It allows the delivery of high doses. Although the follow-up is still insufficient, the local control rates are satisfactory [25-28]. Han *et al.*, published the largest series with a 5-year local control rate of 85.8% [26]. Stereotactic radiotherapy is another innovative technique that allows the delivery of a high dose in a very limited volume with a high dose gradient. It can be delivered in one or more sessions. It can be used as a boost in addition to another re-irradiation technique. Local control rates are better with the multifractionated modality, with a lower rate of late complications [4, 12]. Local control rates are in the range of 51 to 83% at 5 years in published series [21-24, 29].

Leung *et al.*, reported a 3-year local recurrence-free survival of 64%, 61.5% and 18.4% respectively for recurrences classified as rT1, rT2, rT3 ($p = 0.001$) [8]. The dose of re-irradiation is also a prognostic factor for local control and consequently for overall survival. The impact of dose levels on local control has been reported in some retrospective series: re-irradiation doses above 60 Gy were associated with an increased probability of survival without local recurrence at 3 years [12, 30]. The consensus dose should be greater than or equal to 60 Gy in conventional or biologic equivalent spread and fractionation. Data on the role of chemotherapy in the salvage treatment of cavum cancer are conflicting, with published series

including both metastatic and local failures. The best results have been observed with platinum salts. Recent studies testing taxanes are promising. By analogy with the treatment of primary tumors, chemotherapy should be indicated for locally advanced recurrent tumors and/or associated lymph node involvement, ideally in a concomitant modality.

CONCLUSION

In our series we have obtained a satisfactory rate of complete remission but at the cost of significant toxicity. Local therapeutic failures of the cavum constitute an unfavorable event. Salvage treatment involves radiotherapy associated in some cases with chemotherapy. Toxicity related to re-irradiation is its main limiting factor. New irradiation techniques are promising and should reduce the incidence of late complications while ensuring satisfactory local control.

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