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Case Report

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RADIO-INDUCED SARCOMA AFTER TREATMENT OF A UCNT OF THE NASOPHARYNX: A CASE REPORT

S. Boughanmi*, S. Tebra Mrad, S. Tbessi, I. Zrafi, H. Bhiri, S. Soltani and N. Bouaouina

Radiation Therapy Department, Farhat Hached University Hospital, Faculty of medicine Ibn El Jazzar, University of Sousse (Tunisia).

***Corresponding Author: S. Boughanmi**

Radiation Therapy Department, Farhat Hached University Hospital, Faculty of medicine Ibn El Jazzar, University of Sousse (Tunisia).

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INTRODUCTION

Radiotherapy is one of the major components of cancer curative care. Due to improved treatments and to the overall increase in lifespan, we more often face dealing with late adverse effects including second cancers. The occurrence of radiation-induced sarcomas or radio-chemotherapy-induced ones, better known after Hodgkin disease treatment, breast cancer, has been exceptionally reported after treatment of an epidermoid carcinoma of the nasopharynx.

MATERIAL AND METHOD

We report the observation of sarcoma occurring after 12 years in a patient at the age of 35, first treated by chemotherapy then by radiotherapy for nasopharyngeal undifferentiated carcinoma (UCNT), diagnosed in radiation therapy department of Farhat Hached hospital in Sousse.

OBSERVATION

On January 2001, B.A aged 35, was referred to our department for irradiation of undifferentiated nasopharyngeal carcinoma, and revealed by epistaxis and cervical mass. The initial examination revealed a firm and mobile middle left jugular-carotid lymphadenopathy measuring 4×2 cm. The initial CT scan of the nasopharynx detected a thickening of the posterolateral wall of the nasopharynx filling the Rosen Muller dimple and the Eustachian tube and infiltrating the choanae. The parapharyngeal fat, the base of the skull and the endocranium were respected. The extension check-up (chest X-ray, abdominal ultrasound and bone scan) was normal and the tumor was classified T3N1Mo (TNM 1997). The patient underwent 3 cycles of chemotherapy (CT) based on adriamycin and cisplatin with partial clinical and radiological response followed by locoregional cobalt-60 radiation at a dose of 74 Grays (Gy) in 37 fractions (2 Gy / fraction; 5 fractions / week) on the nasopharynx and cervical lymph nodes initially invaded. Prophylactic irradiation was delivered to the rest of cervical areas at a dose of 54 Gy. The treatment was completed in September 2002. The patient was regularly monitored at the consultation and the follow-up clinical examinations found radiation induced cutaneous sclerosis grade 3 (RTOG) .In September 2014, 12 years after the end of the locoregional radiation, the patient consulted again for a left latero cervical mass who had appeared and had been growing up since 3 months. The CT scan of the nasopharynx and neck showed an expansive process infiltrating the left muscular structures. This process is heterogeneous with necrotic zone non enhanced by the PDC. A biopsy of this mass was practiced and the histological examination revealed a malignant tumor proliferation made of fusiform cells corresponding to a grade II sarcoma. The radiation fields were reviewed and we concluded that the tumor occurred in the irradiated area. A new check-up was ordered and returned negative. The decision of the multidisciplinary meeting was to begin a CT before a new evaluation.

DISCUSSION

Nasopharyngeal carcinomas (NPC), are rare and sporadic in Western countries, and endemic in countries of the Mediterranean basin and North Africa and especially South-East Asia. In the intermediate frequency areas that are the Maghreb and Mediterranean countries, the incidence varies from 3 to 7/100 000 with a bimodal distribution with a first peak between 10 and 24 years and a second one at 50 years. Undifferentiated form or UCNT is most common in middle or high impact areas, representing 80 to 99% of cases.[1]

Radiotherapy is one of the major components of the treatment with curative intent of these cancers. Due to improved treatments and the subsequent increase on survival, we more often face handling late adverse effects.

Late complications are often infrequent, including cervical cutaneous sclerosis, trismus, hyposialia, hypoplasia of the mandible, and failure to thrive or amenorrhea in case of irradiation of the skull base. The most serious late complication is the occurrence of a

secondary cancer in irradiated areas. They are more frequent in younger patients and in case of chemotherapy with alkylating agent.[1]

Squamous cell cancers comprise the commonest histologic sub-type of radiation-induced malignancy occurring in the head and neck region. Radiation induced sarcoma is the second most common, accounting for approximately 12% of radiation-induced malignancies. Lifetime risk of developing secondary sarcoma is low has been estimated to be 0.03%-0.3% in patients who have been previously irradiated, higher after treatment for Hodgkin's disease than for breast cancer, cervical or head and neck tumors. The secondary sarcomas are even rarer after treatment of nasopharyngeal cancer.[2; 3; 4; 5]

In 1948, Cahan et al. proposed four diagnostic criteria for bone sarcomas in irradiated areas: medical history of radiation, a latency period of at least five years, a clearly-distinct histology from the index lesion and its location within the irradiated field.[6] Arlen et al. used the same criteria with minimal latency, three years.[7] In our case, the second cancer is a grade II sarcoma, which occur 12 years after an UCNT treated with combined radio-chemotherapy. It is located on the irradiation field border.

Several factors are incriminated in the carcinogenesis of these tumors. Indeed the risk of sarcoma in irradiated areas seems to depend on the dose. Several studies have shown the existence of a dose-response relation with significant increased risk with increasing radiation dose.[5,8,9,10] Greater risks for secondary sarcomas have been associated with younger age at initial diagnosis and combined treatment with chemotherapy. Alkylating agents and anthracyclines have been particularly implicated in this regard.[5]

The vast majority of radiation induced sarcoma are high grade and often poorly differentiated tumors and display significant degree of necrosis. In our case it is a grade II sarcoma.[11]

The diagnosis of sarcoma in irradiated tissue is difficult and often late, because of the radiation-associated tissue changes such as induration that may render them more difficult to be diagnosed, with the corollary of large tumor volume.[5] The tumor in this patient is 4 cm long axis.
Management of these patients is complex. Optimal surgical resection has a major impact on patients' survival, but the tumor location often makes this therapeutic difficult to implement because of the complex anatomy of this region even in de novo sarcomas. Besides resection of radiation induced sarcoma presents added challenges-entailing surgery in irradiated tissue.[12]

Patients rarely benefit from adjuvant radiation after tumor resection while it is a standard care for de novo soft tissue sarcomas. Its major limitation is the amount of prior radiation in the same field. Factors that need to be considered include the previously treated volume and dose fractionation schedule, critical tissues and organs at risk, and time elapsed since the first treatment course[13] Recently, thanks to advances in radiation therapy and the emergence of highly comformal technique such as IMRT, it is now possible to do it for selected patients. Therefore, the feasibility of re-irradiating this type of tumor is discussed case by case.[13, 14]

Chemotherapy may be used alone, but the response rate is low. This is probably due to patients' poor general condition, not allowing to perform optimal cures. The role of fibrosis in irradiated tissue was also incriminated. There are limited data to guide the best treatment for radiation-induced sarcoma, therefore, the standard chemotherapy options are reasonable choices. These include doxorubicin, ifosfamide, gemcitabine, docetaxel, and pazopanib. Patients with radiation-associated sarcomas may have received prior anthracyclines to treat antecedent malignancies. Thus, if additional doxorubicin cannot be used, liposomal doxorubicin is a reasonable substitute.[15] The protocols should be adapted to the patient's general condition and age, and the prescription is made after evaluation of the benefit / risk.[16]

The radiation induced sarcoma prognosis is poor, with an overall survival rate at five years of 10 to 30%. This unfavorable prognosis seems to be related to tumor grade, size at diagnosis, location and the difficulty of surgery and re-irradiation implementation making such a management challenging.[14]

CONCLUSION

Radiation induced sarcoma even rare remain a serious late toxicity of radiotherapy. Since accurate survival rates are achieved, radiation induced sarcoma are increasingly seen. Radiotherapy remains mandatory in the management of solid tumors for which the risk of developing a radiation induced sarcoma is very low with regard to the risk of recurrence without radiation. Growing awareness of this late complication, lead doctors to biopsy any suspicious mass. When a radiation induced sarcoma is diagnosed, the treatment of choice is surgical resection with clear margin where possible. Adjuvant chemotherapy and re-irradiation may have a role in carefully selected patient. Decision should be undertaken in a multidisciplinary team.

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