

RADIO-INDUCED SARCOMAS

Summary

Objectif - discuss epidemiology, histology, onset time, treatment and prognosis of these secondary tumors.

Observation - We report one case of radio induced sarcoma having appeared in radiated area, in patient treated by radiotherapy for cancer of the left orbit

Discussion- the occurrence of another local tumor after radiation therapy is a rare complication but catastrophic. Their overall incidence in patients surviving more than 5 years after radiation is low. The prognosis of radiation-induced sarcomas is disastrous. The curative treatment of this disease is based on the extended surgery.

Conclusion - Radiation can induce cancer after a latency period of several years. These second cancers are of poor prognosis. Treatment is primarily surgical

Keyword: Sarcoma, radiotherapy, orbit Cancer

1. Introduction:

Radiation therapy is loco regional treatment of tumors, especially malignant (95%) by ionizing radiation. Radiation therapy is used in half of the cancer, either alone or combined with surgical treatment or chemotherapy. Complications are sometimes observed. The most serious radiation-induced sarcoma. Radiation-induced sarcomas occur in or bordering the irradiation field, their histology is different from the initial lesion, they occur at least five years after the initial lesion, (criterion Cahan et al in 1948) [1]. These second cancers are generally of higher grade and grafted a poor prognosis [2-5]. Most published studies of radiation-induced sarcomas described tumors that occur after breast cancer treatment. The first case of parietal osteosarcoma after breast radiotherapy was described by Beck in 1922 [5]. The soft tissue sarcoma occurring after breast cancer irradiation has been described by Warren and Sommer 1936[6]. Chauveinc L et al. described cases of radiation-induced leiomyosarcoma of the thoracic region [7]. Important series were published by Robinson et al [8] and Weatherby et al [9], but the majority of cases were reported separately, often with few details; making it difficult to assess the prevalence of this tumor. From one case of radiation-induced sarcomas occurred in patient treated for cancer of left orbit at the National Institute of Oncology Rabat, Morocco in 1993 and literature review, we discuss epidemiology, histology, onset time, treatment and prognosis of these secondary tumors.

PATIENTS AND METHODS

Observation 1: Patient 64 years old, without personal or familial antecedent, consults for a nodule in the left lower eyelid in 1993. Clinical examination found a large tumor budding of the left orbit. Lesion extends into the cheek and right temple. The eyeball is completely destroyed. There was no palpable cervical lymphadenopathy. Biopsy revealed a basal cell carcinoma. The assessment of extension is normal. The patient was operated, total excision,

the histological study revealed a basal cell carcinoma. The limits of resection were healthy. The patient received external beam radiotherapy by Cobalt 1.25 MeV to the total dose of 30Gy in 10 fractions and a complement to electrons of energy 10.5 MeV to the total dose of 24Gy in 8fractions with a spreading 38jours. He remained in good locoregional control until 1995, where he presented a recurrence in left cheek and orbital. The assessment of extension is normal. The patient was operated, total excision, the histological study revealed a basal cell carcinoma. The limits of resection were healthy. Then the patient is lost sight of from 1996 to 2010, date on which he presents with swelling cheek left. A CT scan of the maxillary sinus and left nasolabial furrow was realizing (**Fig 1**). Highlighted the presence of a heterogeneous tissue tumor process encompassing the entire left maxillary sinus of 47mm x 57mm x 77mm. It is accompanied by lysis of the anterior wall of the sinus with extension to the soft parts facing; and lysis of the orbital floor with intra orbital extension. We also observe an invasion of the left nostril with blown aspect of the nasal septum, and filling the left frontal sinus. Biopsy showed a morphological appearance and immunohistochemical profile of a leimyosarcoma. Surgical treatment was not performed given the extent of lesions. He received palliative radiotherapy to the analgesic dose 8 Gy in one session, the patient died two months later.

2. Discussion

The appearance of another local tumor after irradiation is a very rare but serious complication. The overall incidence of radiation-induced sarcomas in patients who survive more than 5 years after radiation is about 0.1% [10]. In a large series, the incidence has been estimated at 0.11% after orthovoltage radiotherapy and 0.09% after the high-energy radiation [10]. Prevalence is low of the order of 0.14 to 0.20% [11, 12]. The Treaties patients have a relative risk (RR) to develop sarcoma of about 1- 5 [13, 11, 12, 14]. Phillips and Sheline [15] estimate the frequency of 0.23% sarcoma after irradiation for breast cancer. Other [16, 17] reported a lower incidence if all patients treated with radiation are taken into account. Several factors are recognized in carcinogenesis. Genetic predisposition, chemotherapy and radiotherapy.

Role of genetic predisposition

Frequency of irradiated tissue sarcomas is greater for patients with underlying génopathie, specially the bilateral retinoblastoma, Recklinghausen disease peripheral, ataxia telangiectasia and Li-Fraumeni syndrome [18]. For the patients with unilateral retinoblastoma, the risk of second cancers is not significantly increased after irradiation. On the other hand, for those with bilateral retinoblastoma, the risk of developing soft tissue sarcoma is zero without

irradiation and reached 880 after radiotherapy. Le risque de sarcome des os est 270 sans irradiation et 630 après irradiation [19].

Role chemotherapy

Valagussa et al. [20] studied the incidence of secondary cancers in a group of 845 women having had a mastectomy whose 666 had received adjuvant chemotherapy teaming up cyclophosphamide, methotrexate and 5-fluorouracil, without irradiation. In this group, 21 patients had solid tumors no sarcomatous. This confirms the role of chemotherapy in carcinogenesis.

Role of radiotherapy

The carcinogenic effects of ionizing radiation are well known, in particular the action of water radiolysis resulting in the creation of ions hydroxides causing double-strand DNA breaks The dose-response relationship was demonstrated in some tumor types and tissues [21]. Monitoring the population irradiated in nuclear explosions of Hiroshima and Nagasaki provided evidence on this subject [22, 23]. The dose provided to induce a sarcoma is 60 to 80 Gy at five fractions of 2 Gy per week [21].

histological type:

In the littérature, osteosarcoma is the most frequent, followed by fibrosarcoma and malignant fibrous histiocyoma. [24]. Hardy et al. also observed a predominance of osteosarcoma and fibrosarcoma in radiation-induced sarcomas of the wall [25]. Chauveinc L et al. described four cases of radiation-induced leiomyosarcoma of the thoracic region [7]. The leiomyosarcoma induced radio of orbit, jejunum and uterus was reported after irradiation for retinoblastoma, hodgkin's disease and uterine adenocarcinoma [26-28]. Histologically, the radiation-induced tumors do not possess specific characteristics that can distinguish spontaneous tumors [29], otherwise they have a very high grade with a sometimes very rapid development.

The latency period:

Kim et al. [30] considered that four years is the minimum period for the onset of radiation-induced sarcoma (4 to 27 years in their study on bone sarcomas). The analysis of the literature highlights development times from three months to 50 years depending on the series [31], with an average of between 10 years [39, 40] and 12 years [33]. In our study, the latency period is 17 years.

Prognosis:

The prognosis of radiation-induced sarcomas is disastrous in most series. The 5-year survival is only 10 to 30% [32-35]. In a literature review, we found a median survival reported 15

months [36], which is similar to the results presented later by Robinson et al [8], who found a median survival of 12 months with a survival rate of 22% at 2 years and 11% at 5 years. This poor prognosis was confirmed with the results of other studies [37-40]. Taghian et al. reported a median survival of 2.4 years (from four months to nine years) [41]. Many factors may help explain the poor prognosis in patients with secondary sarcoma. These tumors are generally aggressive and have a high potential for local recurrence. Sarcomas are also a high potential for metastasis [1, 42, 43].

Therapeutic strategies of radiation induced sarcomas

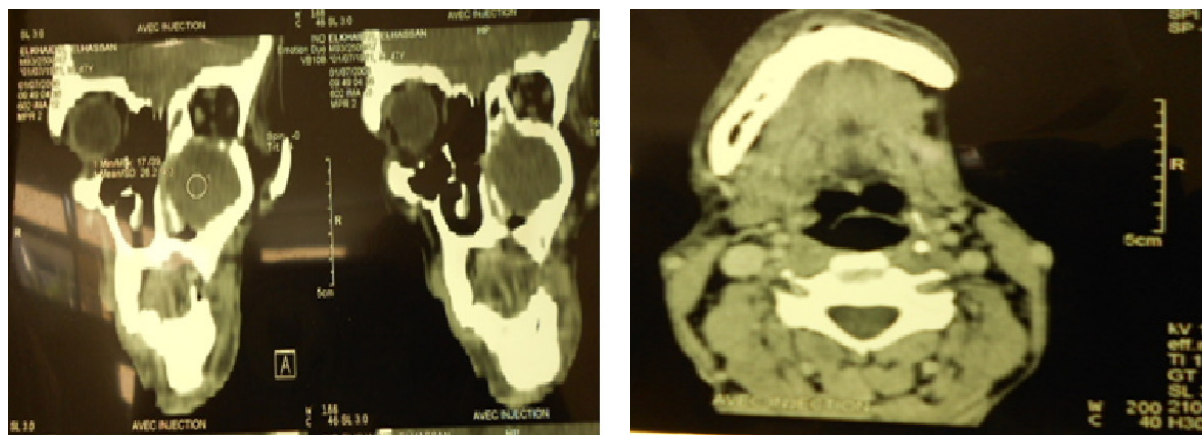
The curative treatment of this disease is based on the extended surgery, often requiring reconstruction shreds. Robinson et al. [44] have written that radical surgery is the only chance of recovery. Cha et al. [45] stressed that this surgery is difficult to perform, because on one hand, the majority of these tumors are diagnosed at a late stage and secondly, they are often located in areas where radical surgery cannot be performed. Chemotherapy is often used in the treatment of radiation-induced sarcomas but the response rate is low. [46], seven cases of sarcoma were treated with the CYVADIC protocol (cyclophosphamide, vincristine, adriamycin, dacarbazine). A partial response was obtained in only two patients respectively two and three months. In a study of osteosarcoma and soft tissue sarcoma, adding the chemotherapy to surgery does not significantly modify the survival compared to surgery alone [47].

Conclusion

Radiation can induce cancer after a latency period of several years. The leiomyosarcoma like other radiation-induced sarcomas are of poor prognosis. The diagnosis is often late and the therapeutic possibilities are then reduced. Their Treatment is primarily surgical and warrants a long-term monitoring of irradiated patients to enable early diagnosis and complete resection.

Fig1

CT scan: Highlighted the presence of a heterogeneous tissue tumor process encompassing the entire left maxillary sinus with lysis of the anterior wall of the sinus; the floor of the orbit and orbital intra extension.



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