A Case of Radiation Induced Osteosarcoma of Proximal Humerus in Undifferentiated Nasopharyngeal Carcinoma

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Abstract

Radiation-induced osteosarcomas (RIOS) after nasopharyngeal carcinomas are rare complication of radiotherapy and are associated with poor prognosis. Few cases are reported in the literature.

Case report: We report a case of radiation-induced osteosarcoma involving the proximal humerus in a patient treated with radiotherapy for nasopharyngeal carcinoma (NPC) nine years ago. Surgical treatment could not be performed, and the patient received induction chemotherapy. He died from disease spread after three cycles.

Conclusion: RIOS after treatment of NPC is very aggressive complication. Only a regular follow up of treated patient allow early detection of these tumors and best chances of survival.

Keywords: Radiation therapy; Osteosarcoma; Nasopharyngeal carcinoma; Prognosis

Background

Radiation-induced osteosarcomas (RIOS) are rare complication of radiotherapy and are associated with poor prognosis. They represent 5.5% of all osteosarcomas [1]. RIOS occur mostly after treatment of breast cancer, lymphoma, pelvic cancer, or Ewing sarcoma [2-3]. Nasopharyngeal carcinoma is the most frequent tumor of head and neck in North Africa and high doses of radiotherapy in localized stages is the mainstay of treatment. Reports of patients in who were treated for nasopharyngeal carcinoma are limited. We report here in a rare case of RIOS of proximal humerus having occurred nine years after treatment of nasopharyngeal carcinoma, and we review the existing literature data of RIOS after treatment of nasopharyngeal carcinoma [4].

Case Report

A 25 year-old man was treated in 2007 for stage III (T2bN2M0) undifferentiated nasopharyngeal carcinoma. He had received three courses of induction chemotherapy based on Bleomycin-Etoposid-Cisplatin regimen followed by radiotherapy. The radiation dose was 70 gray, in 35 fractions, five days per week, delivered using the classic 3 field’s technique (2 lateral opposed fields abutted to an anterior low-field field). He presented nine years later to emergency department for pathologic fracture of his left shoulder. Radiograph showed medullary and cortical bone destruction of proximal humerus with an underlying pathologic fracture (Figure 1). CT scan showed a locally advanced lytic neoplastic lesion of proximal humerus (Figure 2). Ct scan of chest and abdomen revealed no distant metastases. Histological examination of the bony mass showed proliferation of spindle shaped cells with atypical mitosis and associated with osteoid matrix. Immunohistochemistry showed expression of vimentin and S100 protein. These findings were consistent with osteosarcoma. As the tumor was unrespectable, neoadjuvunt chemotherapy was then started with doxorubicin 60 mg/ m² (days 1 and 15), cisplatin 100 mg/m² (day 1), and Ifosfamide 5 g/m² (days 2 and 15), with an equivalent dose of mesna and growth factor support. The tumor showed clinical and radiological progression after three cycles of chemotherapy and the patient died one month later (Figures 1 and 2).

Discussion

Radiation-induced sarcomas are rare but a well-known late complication of radiotherapy. The incidence of RIOS is rising due to increased survival as a result of improved treatments of nasopharyngeal carcinoma (NPC) [5,6]. RIOS account for 0.01–0.03% of all irradiated patients [1,7], and 0.03-0.8% of all NPC patients [5,8]. The most frequent radiation-induced tumors are fibrosarcoma and osteosarcoma. The maxilla and the mandible are the most common RIOS sites in NPC followed by nasal cavity and para-nasal sinuses [5]. To the best of our knowledge, our case is the first to describe proximal humerus as a site of RIOS in NPC. The diagnosis of RIOS is based on four criteria established by Cahan et al in 1984 that are still valid today: the origin of the neoplasm in the radiation field, the nonmalignant nature of the initial bone condition, the histological diagnosis of the primary bone lesion, and the exclusion of other malignancies [5].

Figure 1: Radiograph showing pathologic fracture of proximal humerus.

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neoplasm, and a relatively long latency period [9]. Our patient fulfilled all these criteria. The latent period following radiation therapy for nasopharyngeal carcinoma and the development of secondary tumors is 5-30 years with a mean of 12.9 years [5,10]. Some researchers have suggested that the minimum radiation dose needed for development of radiation-induced sarcoma is 30 Gy [11,12]. The radiation doses in reported cases varied from 25 to 110 Gy, with a median dose of 45 Gy [13]. Our patient received 70 Gy which is much higher than the median dose previously mentioned. The pathogenesis of RIOS is unknown. It is suggested that the patients who have genetic predisposition like Li-Fraumeni syndrome, von Recklinghausen’s disease, mutations in tumor suppressor genes including p53 and RB1, are more prone to develop RIOS [14,15]. The patient age at radiation exposure and association of chemotherapy have also been identified as risk factors for RIOS [16]. The CT scan shows bone destruction, soft tissue mass and osteoneogenesis while the MRI is good in defining the extension into the adjacent soft tissues in osteosarcomas. In our case, the MRI was not performed before treatment because of financial considerations, but it was programmed after the first three cycles to evaluate respectability.

The treatment of high grade osteosarcomas, irrespective of etiology includes radical surgery with perioperative chemotherapy. Although formal proof that giving chemotherapy preoperatively improves the outcome per se is lacking, disease free survival probabilities increases with multimodal treatment from 10-20% to up to 60% compared with surgery alone [17]. The goal of surgery is to remove the tumor with adequate surgical margins and yet preserve as much function as possible. Obtaining negative margins is crucial to local control as well as recurrence-free survival [18].

The prognosis of radiation-induced sarcoma is generally thought to be worse than primary sarcomas, regardless of site. The cumulative disease-free survival at 5 years for patients with a RIOS was 17%, with a median survival estimate of 1 year [14]. In order to prevent radiation-induced tumors, it is important to be meticulous in radiation doses in planned fields. In our case, the preferred radiation dose is lower now than in the past for the treatment of nasopharyngeal carcinoma. Moreover, the exposure of normal tissue to radiation is decreased by intensity modulation radiotherapy and the addition of chemotherapy [13].

Conclusion

Radiation-induced osteosarcoma of proximal humerus after treatment of nasopharyngeal carcinoma is exceptional but very aggressive complication with poor prognosis as highlighted in this case. Regular follow up of treated patients should be considered.

Conflicts of Interest

All the authors declare no conflict of interest.

References