Maxillary Osteosarcomas after Irradiation for Nasopharyngeal Carcinoma: A Case Report and Review of the Literature

Author(s): Dr. Sarah Naciri, Dr. Houda Mouzount, Dr. Samia Arifi, Prof. Tayeb Kebdani, Prof. Noureddine Benjaafar, Prof. Hassan Errihani

Corresponding Author:
Dr. Houda Mouzount,
Medical Oncology, National Institute of Oncology, 10000 - Morocco

Submitting Author:
Dr. Sarah Naciri,
Medical Oncology, National Institute of Oncology, 10000 - Morocco

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Abstract

Radiation induced sarcomas (RIO) are rare tumors that develop after a latent period after radiation, within the field of radiation. A 22-year-old woman with a history of nasopharyngeal carcinoma, treated with standard neo-adjuvant chemotherapy followed by irradiation. 4 years after, computed tomography showed an extensive loco regional lesion of the left maxilla. Biopsy revealed high-grade osteosarcomas. The patient was treated by chemotherapy. There was no response and the tumor remained unresectable. RIO is particular form of osteosarcomas; diagnosis and treatment are still a dilemma.

Introduction

Radiotherapy is the standard treatment for nasopharyngeal carcinoma (1). Unfortunately, it can produce undesirable complications after treatment. When radiotherapy is used with curative intent, the possibility of late complications in the irradiated tissues must be considered. Radiation induced sarcomas are defined as tumors that develop after a latent period after radiation, within the field of radiation, and have histological confirmation of a sarcoma. Radio induced osteosarcomas (RIO) are rare, accounting for 3.1–5.5% of all osteosarcomas. However, it is the most common second malignant neoplasm (2). RIO can arise from all sites of radiation including skull base, maxilla, mandible, pterygoid bones, skin, and thyroid. The rarity of RIO has made studies difficult for this particular form of osteosarcomas. As a consequence, very few articles report outcome after modern treatment of RIO. The low incidence rate of radio induced osteosarcomas after nasopharyngeal carcinoma management does not rule out the use of radiotherapy because of its efficacy in this neoplasm. Early detection of radiation-induced tumors is important; it is difficult since changes seen after radiotherapy have often been attributed to other causes such as osteonecrosis.

Case report

22-year-old woman presented with epistaxis and a mandibular mass. History revealed a nasopharyngeal carcinoma in 1999, treated with neo-adjuvant chemotherapy (3 cycles of adriamycin 50mg/m2 and cisplatin 100mg/m2) followed by external beam irradiation (70 Grays). Computed tomography showed an extensive locoregional lesion of the left maxilla (fig1 A). Biopsy revealed a high-grade osteosarcoma containing a mixture of fibroblastic and osteoblastic elements.

The patient received chemotherapy: adriamycin 50 mg/m2 and Cisplatin 100 mg/m2. The patient was progressive after four cycles of chemotherapy (fig 1B, 2), and the tumor remained unresectable. Patient received a second line chemotherapy; cyclophosphamide 100 mg X 2/day and prednisolone 40 mg/day for 7 days/14 days. Patient developed severe flare-up of hepatitis B following chemotherapy. Prior to chemotherapy, the patient had normal liver function test, chemotherapy was interrupted.

Discussion

Osteosarcomas after radiation characteristically occur at the edge of the radiation field, because the administered radiation is unable to cause cell death but is sufficient to induce malignant transformation. In general, a radiation dose of at least 30 Grays is required for the development of radiation-induced osteosarcomas (3).

The observation we report here reveals a severe and aggressive case as the patient developed an RIO only 4 years after radiation, which is a low latency period compared to previous reports. In fact, studies stated that the latency period between radiotherapy for nasopharyngeal carcinoma and the presentation of temporal bone tumors ranged from 5 to 30 years with a mean of 12.9 years (4,5).

Cahan et al. described 11 cases of sarcomas arising from irradiated bones (3). They established four
criteria for the diagnosis of RIO that are still valid to date: (a) the origin of the neoplasm in the radiation field, (b) the nonmalignant nature of the initial bone condition (this criteria was modified by Arlen et al. to “the tumors developed in bone not known to have a primary malignant osteoblastic lesion when the radiotherapy was given” (4, 6)), (c) the histological diagnosis of the neoplasm, and (d) a relatively long latency period. Our patient fulfilled the above-mentioned criteria.

The pathogenesis is unknown; various predisposing factors have been suggested (7). Gaetano et al. reported a higher rate of females in RIO. However it’s interesting to note that the female gender proved to be an independent risk factor for the development of second tumors unrelated to radiotherapy (8).

RIO may occur after megavoltage or orthovoltage radiation. In addition to radiation dose, development of RIO is probably influenced by other factors: age of the patient at radiation exposure, association of chemotherapy, and genetic predisposition (such mutations in tumor suppressor genes like p53 and RB1) (9). The Li-Fraumeni syndrome, von Recklinghausen's disease, and other hereditary syndromes are also risk factors for RIO (10). In fact, some studies have proved that RIO risk may be increased after treatment of Hodgkin's lymphoma with radiotherapy. In addition, radiation therapy given during childhood can also increase the relative risk of RIO to 30 (9). Leclercq et al. suggested that addition of alkylant-based chemotherapy to radiotherapy will increase the risk of developing RIO (9).

Metastases, especially to the lungs, are common in osteosarcomas. In contrast, radiation-induced osteosarcomas do not exhibit this tendency. These tumors, however, often carry a poor prognosis because of rapid local growth regardless of site (11). The cumulative disease-free survival at 5 years for patients with a postirradiation osteosarcoma was 17%, with a median survival estimate of 1 year (10).

Often, there is a delay in diagnosis until an advanced stage of disease because of the difficult distinction between neoplastic and radiation changes. In addition, RIO occurs often in anatomic sites (head and neck, pelvic, thorax) where complete surgical resection is difficult (11). The mainstay of treatment is surgical resection with negative margins. The role of neo-adjuvant chemotherapy is not well established. Small series evaluate neoadjuvant chemotherapy combined with surgery in RIO (1, 2). For example Gaetano et al showed that RIO treated with neoadjuvant chemotherapy, seem to have an outcome that is not significantly different from that of patients with conventional primary high grade osteosarcoma:

5-year event-free survival: 40% vs. 60%; 5-year overall survival 40% vs. 67%, with p < 0.01. In this study a reduced rate of good histological response to preoperative treatment in comparison to conventional osteosarcoma was noted (44% vs. 63%) (2).

To prevent radiation-induced sarcoma, it is important to use radiation dosimetry in carefully planned fields. Also, intensity modulation radiotherapy (IMRT) will reduce the exposure of normal tissues to radiation (11). Because of the aggressive nature of RIO, careful long-term follow-up of irradiated patients is preferable (12).

Conclusion

The rarity of RIO has made studies difficult for this particular form of osteosarcomas. As a consequence, very few articles report outcome after modern treatment of RIO. The low incidence rate of radio induced osteosarcomas after nasopharyngeal carcinoma management does not rule out the use of radiotherapy because of its efficacy in this neoplasm. Early detection of radiation-induced tumors is important; it is difficult since changes seen after radiotherapy have often been attributed to other causes such as osteonecrosis.

References

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Illustrations

Illustration 1

Computed tomography: (A) Before chemotherapy; (B) After four cycles of chemotherapy

Illustration 2

Patient after 4 cycles of chemotherapy
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