Mastoid Osteosarcoma Post Radiation Exposure

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Introduction

Many of the malignancies afflicting the head and neck region are confined within intricate anatomic locations to make wide resection a challenging task. This has established the role of radiation therapy both as a primary as well as adjuvant modality for head and neck cancer management. However, as with all management modalities, there are potential short- and long-term complications. Frieben reported the first cases of radiation-induced skin cancers at the turn of the twentieth century[1], shortly after Roentgen first discovered x-rays. Since then, cases have emerged in the world literature documenting radiation-induced malignancies in various body sites. It remains a rare entity, however, with an estimated incidence of 0.4% to 1.0%.

This paper adds to the English literature a case of radiation induced sarcoma of the temporal bone that arose within a relatively short latency period of 4 years, with a current review of the English literature on management of this challenging disease.

Case Presentation

A 55-year-old woman initially presented with a 2.5 cm lesion within the right parotid gland. She underwent right parotidectomy and neck dissection in April 2015. Her surgical pathology was in keeping with low grade mucoepidermoid carcinoma of the right parotid gland, with focal positive margins, focal perineural invasion, and microscopic extra-parotid extension that involved the surrounding skeletal muscle. She received adjuvant radiotherapy with 6600 centiGray over 33 fractions delivered between July and September 2014. In April 2019, she presented with progressive hearing loss in the right ear. She was referred to the otology clinic and on examination she was found to have a red hue in the middle ear.

A subsequent computed tomography (CT) scan revealed an aggressive and destructive soft tissue density centered on the right mastoid air cells. The differential diagnosis included osteosarcoma, chondrosarcoma, osteochondroma, giant osteoma, organizing scalp hematoma, and parosteal osteogenic sarcoma.

Right mastoidectomy and biopsy was done in July 2019, and the pathology demonstrated multiple fragments of a high-grade spindle cell and epithelioid malignancy, throughout which were irregular seams of osteoid and mature bone, as well as tumor giant cells and osteoclast-like giant cells. Immunohistochemistry results showed diffuse strong positivity for vimentin, partial moderate positivity for AE1/AE3 and CK8/18 (similar expression), and focal weak membranous positivity for CD10. Leukocyte common antigen, p40, CK5/6, CD3, CD20, S100 and HMB-45 were negative. Those findings were in keeping with a high-grade osteosarcoma. In October 2019, the patient underwent surgery in the form of a subtotal temporal bone resection, revision parotidectomy, and ipsilateral neck dissection with resection of the upper sternocleidomastoid. Reconstruction was undertaken using a regional submental island flap reconstruction. The final pathology confirmed the lesion as osteosarcoma, with one positive lymph node, and a mitotic range 44 per 10 high powered field.



Figure 1. CT scan of the temporal bones with contrast, bone window and axial view, showing an aggressive right mastoid mass with bony destruction.

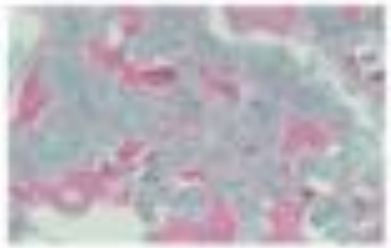


Figure 2. osteosarcoma infiltrating bone. The tumor has a cellular component with abundant strands of pale pink stroma, which is osteoid, characteristic of an osteosarcoma (H&E, 40x).

Postoperatively, the patient was deemed not a candidate for any further radiotherapy. Instead, she received a first cycle of chemotherapy (Doxorubicin and Cisplatin) in December 2019 before undergoing restaging CT head, chest, abdomen and pelvis in January 2020. The scan showed redemonstration of the lesion centered within the right mastoid with extension into the intracranial cavity. This was in keeping with rapid regrowth of the tumor during the interval three months since her surgery. There was no evidence of metastatic disease. She completed 3 cycles of chemotherapy, and this was complicated by an episode of severe neutropenia requiring admission for observation and blood transfusion. Follow up imaging showed stable findings, with no progression but also no regression of the tumor. The case was reviewed again in multidisciplinary rounds, and it was felt that no further surgical options were plausible for repeat resection. Palliative care was involved, and the patient succumbed to her disease in August 2020.

Discussion

Sarcomas comprise a heterogeneous group of mesenchymal neoplasms. They can be grouped into 2 general types: soft tissue, and primary bone sarcomas. It is estimated that approximately 7800 new sarcoma cases in adults are diagnosed annually in the United States[3].

Occurrence in the head and neck is rare, accounting for less than 1% of all malignant tumors in this region. Conversely, approximately 4% of all soft tissue sarcomas arise in the head and neck[4, 5]. Radiation induced head and neck sarcomas arise in previously radiated fields with no site predilection[7], and early on may share clinical features with more common radiotherapy complications including radionecrosis.

Radiation therapy has been commonly utilized in the management of head and neck malignancies, and it has long been recognized that there exists a risk of long term malignant sarcomatous transformation. There are some challenges in the study of head and neck radiation-induced malignancy. Certain primary tumor histologies predispose to an increased risk of sarcoma development, irrespective of the treatment utilized in their management[6, 7]. Examples include retinoblastomas and rhabdomyosarcoma. It is suggested that an underlying genetic abnormality may play a prominent role in the carcinogenesis mechanisms of these tumors. Furthermore, there is an inherent risk of second primaries in patients with head and neck oncologic disease. This has been explained using a carcinogenesis model in which, in light of common risk factors including tobacco and alcohol consumption, there develops a field with genetically altered cells that plays a central role in the development of a second malignancy. This "field cancerization" concept was introduced by Slaughter et al. in 1953[10], and was initially described in patients with oral squamous cell carcinoma (SCC).

SCC remains the most common histologic subtype of head and neck cancer and the one to which most field cancerization studies have been applied. However, recent studies have explored the potential role of carcinogenic endothelial cells themeselves in the development of secondary malignancies via chemokines secreted by these endothelial tumor cells[11]. These studies may alter our understanding of the interplay of the various risk factors, including that of radiation therapy, in the development of secondary malignancies. While there are no definitive diagnostic criteria for the diagnosis of radiation induced malignancy of the head and neck, Cahan and others[11, 12] have defined criteria for the diagnosis of radiation-induced tumors, most commonly sarcomas:

Conclusion

Radiation-induced sarcomas of the head and neck are rare clinical entities, but their true incidence is difficult to establish in light of non-uniform diagnostic criteria, and often confounding risk factors for head and neck carcinoma. They may present after a variable latency period following radiation therapy and can be challenging to diagnose on clinical and radiographic assessment secondary to fibrosis and often altered post-operative surgical anatomy. Early diagnosis is important, but these tumors are often only amendable to subtotal surgical resection and are associated with an overall poor prognosis. With radiation therapy becoming more commonly used in the management of a myriad of head and neck pathologies, it is paramount for contemporary otolaryngologists to be aware of radiation-induced malignancies, their diagnostic approach, and management strategies.