The Role of Radiation in Carcinoma Ex Pleomorphic Adenoma

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Background

Carcinoma ex pleomorphic adenoma (CXPA) is a rare and aggressive tumor that accounts for ~11% of salivary gland malignancies. Tumors most commonly occur in the parotid gland but can also occur in submandibular glands, minor salivary glands, lacrimal gland and breast tissue. The tumor is comprised of a mixed histology of malignant tissue in the presence of benign pleomorphic adenoma which makes pathological diagnosis challenging. Prognosis is extremely variable and multifactorial, which explains the wide range of reported 5-year survival, 25-75%.

CXPA is a heterogeneous class of tumors and treatment varies accordingly. Clinical management typically involves surgical resection with or without post-operative radiotherapy; however, the role and efficacy of radiotherapy is not well defined. Given the rarity of the diagnosis, little data are available to guide therapeutic management and there are no randomized data on this entity. Single institution retrospective reviews have suggested that post-operative radiation can significantly improve local control rates.

Overall Survival (OS) was improved with radiation only in those patients with negative LNs. The overall trend was for shorter OS in those who received adjuvant radiation.

Here we investigate the patient and tumor characteristics as well as treatment modality in the outcome of patients with CXPA using the National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) database.

Methods

The present study is a retrospective review of patients with CXPA extracted from the National Cancer Institute’s SEER database. Patients from 1986-2008 provided by 17 registries were identified using the November 2010 submission. Cases of CXPA were identified using the International Classification for Childhood Cancer site recode extended ICD-0-3 histology code 8941/3.

Patient and Disease Characteristics

A total of 246 patients were identified who were diagnosed with CXPA which originated in the parotid or submandibular glands and who had surgical resection with or without adjuvant radiation. Patients whose stage was unknown, whose disease originated in other sites, or who had distant disease were excluded.

Prognostic Factors

On multivariate analysis, regional LN involvement, male gender, and older age were negative prognostic factors. For node negative patients, median survival was 60 months as compared to 28 months for node positive patients (p<0.01).

CXPA location, use of adjuvant radiation, and tumor extension through capsule were not significant prognostic factors.

OS for high grade tumors was significantly less than low or unknown grade tumors (p=.001).

Benefits of Radiation

Median overall survival of patients who received post-operative radiation was 46 months as opposed to 53 months for those who had surgery only (non-significant, p=0.2). This trend is likely due to the increased use of post-operative radiation for high risk patients (e.g. high grade, regional LN spread, ECE).

Adjuvant radiation was shown to provide significant OS benefit for patients with high grade tumors. This was not seen for low grade or tumors of unknown grade.

Discussion

This review of the SEER database provides prognostic information for patients diagnosed with non-metastatic CXPA of the parotid or submandibular glands who are able to have surgical resection +/- adjuvant radiation.

--Older age, male gender, and regional LN involvement were all significant independent poor prognostic factors. Age may be a surrogate for KPS in this patient population.

--Regionally involved LN demonstrated the largest Hazard Ratio (3.41, 2.11-5.51)

--CXPA arising from the submandibular gland had a shorter median OS as compared to those of parotid origin, though this did not hold through multivariate analysis. Submandibular CXPA on average tended to be of higher grade and more likely to have capsular penetration as compared to parotid CXPA.

--Radiation was utilized more frequently in high risk patients and which may explain the trend toward shorter median OS.

--Adjuvant radiation did not provide any OS benefit for patients with involved regional LNs or with uninvolved regional LNs.

--Adjuvant radiation was shown to provide significant OS benefit for patients with high grade tumors. This was not seen for low grade or tumors of unknown grade.

--Thus this study helps to further provide clinical evidence for when to recommend adjuvant radiation in this relatively rare and heterogeneous tumor.

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References