Carcinoma Ex Pleomorphic Adenoma: Is It a High-Grade Malignancy?

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Purpose: The objective of this study was to investigate the clinicopathologic features of carcinoma ex pleomorphic adenoma (CXPA) and comprehensively improve an understanding of this disease.

Materials and Methods: This retrospective study investigated 151 cases of histologically confirmed CXPA. Disease-specific survival, local recurrence, and regional and distant metastases were analyzed.

Results: Most cases were classed as frankly invasive CXPA (135 of 151). More than half these cases (73 of 135; 54.1%) developed local recurrence; 25 (18.5%) developed cervical metastasis; 21 (15.6%) developed distant metastasis; and 60 patients (55.6%) died during follow-up. In contrast, only 1 patient in the noninvasive CXPA group (n = 10) died after treatment for lung metastasis and 1 patient developed cervical metastasis. Similarly, only 1 patient in the minimally invasive CXPA group (n = 6) died of lung metastasis and the remaining 5 patients had an uneventful recovery after treatment.

Conclusions: Frankly invasive CXPA was a high-grade malignancy with an unfavorable prognosis. Elective neck dissection should be performed in cases of frankly invasive CXPA that originate in the submandibular gland. Patients with minimally invasive and noninvasive CXPA should be followed closely after primary treatment because regional or distant metastasis can occur.

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Benign pleomorphic adenoma is the most common form of salivary neoplasm, accounting for almost 80% of all salivary tumors. Malignant degeneration arising from pleomorphic adenoma often occurs in patients with a prolonged history of untreated or recurrent benign pleomorphic adenoma. A report has suggested that the median onset of pleomorphic adenoma is 10 years of age.[1] According to the World Health Organization (WHO) classification system,[2] there are 3 main categories of malignant pleomorphic adenoma: carcinoma ex pleomorphic adenoma (CXPA), carcinosarcoma, and metastatic benign pleomorphic adenoma. Although cases of CXPA greatly outnumber those for the other 2 subtypes, it is a relatively rare carcinoma. Estimates suggest it accounts for 5 to 15% of salivary malignancies and 3.6% of all salivary tumors.[3-6] These proportions could increase as knowledge of this disease increases. CXPA generally has been recognized as a high-grade carcinoma owing to its potential for regional and distant metastases, resulting in a high rate of mortality.[7,8] However, this categorization might not be conclusive.

CXPA presents with epithelial malignancy mixed with benign pleomorphic adenoma in variable proportions.[9] CXPA can be divided into 3 subtypes based on the extent of the malignancy[2]: noninvasive CXPA if the malignancy is confined by the tumor capsule; minimally invasive CXPA if invasion extends no farther than 1.5 mm beyond the capsule; and frankly invasive CXPA if invasion extends farther than 1.5 mm beyond the capsule.[2] Not all these subtypes are aggressive; minimally invasive and noninvasive forms of CXPA generally behave in a benign manner, with a prolonged and uneventful clinical

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course, especially after standard treatment,[10] whereas frankly invasive CPXA frequently results in disease-related death. Therefore, not all cases of CXPA can be conclusively categorized as a high-grade malignancy.

Despite considerable research into CXPA and data on prognostic factors, including tumor size, grade, proportion of carcinoma, extent of invasion extent, proliferation index, and clinical outcome,[4,5,11] CXPA remains a poorly understood neoplasm. Therefore, the aim of the present study was to analyze retrospectively the clinical and pathologic features and survival outcome of 151 cases of CXPA to improve an understanding of this disease.

Materials and Methods

PATIENT SELECTION AND CHARACTERISTICS

This study was approved by the institutional review board of the Peking University School of Stomatology (Beijing, China). The medical records of all patients treated for malignant pleomorphic adenoma of the salivary gland at the Department of Oral and Maxillofacial Surgery at the Peking University School and Hospital of Stomatology from 1960 through 2015 were retrospectively reviewed, as were available pathologic specimens. Diagnosis was histologically confirmed by an experienced pathologist (Y.G.) and 151 cases of CXPA were selected for this study. Excluded were 10 cases that were previously misdiagnosed (4 were definitively identified as myoepithelial carcinoma, 4 as mucoepidermoid carcinoma, 1 as salivary duct carcinoma, and 1 as carcinosarcoma). Tumor size, TNM staging, type of carcinomatous element, and extent of invasion were recorded. The cases were subclassified as noninvasive (intracapsular), minimally invasive, and frankly invasive CXPA, in accordance with the WHO classification system.[2] Demographic data, treatment, and clinical and prognostic information were obtained from the patients' medical records and follow-up telephone calls. The mean follow-up time was 61 months (range, 6 to 228 months).

STATISTICAL ANALYSIS

Statistical analysis was carried out using SPSS 20.0 (SPSS, Inc, Chicago, IL). Survival data were compared by the Kaplan-Meier method. Univariate analysis with log-rank test was applied to identify potential prognostic factors. A P value less than .05 was considered statistically significant.

Results

PATIENTS' CLINICOPATHOLOGIC CHARACTERISTICS AND TREATMENT

The 151 patients with CXPA included 80 men (53.0%) and 71 women (47.0%) with a mean age of

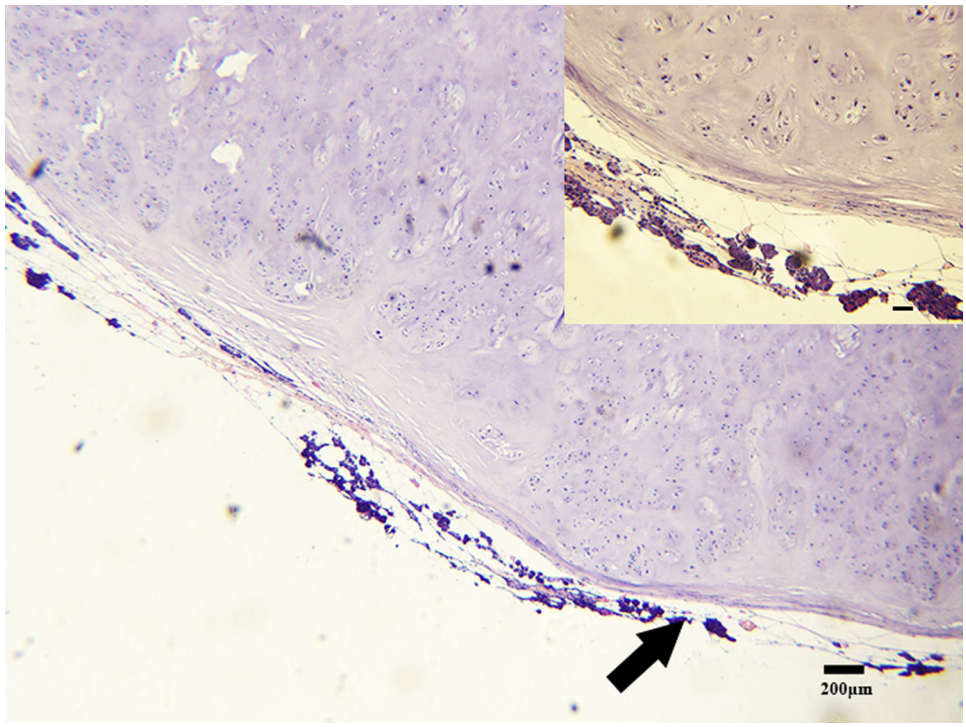

FIGURE 1. Photomicrograph (magnification, ×4) of noninvasive carcinoma ex pleomorphic adenoma with well-circumscribed malignancy (*arrow*). *Inset*, Photomicrograph at higher magnification (×20) showing the well-defined capsule (bar = 50 μm).

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