



From Indolent to Invasive: High-Grade Salivary Duct Carcinoma ex Pleomorphic Adenoma in a Long-Standing Parotid Lesion

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ABSTRACT

Pleomorphic adenomas are the most common salivary gland neoplasms and are typically benign; however, the risk of malignant transformation increases with prolonged lesion duration.¹ Carcinoma ex pleomorphic adenoma is a rare malignant salivary gland tumor that originates from a preexisting lesion with a 61.9% 5-year median survival rate.² In this case study, a 68-year-old woman presented with pain associated with a 20-year-old parotid lesion following a COVID-19 infection. Computed tomography (CT) demonstrated a large mass involving the majority of the parotid gland with extension into the sternocleidomastoid muscle. Ultrasound-guided fine needle aspiration (FNA) revealed malignant cells consistent with carcinoma, prompting surgical intervention. The patient underwent a total right parotidectomy with facial nerve dissection and a right modified radical neck dissection (levels I-III). Gross examination revealed a large, firm, tan-white lesion abutting the deep margin with focal extension into skeletal muscle. Histologic evaluation provided the diagnosis of invasive high-grade salivary duct carcinoma ex pleomorphic adenoma with focal mucoepidermoid differentiation. Postoperatively, the patient underwent adjuvant radiation therapy; however, follow-up FNA revealed persistent malignant cells consistent with the primary tumor. The findings in this case emphasize the important role of the pathologists' assistant in careful gross examination and representative tissue sampling for the identification of malignant transformation in long-standing lesions.

BACKGROUND

Introduction

Salivary neoplasms most commonly arise in the parotid gland, with pleomorphic adenoma representing the most frequent benign subtype. Although typically benign, the risk of malignant transformation increases with tumor duration, rising from 2% in lesions present for less than 5 years to 10% in those present for more than 15 years.¹ Malignant transformation to carcinoma ex pleomorphic adenoma is a rare but serious complication. Clinical findings such as rapid growth, new-onset pain, and facial nerve deficits may suggest malignant change.³ Because benign and malignant components can coexist, diagnosis may be challenging, making thorough gross examination and representative tissue sampling essential for appropriate patient care.⁴

Case Presentation

A 68-year-old female with stage 2 hypertension presented with a 20-year history of a right parotid mass. Surgical excision of the **slow-growing** mass had been recommended 14 years earlier, but the patient declined treatment, as the lesion was **small and painless**. Following a COVID-19 infection, the mass became painful, prompting surgical evaluation. Examination revealed left-sided facial weakness attributed to remote Bell's palsy and unrelated to the right parotid lesion. Normal motility was noted on her right side. CT imaging demonstrated a 6.6 cm right parotid mass with mixed cystic and solid components. Fine needle aspiration identified malignant cells consistent with carcinoma. Given the lesion's size and malignant findings, surgical resection was performed.

RESULTS



Figure 2. Photomicrographs of the right parotid gland. **A.** Smooth surface of the parotid gland. **B.** The deep roughened surface with a circular defect. **C.** The cut surface displaying the tan-white firm mass to nearest margins.

Gross Description: Received in formalin is a 119 g, 10.2 x 7.5 x 5.5 cm unoriented portion of tan-brown soft tissue with one aspect being smooth and the opposite being lobulated with a 1.6 x 0.9 cm circular defect on the deep margin. The superficial smooth surface is inked green, the roughened deep margin is inked black, and the defect is inked blue. Sectioning reveals 7.5 x 4.8 x 4.2 cm **tan-white firm mass** that **abuts the deep margin**. The mass at one aspect has a 4.0 x 3.3 x 2 cm cystic component that is congruent with the defect. The cystic aspect is adjacent to a white firm lobulated portion of the mass that is 4.0 x 3.5 x 3 cm with a central hemorrhagic cavity that is 1.6 x 1.5 cm. The uninvolved parenchyma is tan yellow lobulated. Lymph nodes are identified.

- A1:** Mass to superficial margin, perpendicular
- A2:** White firm nodule of mass
- A3-4:** Full-face mass, cystic to solid aspect, to deep margin
- A5-7:** Mass to superficial margin
- A8:** Cystic aspect of mass to defect area
- A9:** Mass to uninvolved parotid gland
- A10:** Cystic aspect within white firm area of mass
- A11:** Lymph node candidates, whole

Key Findings:

- Macroscopic tumor **invasion into extraglandular soft tissue** and focally into **skeletal muscle**
- Negative margins; 0.1 cm to closest deep margin
- All 34 regional lymph nodes assessed (including neck dissection) were negative

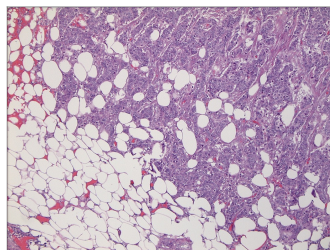


Figure 2: High-Grade carcinoma invading into surrounding adipose by H&E

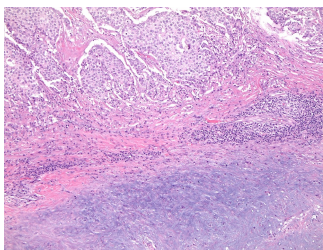


Figure 3: Invasive high-grade carcinoma extending beyond PA by H&E.

DISCUSSION

Microscopic examination demonstrated features characteristic of pleomorphic adenoma, including a heterogeneous admixture of epithelial and myoepithelial elements arranged in ducts, tubules, strands, and sheets within a myxoid and collagenous stroma. Foci of chondromyxoid differentiation were also identified.¹ These findings are consistent with the classic morphological presentation of pleomorphic adenoma and establish the benign precursor component required for the diagnosis of carcinoma ex pleomorphic adenoma. In addition to these benign elements, areas of high-grade salivary duct carcinoma were present, characterized by infiltrative malignant epithelial proliferation with marked cytologic atypia, supporting malignant transformation within a pre-existing pleomorphic adenoma.⁵

The pathogenesis of pleomorphic adenoma remains incompletely understood. Many tumors harbor chromosomal rearrangements resulting in overexpression of *PLAG1*, a transcription factor that promotes cellular proliferation through growth factor signaling pathways. Other tumors demonstrate alteration involving *HMG2*, a DNA-binding protein involved in growth regulation.¹ While these molecular abnormalities are implicated in pleomorphic adenoma development, the mechanism driving malignant transformation to carcinoma ex pleomorphic adenoma remains poorly defined. The strongest established risk factor is prolonged tumor duration, with the risk of malignant transformation increasing in long-standing lesions.³

Pathologic staging was assigned according to the American Joint Committee on Cancer (AJCC) 8th Edition staging system for major salivary gland carcinomas. Primary tumor (T) classification is based on tumor size and extension, with **pT3** defined as **tumors greater than 4 cm and/or demonstrating extraparenchymal extension**.⁶ In this case, the tumor measured 7.5 cm and showed extraglandular extension, meeting criteria for pT3 staging. Regional lymph nodes were negative for metastasis (pN0), and no distant metastasis was identified (M0). Collectively, the Tumor was staged as PT3N0M0, corresponding to AJCC Stage III disease, indicating a locally advanced malignancy.

Given that the vast majority of salivary gland resections are initially evaluated by Pathologists' Assistants (PAs), their expertise is a critical step in the diagnostic workflow. In this specific case of invasive salivary duct carcinoma arising from a pleomorphic adenoma, the PA played a pivotal role. As malignant transformation in these heterogeneous tumors can be focal and easily missed, the PA's careful gross examination and strategic sampling were essential. The PA meticulously selected sections from variable parenchymal regions, accurately measured tumor dimensions, and targeted the deepest areas of tumor invasion. This precise dissection translated complex gross findings into actionable diagnostic material, directly enabling reliable classification and staging.

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