

# Carcinoma ex Pleomorphic Adenoma: Salivary Duct Carcinoma with Squamous Differentiation: A Case Report and Review of the Literature

James Hamilton<sup>1</sup>, MD, Phoebe Holmes<sup>2</sup>, MD, Katherine McKee-Cole<sup>1</sup>, MD, Madalina Tuluc<sup>2</sup> MD, Joseph Curry<sup>1</sup>, MD

<sup>1</sup>Dept. of Otorhinolaryngology, Thomas Jefferson University Hospital, Phila., PA; <sup>2</sup>Dept. of Pathology, Thomas Jefferson University Hospital, Phila., PA

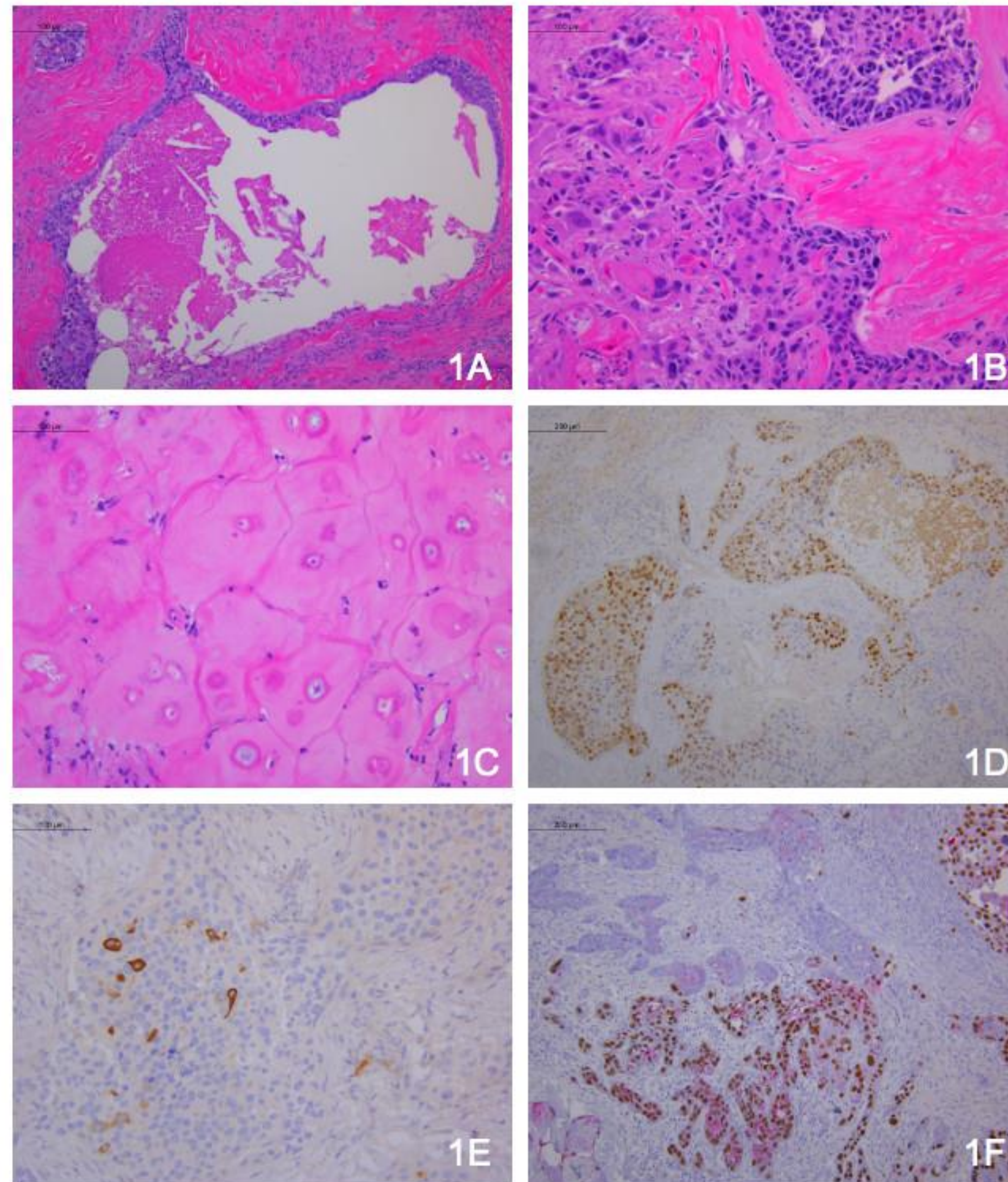
## Introduction

Carcinoma ex pleomorphic adenoma (CXPA), a rare malignancy of the salivary glands.<sup>1</sup> It is defined as a malignant epithelial tumor arising from a pleomorphic adenoma (PA),<sup>2</sup> most often arising in the parotid gland.<sup>3</sup> Any form of carcinoma can be found in the malignant component but it most commonly takes the form of poorly differentiated adenocarcinoma not otherwise specified (NOS) or salivary duct carcinoma (SDC). Its wide range of histologic presentations presents diagnostic difficulties<sup>4</sup> which may be compounded by the rare presence of a mixture of carcinoma subtypes. Classic history is a longstanding mass that suddenly undergoes rapid growth.<sup>3</sup> We report an extremely rare case of CXPA comprised of high-grade carcinoma with features of SDC with squamous differentiation, which has thus far been reported twice in the literature with only one case occurring in the parotid gland.

## Case Presentation

A 64-year-old female presented with a 15 year history of a right-sided parotid mass that had recently increased in size. Physical exam revealed a firm 3.5 cm mass involving the posterior inferior right parotid with no palpable adenopathy, normal overlying skin, and intact facial nerve function. FNA was positive for keratinizing squamous cell carcinoma with no detectable microscopic features of PA. CT scan described a 3 cm exophytic mixed solid and cystic mass with peripheral enhancement. PET scan demonstrated increased metabolic activity in the solid components (SUV 10.25) but no evidence of hypermetabolic adenopathy. The patient underwent right near-total parotidectomy and right neck dissection

Gross examination showed a firm, infiltrative 4.5 x 3.5 cm mass with cystic degeneration. Microscopic examination revealed high-grade malignant neoplasm with two distinctive components. One exhibited the characteristics of high-grade SDC, with round solid and cystic tumor nodules resembling intraductal carcinoma of the breast. The cystic tumor nodules exhibited comedo necrosis. Nuclear pleomorphism, increased mitotic activity, numerous apoptotic bodies were also present (FIG. 1A).



The second was represented by SCC, NOS, characterized by pleomorphic squamous cells with intercellular bridges and squamous whorls. In areas there was a subtle transition from the SDC component to the squamous component and the patterns appeared to merge (Fig. 1B). Perineural and lymphovascular invasion and gross extraglandular extension were identified. It arose in a background of hyalinized and hypocellular PA, represented by chondroid stroma (Fig. 1C). On IHC, areas of tumor that were morphologically consistent with SDC were positive for androgen receptor (AR) (Fig. 1D) and focally for GCDFFP-15/mammaglobin (Fig. 1E), while areas with squamous differentiation were negative (Fig. 1D). The squamous marker p40/CK5/6 was positive in the squamous areas and negative in the SDC component (Fig. 1F). ER/PR staining was universally negative.

## Discussion

Carcinoma may develop in up to 25% of untreated PAs.<sup>1</sup> CXPA is typically high-grade, leading to metastasis and disease-related death.<sup>1</sup> SDC accounts for 10-34% of carcinoma subtypes. Immunohistochemically, SDC is characterized by AR and GCDFFP-15 positivity but ER/PR negativity.<sup>4</sup> Histologically, it is similar to ductal carcinoma of the breast and overexpression of the HER-2/*neu* protein is associated with poorer prognosis.<sup>4</sup>

Malignant squamous component is rare, especially when mixed with other malignant subtypes. In the two largest series of CXPA, no malignant components were classified as SCC.<sup>1,5</sup> Case reports include a malignant component of SCC in a CXPA of the upper lip<sup>2</sup>, submandibular gland,<sup>6</sup> and palate.<sup>7</sup> There are two reports of CXPA consisting of a malignant squamous component mixed with SDC. Nakamori described a non-invasive CXPA of the buccal mucosa with histological characteristics consistent with SCC and SDC<sup>8</sup> and Magaki reported a CXPA consisting of keratinizing SCC and high-grade SDC in the parotid gland.<sup>4</sup>

This case is extremely rare and only the second report of SCC and SDC found together in a CXPA of the parotid gland. It is important to maintain awareness of these rare tumors as the combination of multiple malignant subtypes may lead to diagnostic difficulty. A slow growing parotid mass exhibiting a growth spurt should raise concern for CXPA. At one year following treatment our patient remains well with no clinical or radiographic evidence of recurrence. Given the aggressive behavior of these rare lesions, a high index of suspicion should be maintained, and careful follow-up.

## References

- Olsen KD, Lewis JE. Carcinoma ex pleomorphic adenoma: A clinicopathologic review. *Head Neck*. 2001;23(9):705-712. doi:10.1002/hed.1100.
- Mitate E, Kawano S, Kiyoshima T, et al. Carcinoma ex pleomorphic adenoma of the upper lip: a case of an unusual malignant component of squamous cell carcinoma. *World J Surg Oncol*. 2013;11(1):234. doi:10.1186/1477-7819-11-234.
- Magaki SD, Bhuta S, Abemayor E, Nabili V, Sepahdari AR, Lai CK. Carcinoma ex-pleomorphic adenoma of the parotid gland consisting of high-grade salivary duct carcinoma and keratinizing squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;120(3):e169-e173. doi:10.1016/j.oooo.2015.01.014.
- Kim KM, Lee A, Yoon SH, Kang JH, Shim SI. Carcinoma ex pleomorphic adenoma of the palate--a case report. *J Korean Med Sci*. 1997;12(1):63-66. doi:10.3346/jkms.1997.12.1.63.
- Nakamori K, Ohuchi T, Hasegawa T, Hiratsuka H. Carcinoma ex pleomorphic adenoma of the buccal region is composed of salivary duct carcinoma and squamous cell carcinoma components. *Int J Oral Maxillofac Surg*. 2009;38(10):1116-1118. doi:10.1016/j.ijom.2009.04.016.
- Antony J, Gopalan V, Smith RA, Lam AKY. Carcinoma ex Pleomorphic Adenoma: A Comprehensive Review of Clinical, Pathological and Molecular Data. *Head Neck Pathol*. 2012;6(1):1-9. doi:10.1007/s12105-011-0281-z.