

Title: Salivary Gland Carcinoma Ex-Pleomorphic Adenoma: The role of long-term surveillance for early detection of malignant transformation

INTRODUCTION: Pleomorphic adenomas (PA) of the salivary glands, also known as benign mixed tumors (BMTs), are the most common salivary gland tumors and account for 70-80% of benign salivary tumors. They are usually found in the larger parotid and submandibular glands (SMG). The vast majority of these have a benign natural history. Approximately 25% of these tumors have the potential to undergo the adenoma-carcinoma sequence, whereby they lose important tumor suppressor oncogenes such as APC, KRAS, TP53 and Cyclin D1 and degenerate into invasive neoplasms.

CASE DESCRIPTION: An 84-year-old man presented to our clinic with a past medical history of smoking, right tempo-mandibular joint pain, and enlargement of right SMG with recurrent episodes of sialadenitis. He had previously been diagnosed with an incidental right SMG PA four years ago, for which he was being observed by serial imaging. He now developed a secondary painful mobile nodule adjacent to the right SMG. Contrast enhanced Head CT scan revealed the new mass was homogenous, non-enhancing, and partially-calcified and encapsulated within an enlarged right SMG. Ultrasound (U/S) showed a partially calcified solid mass and associated cervical adenopathy, and U/S-guided FNA biopsy was performed and demonstrated histologic features consistent with pleomorphic adenoma. However, given the high clinical index of suspicion as well the rapid increase in the size of the right SMG, the patient underwent uneventful excisional biopsy of this mass. The final pathology report revealed a focus of carcinoma ex pleomorphic adenoma (CEPA) with flow cytology showing no evidence of monoclonality.

DISCUSSION: The largest retrospective analysis of 41 cases of Metastasizing PA from 1953 to 2005 concluded that an average of 16 years elapsed following the initial surgical resection of a benign PA. The primary tumor arose most commonly from the parotid gland. Incomplete tumor clearance has been strongly linked with local recurrence. Malignant changes in pleomorphic adenoma have been associated with a long duration, tumor recurrence, radiation therapy, advanced age, and initial tumor size.

CEPA is a rare, usually high-grade malignancy whose hallmark feature is frequent local recurrences and distant metastases underscoring the importance of meticulous and thorough initial resection. Diligence is required in follow-up with serial imaging and a high index of suspicion is required when monitoring these patients over time. In our case, MRI had been done 2 years prior and CT head and neck was done a year ago, and U/S had been done six months prior to presentation.

CONCLUSION: Malignant tumors can coexist in or arise from a PA. This is most commonly manifested by sudden growth of a previously stable mass. Fine Needle aspiration has limited sensitivity and accuracy. The early identification and timely appropriate treatment of presumed benign lesions that may undergo malignant transformation into CEPA over time is paramount.

This case report emphasizes the importance of long-term follow-up with close monitoring, regular clinical examinations and role of serial multiple imaging modalities.

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