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CASE REPORT

# Carcinoma Ex Pleomorphic Adenoma of Upper Lip: An Unusual Presentation

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**ABSTRACT**

Carcinoma ex-pleomorphic adenoma is a rare salivary gland malignancy, usually derived from a long-standing or recurrent benign tumor, the pleomorphic adenoma.[1] This rare tumor comprises less than 4% of salivary gland neoplasms and 11.6% of salivary gland carcinomas. They mostly involve the "major" salivary glands[1] and their occurrence in the minor salivary gland is considered rare, especially in the upper lip. So far there is only one report of CXPA occurring in the upper lip in the literature.[13] Hereby, we present a case of carcinoma ex-pleomorphic adenoma in a 52-year-old woman who reported to our department with a painful swelling on the upper lip which was diagnosed and treated successfully.

**Keywords:** Carcinoma, Carcinoma ex Pleomorphic adenoma, Carcinoma of upper lip.

## INTRODUCTION

Carcinoma ex-pleomorphic adenoma (CXPA) is a malignant neoplasm that arises in association with a primary or recurrent benign pleomorphic adenoma (PA). This rare tumor comprises less than 4% of salivary gland neoplasms and 11.6% of salivary gland carcinomas. The patients are 60 to 70 years old, approximately a decade older than patients with PA.[1] These tumors are typically high grade and have similar histology to their *do novo* counterparts. CXPAs are subclassified into intracapsular (IC) or noninvasive, minimally invasive (MI), and widely invasive (WI) based on the degree of tumor invasion through the fibrous capsule of the PA into the surrounding tissues.[2] It is a rare entity and when it does occur, the palate is the most common site. So far there is only one report of CXPA occurring in the upper lip in the literature.[3] Hereby, we present a case of carcinoma ex-pleomorphic adenoma in a 52 year-old-woman who reported to our department with a painful swelling on the upper lip.

## CASE REPORT

A 52-year-old female patient came to our department with the complain of swelling in the upper lip since 3 months. It was initially the size of a small nodule and gradually progressed to present dimension. It was associated with pain, which was insidious in onset, localized, intermittent, nonprogressive, mild in intensity and aggravated on touching. She had a habit of chewing betel quid thrice daily since 20 years.

Right and left solitary submandibular lymph nodes were palpable and enlarged, measured about 1 × 1.5 cm in size, oval in shape, soft in consistency, mobile and tender. Extraoral examination revealed a solitary diffused swelling (Fig. 1) involving philtrum and vermilion border of upper lip on left side, measuring 2 × 1.5 cm, oval in shape extending from midline to left ala of the nose and inferiorly from vermilion border of upper lip to nasolabial fold and inferior aspect of nostrils. On palpation, the swelling was firm in consistency with well-defined borders and mildly tender.

Intraoral examination revealed a solitary diffuse swelling on the left upper labial mucosa (Fig. 2), measuring 1.5 × 1 cm, oval in shape extending from vermilion border of lip to depth of labial vestibule and medially from 1 cm right of the labial frenum to 2 cm lateral to it. Mucosa over swelling appeared mildly purplish but blanches and became yellowish on stretching. No visible pulsations or sinus were evident and margins were ill-defined. On palpation, the swelling was firm in consistency, mildly tender and blanched on palpation. Hard tissue examination revealed clinically missing 32, 42 and anterior traumatic bite. No pathology was noted in relation to the maxillary anterior teeth.

A provisional diagnosis of a benign tumor of mesenchymal origin on upper lip was made.

The differential diagnosis considered was lipid proteinosis and minor salivary gland tumors, which included pleomorphic and canalicular adenoma. Other considerations were tumors of

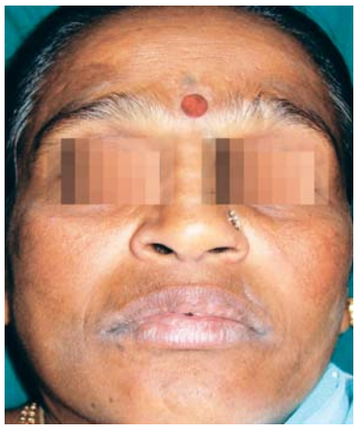

**Fig. 1:** Extraoral photograph showing diffuse swelling on upper lip and philtrum

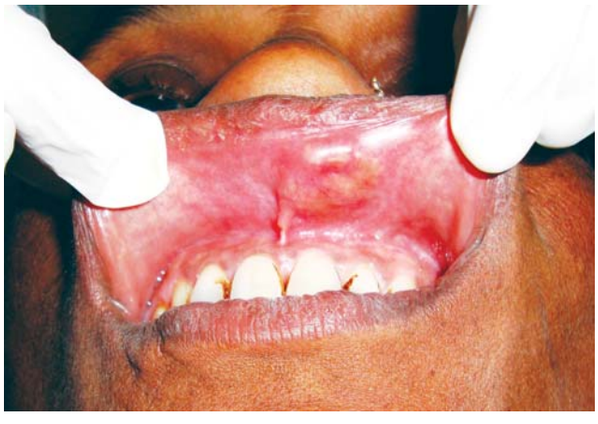

**Fig. 2:** Intraoral photograph showing diffuse swelling on the left upper labial mucosa

neural origin namely palisaded encapsulated neurofibroma and schwannoma.

Lipid protienosis is an autosomal recessive trait characterized by deposition of waxy amorphous lipids in the dermis. In the oral mucosa, it presents commonly in the second decade of life as a nodular thickened enlargement with waxy, yellow-white plaques or nodules, frequently in the tongue and upper labial mucosa. The clinical appearance as well as the site of occurrence led us to consider this entity as one of the differential diagnoses.

Palisaded encapsulated neurofibroma is a benign neural tumor that shows predilection for the nose and cheek occurring commonly between fifth and seventh decade of life. It presents as a smooth surfaced painless dome shaped papule or nodule usually less than 1 cm in diameter.

The neurilemmoma (Schwannoma) is a slow growing encapsulated tumor of Schwann cell origin, which presents as a painless swelling though the occurrence is rare, more so in the upper lip.

Pleomorphic adenoma (PA) is the most common neoplasm in both the major and minor salivary glands. Though the palate is the most common site for occurrence of the entity, considering the high incidence of occurrence, asymptomatic nature of the swelling and the presentation as a nodular growth, it was considered a probable diagnosis.

The canalicular adenoma is an uncommon tumor that occurs almost exclusively in the minor salivary gland. The lesion has a striking predilection for the upper lip with nearly 75% occurring in this location. The age of incidence (50-70 yrs), site as well as the asymptomatic nature of the swelling led us to consider the entity as a differential diagnosis.

Excisional biopsy of the lesion was carried out (Fig. 3) and the specimen was sent for histopathologic examination (Fig. 4). It demonstrated malignant glandular epithelial cells arranged as nests separated by connective tissue septa and neoplastic epithelium arranged as sheets in other areas (Fig. 5). Chondroid metaplasia and adjacent normal salivary gland tissue spindle shaped cells, stellate cells and plasmacytoid cells were seen. Hyaline like material was visualized in profusion (Fig. 6). Special staining with Mucicarmine and Periodic Acid Schiff were carried out to rule out mucin secreting tumors, which turned out to be negative.

Based on the histopathological reports, a final diagnosis of Carcinoma ex-pleomorphic adenoma (invasive) of minor salivary gland involving upper lip was made.

Excision in toto with safe margins was deemed adequate for the management of the lesion as it did not show any invasive features and was well circumscribed. The literature mentions that malignant areas, extending beyond tumor capsule, carry a poor prognosis, the 5-year survival ranging from 25 to 65%, regional lymph nodes metastases occurring in 25% of the cases.[4] In our case, regional lymphadenopathy could not be correlated to the lesion and no signs of distance metastasis were noted. The patient is currently under follow-up and has been recalled after 3 months.

## DISCUSSION

Pleomorphic adenoma is the most frequent neoplasm in both the ''major'' and ''minor'' salivary glands, and rarely undergoes malignant transformation. Invasiveness features and histological differentiation define three distinct categories: carcinoma ex pleomorphic adenoma, carcinosarcoma or true malignant mixed tumor, and metastasising pleomorphic adenoma.[5] Subtyping carcinoma expleomorphic adenoma, into noninvasive and invasive categories, correlates with prognosis.[5]

Carcinoma ex pleomorphic adenoma is a rare salivary gland malignancy usually derived from a long-standing or recurrent benign tumor, the pleomorphic adenoma.[1] So far there is only one report of CXPA occurring in the upper lip in literature.[3]

They account for 11.6% of all malignant neoplasms of the salivary gland and mainly affect patients in their sixth to eighth decades of life. They mostly involve the major salivary glands.[1] A slight female predominance (63%) has been noted.[6]

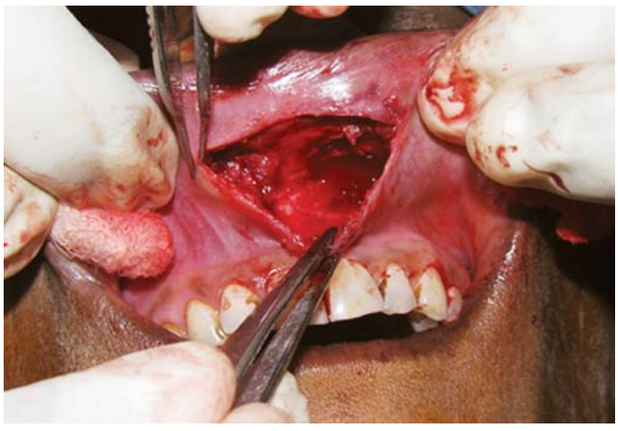

**Fig. 3:** Intraoperative photograph

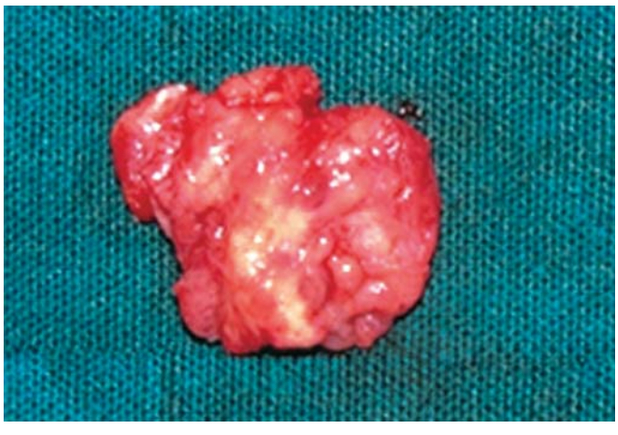

**Fig. 4:** Gross specimen

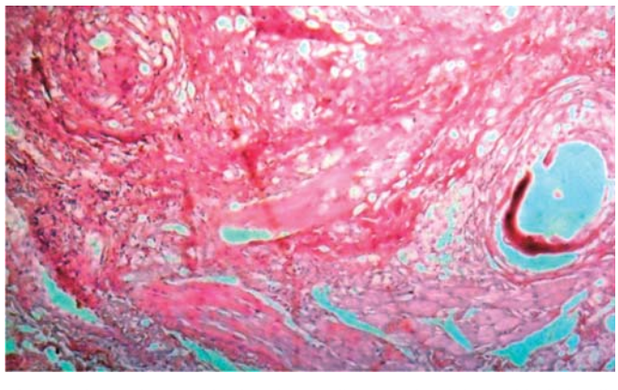

**Fig. 5:** Photomicrograph showing malignant glandular epithelial cells arranged as nests separated by connective tissue septa and neoplastic epithelium arranged as sheets in other areas (H and E 10x)

A relatively high rate of mutations (loss of heterozygosity (LOH) and microsatellite alterations) at the *p53* gene was detected in CXPAs (58%), and at somewhat lower frequencies at the *retinoblastoma* gene (33%) and chromosomal location 5q (17%).[7]

Most of the patients present with a painless mass that slowly increases in size. Other symptoms include a painful mass (9.3%), facial nerve palsy (5%), facial tingling (2%), and trismus (2%).[6]

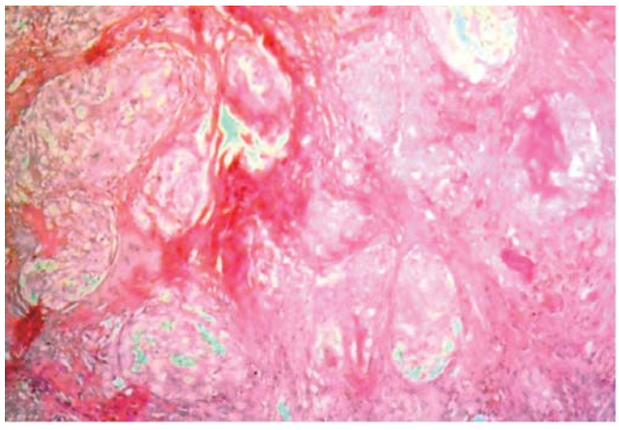

**Fig. 6:** Photomicrograph showing adjacent normal salivary gland tissue spindle shaped cells, stellate cells and plasmacytoid cells

Loss of myoepithelial differentiation is important in the evolution of Ca ex-PA, and corroborate the hypothesis that p63 antigen may be a useful marker of myoepithelial cells in salivary glands neoplasms.[8] Studies have demonstrated that the expression of α-smooth muscle actin, calponin, cytokeratin 14, P63, CD10, D2-40, laminin and maspin were stronger in benign myoepithelial cells surrounding the malignant epithelial cells than in benign myoepithelial cells of duct like structures of PA.[3,9]

The single most reliable prognostic marker is the extent of tumor infiltration beyond the capsule.[4,12,13] Tumor necrosis, a high mitotic rate and atypical mitoses have been shown to be important prognostic factors in other types of malignant salivary glands tumors.[10,11] Although proliferative rate and tumor necrosis were able to predict the clinical outcome, nuclear pleomorphism correlated weakly with prognosis.[2]

A wide surgical excision with adequate margins is the treatment of choice. Postoperative radiotherapy should be reserved for patients with highgrade tumor histology, large primary lesions, perineural invasion, bone invasion, cervical lymph node metastasis, and positive margins, although clear-cut survival advantage has not been proven.[14]

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