Research Article

# Carcinoma Ex Pleomorphic Adenoma in Lacrimal Gland: A Rare Malignant Neoplasm

**Renuka Verma[1], Nidhi Kaushik[1*], Monika Dhankher[1], Niharika Taunk[1], Sonia Chhabra[1], Rajeev Sen[1]**

[1]Department of Pathology, PGIMS, Rohtak, Haryana

**Corresponding author: Nidhi Kaushik, Department of Pathology, PGIMS, Rohtak, Haryana, Tel: 8295154196; E-mail: yudisharma2985@gmail.com**

## Abstract

Carcinoma ex pleomorphic adenoma (CXPA) is a rare malignancy which arises from a previously benign pleomorphic adenoma (PA). It has high aggressive behavior and poor prognosis. It is often difficult to diagnose because of similar clinical presentation to benign tumors and various other histological variants. Histological diagnosis is the gold standard for making the diagnosis. This tumor is rare in salivary gland and even rarer in lacrimal gland with only 0.3% of all orbital tumorous lesions. Patients with PA of the lacrimal gland clinically present as insidiously enlarging painless swelling of the orbit and if transformed to CXPA bulbar enlargement, displacement, and proptosis are the chief presentation. Here, we report a case in 68 year old female who was previously operated for Pleomorphic Adenoma. Now, she underwent an en bloc resection of the mass with orbital exoneration. Histopathology together with IHC demonstrated a carcinoma arising from a PA which led to the diagnosis of CXPA. This case highlights the challenges in clinical and pathologic diagnoses and the need for more literature to guide appropriate treatment.

**Keywords**: Salivary gland; Pleomorphic adenoma; Carcinoma ex pleomorphic adenoma

## Introduction

The lacrimal gland is an almond-shaped, bilobed, eccrine gland present in the super lateral aspect of the orbital wall and is composed of small lobules separated by connective tissue.

Incidence of Lacrimal gland tumors is 1 in 1,000,000 individuals per year and accounts for 5%-25% of all orbital malignancies. Epithelial lesions comprise around 50%-60% of all benign and 40%-50% of all malignant lesions. [1,2]

Pleomorphic adenoma (PA) is the most common benign neoplasm of the lacrimal gland. It is a biphasic tumor with a characteristic fibromyxoid and cartilaginous stroma with populations of epithelial and myoepithelial cells and has excellent prognosis after surgical excision like its salivary counterpart.

It represents around 20% of all lacrimal gland tumors. Carcinoma ex pleomorphic adenoma (CXPA) is a rare transformation of a benign primary PA to a malignant neoplasm. These are rare tumors and show many morphologic variations. CXPA can be noninvasive, minimally invasive or widely invasive. The first two types are treated with surgical resection, radiation and carry a fair prognosis. Data regarding diagnosis and management is very less and the available literature consists mostly of case reports and limited phase. [3,4]

## Case report

A 68-year-old female reported to Ophthalmology OPD in our institute with chief complaint of a recurrent swelling in the right temple area. She was first operated for a swelling over inner eye and diagnosed as pleomorphic adenoma. After 1 year she developed a similar swelling, for which she underwent another surgery. The pathological diagnosis was found to be same as previous i.e. PA. These both surgeries were performed before she came here. Now the swelling was tender in nature and increasing in size leading to proptosis. Other symptoms were tearing, discharge from the right eye with redness over the left temple and orbit.

CT scan showed recurrent neoplastic lesion abutting the optic nerve. Right orbidectomy was done under general anesthesia and resected specimen was sent to Pathology department. We received the biopsy in multiple soft tissue pieces along with eyeball specimen. On gross examination, eyeball was atrophic and tumor tissue was in small tissue bits, measuring



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approximately 5X4X3 cm. Microscopic examination demonstrated tumor with circumscribed margins having variable sized lobules, nests and trabecular of epithelial cells and myoepithelial cells distributed in background of mucomyxoid or chondromyxoid stroma. These nests comprising of atypical epithelial cells show moderate pleomorphic, abnormal chromatin clumping, [6,7] mitosis per 10 high power field. Lymph vascular embolilsation was seen by both epithelial and myoepithelial component. On IHC these tumor cells were positive for Pan CK, 34βE12, NSE, S-100, Vimentin and Ki 67<20%. Micro sections examined from eyeball specimen show atrophic changes with thromboembolic tumor deposits in per orbital soft tissue. Based on these findings, diagnosis of carcinoma ex-pleomorphic adenoma was made.

## Discussion

According to WHO classification published in 2005, malignant changes in the PA include three different types: CXPA, carcinosarcoma, and metastasizing PA. Among these, CXPA is the most common type. [5]

The pathological classification of epithelial tumors of both lacrimal and salivary glands is identical, as the lacrimal gland histologically resembles minor salivary glands. Therefore, lacrimal CXPA may well be clinically/pathologically analogous to salivary gland CXPA. CXPA arises from old case of PA or from recurrent PA after previous excision. [6] It is an uncommon and aggressive tumor which arises from a preexisting PA and carries a poor prognosis. Risk of transformation into CXPA increases with time. PA and CXPA of salivary and lacrimal gland have shown similar clinical and genomic profiles. Patients with PA experience an insidiously enlarging painless swelling of the orbits over the year while transformation to CXPA experience a rapid onset of bulbar enlargement and displacement.1 Therefore, proptosis is a common finding in such cases and present in our patient. It ranges in size from less than 1 cm in greatest dimension to large tumors greater than 20 cm. [8]

Common gross findings include necrosis and hemorrhage. PA often possesses bizarre cells and dense sheets of oval to spindle cells, but the malignant transformed component is usually distinct. Malignant component is characterized by profound pleomorphic, high nuclear to cytoplasmic ratios, necrosis, hemorrhage, frequent mitotic figures including atypical forms, perineural and perivascular invasion. [4] There are many histologic variants of carcinoma ex pleomorphic adenoma including adenocarcinomas, myoepithelial carcinoma, adenoid cystic carcinoma, epithelial-myoepithelial carcinoma, squamous cell carcinoma, clear cell carcinoma, adenosquamous carcinoma, mucoepidermoid carcinoma, and acinic cell carcinoma. [3] Adenocarcinoma is the most common type of CX PA in salivary glands but there is insufficient information to comment on lacrimal CXPA. [4]

CXPA can be noninvasive, minimally invasive, or invasive depending on its extension into the adjacent tissue. Noninvasive CXPA remains within the fibrous capsule of the original PA. A minimally invasive tumor invades less than 1.5 mm in the extra capsular structures whereas an invasive CXPA is characterized by greater than 1.5 mm invasion of the malignant component into the surrounding tissues. [2] In our case, comment on margins was not possible due to fragmented small pieces of biopsies received.

Extensive hyalinization was the factor that was most significantly associated with malignant transformation in few studies. [7] The stromal hyalinization seen in our case was in accordance with this report.

Immunohistochemical stains can be invaluable in defining CXPA, especially given the numerous variants and potential for mixed variants. Ki-67 is a marker of DNA proliferation, PA show a low expression while CXPA is known to have a higher expression. GCDFP-15 has been shown to be a biomarker for adenocarcinoma of the lacrimal gland, but its role in management is uncertain. P63 is a marker of myoepithelial elements and is positive in PA, whereas CXPA is generally characterized by loss of P63 expression. [4]

Possible treatments of CXPA include four different modalities; surgical therapy, **radiotherapy**, chemotherapy and combined therapy. Suggested that surgery followed by postoperative radiation should be considered as the standard of care for patients with CXPA. [7] Suggested that the histological evidence of invasive growth pattern, neural or vascular invasion, necrosis and focal calcification carries a poor prognosis. [8] There is currently no standard protocol for chemotherapy or targeted therapy even for the more common salivary gland subtype. Reported a case of salivary HER2 positive CXPA that was successfully treated with trastuzumab and capecitabine. [9] Similarly, in the salivary subtype, showed a good response to a combination of cyclophosphamide, doxorubicin, and cisplatin. [10] There is insufficient evidence of the successful treatment with chemotherapy or targeted therapies in lacrimal gland CXPA in literature. [4] As seen with past experiences and in our patient, this rare tumor is aggressive and carries a very poor prognosis with a high predilection for recurrence and metastasis.

There are no guidelines to aid in management of this rare tumor. More case reports or meta-analysis are needed to improve outcomes of this uncommon morbid malignancy. [7]

## Conclusion

CXPA is a rare fascinating tumor that requires a multidisciplinary approach for better patient outcome. This case illustrates the classic presentation of CXPA with regards to clinical, pathological, and radiographic diagnosis. TNM stage, lymph node involvement, histological grade, perineural invasion and extent of invasion are important prognostic factors of CXPA. Treatment is largely dependent on pathological and radiographic findings. Surgery is the primary treatment modality for CXPA and postoperative radiation therapy may be used for more aggressive tumors. Finally, more research is needed in regards to tumor markers,

prognostic factors and adjuvant therapy in the more aggressive cancer types.

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