

Research Article**A Study of Primary Malignant Epithelial Tumors of the Lacrimal Gland**Kavitha Toopalli^{1*}, Sailaja Vallury², Mohammed Ather³, Modini Pandharpurkar⁴¹Assistant Professor of Pathology, Sarojini Devi Eye Hospital, Hyderabad Telangana State, India²Associate Professor of Pathology, MNR Medical College, Sanga Reddy, Telangana State, India³Professor of Ophthalmology, Gandhi Medical College, Telangana State, India⁴Associate Professor of Ophthalmology, Government Medical College, Nizamabad, Telangana State, India***Corresponding author**

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Abstract: Primary malignant epithelial tumors of the lacrimal gland are rare. Forty cases of lacrimal gland tumors were diagnosed at the Department of Pathology, Sarojini Devi Eye Hospital, Hyderabad over a period of seven years from 2008 to 2014. The age range was from the second to eighth decades. Females were more commonly affected. Histologically, malignant epithelial tumors occurred less frequently than the benign. There were nine cases of primary malignant epithelial tumors constituting 22.5% of the total epithelial tumors. Adenoid cystic carcinoma (ACC) was the commonest malignancy. The dominant histologic pattern determines the prognosis of adenoid cystic carcinoma. A rare case each of carcinoma-ex-pleomorphic adenoma (CEPA) and squamous cell carcinoma were reported. Early diagnosis and treatment can significantly alter the prognosis of some of the tumors. Long term follow up is advocated in the management of these tumors.

Keywords: Lacrimal gland tumors, Epithelial, Primary, Malignant, Rare.

INTRODUCTION

Lacrimal gland is a bilobed eccrine secretory gland located in the supero temporal orbit [1]. The two lobes are the larger orbital lobe and the much smaller palpebral lobe. The lacrimal gland is a non-encapsulated structure composed histologically of ducts and acini [2]. It is composed exclusively of serous cells entirely lacking mucinous cells [3]. Lacrimal gland tumors comprise about 5 to 25% of all orbital tumors [4]. Lacrimal gland may be considered as a minor salivary gland and the tumors of the lacrimal gland are classified like salivary gland tumors [5, 6]. Primary malignant neoplasms of the lacrimal gland have a high morbidity and mortality [7]. Adenoid cystic carcinoma of the lacrimal gland is one of the most malignant neoplasm [8]. Some of the primary malignant epithelial tumors may arise from a pre-existing benign tumor through a malignant transformation, but most arise de novo [9]. Recurrence after complete resection of some malignant tumors such as pleomorphic adenoma ex carcinoma and adenoid cystic carcinoma can occur making long term follow up imperative for these tumors [10]. Primary Squamous cell carcinoma of the lacrimal gland is a very rare epithelial neoplasm [11].

MATERIALS AND METHODS

Forty specimens of suspected lacrimal gland tumors, including incisional biopsies, excisional biopsies and subtotal exenteration specimens were

received in the Department of Pathology, Sarojini Devi Eye Hospital, Hyderabad, over a period of seven years from 2008 to 2014. The study group consisted of nine cases of histologically proven malignant epithelial tumors of the lacrimal gland. The clinical and radiological data were obtained by reviewing the case sheets. The histopathology slides of all the cases were reviewed. The collected data was analyzed to know the prevalence of different types of malignant epithelial lacrimal gland tumors. The correlation of histopathology to clinical data was highlighted, comparing with other studies in literature.

RESULTS

Nine cases of primary malignant tumors of the lacrimal gland were diagnosed over a period of seven years from 2008 to 2014. The age range of the patients in our study was between the third and eighth decades. The tumor involved the left lacrimal gland in six cases and the right in three cases. The age of the youngest patient was 23 years and the oldest patient was 75 years. There were five female patients and four male patients (Table 1)

Table 1: Showing the sex distribution of malignant epithelial tumors of lacrimal gland

Malignant Tumors (N=9)	Sex Distribution
Females	05
Males	04

Adenoid cystic carcinoma was observed in a relatively younger age group, most of the cases occurring between 23 to 50 years. Rare malignancies like squamous cell carcinoma and carcinoma-ex-pleomorphic adenoma were noted in the later decades. CT scan of all the malignant tumors showed irregular margins of the lesion. Bone erosion was noted in two cases. Incisional biopsy was done in two cases and excisional biopsy was done in two cases. In five cases, subtotal exenteration was done. Grossly, incisional biopsies ranged in size from 1 to 1.5cm and excisional biopsies on an average measured 2.5 x 2.5 x 2 cm. In subtotal exenteration specimens, the tumor size measured on an average 4 x 3 x 2.5 cm. Histologically, adenoid cystic carcinoma was the commonest epithelial malignancy accounting for seven out of nine cases. There was a single case each of malignant mixed tumor (CEPA) and squamous cell carcinoma (Table 2).

Table 2: Showing the histological types of malignant epithelial tumors of lacrimal gland

Histologic grade (N=9)	(No., %)
Adenoid cystic Carcinoma	07(77.7%)
Carcinoma-ex-pleomorphic adenoma (CEPA)	01 (11.1%)
Squamous cell carcinoma	01 (11.1%)

Microscopic examination in most of the cases of adenoid cystic carcinoma revealed cribriform pattern in most cases (Fig.1). Tubular pattern was seen along with the cribriform pattern in few cases. One case of adenoid cystic carcinoma showed solid (basaloid) pattern in addition to the cribriform pattern (Fig. 2, 3). Higher mitotic activity was observed in the basaloid areas. There was perineural invasion in one case. Vascular and lymphatic invasion was not observed in any of the cases. Muscle invasion was noted in two of the cases studied. One case of adenoid cystic carcinoma recurred ten years after initial resection and radiation therapy. In the single case of carcinoma ex pleomorphic adenoma, multiple sections were taken to search for residual benign component. The malignant component was a poorly differentiated carcinoma. There was a single case of squamous cell carcinoma in a 75 year old female patient. Histology revealed a moderately differentiated squamous cell carcinoma (Fig. 4). Immuno histochemistry with keratin and p63 were positive in this case.

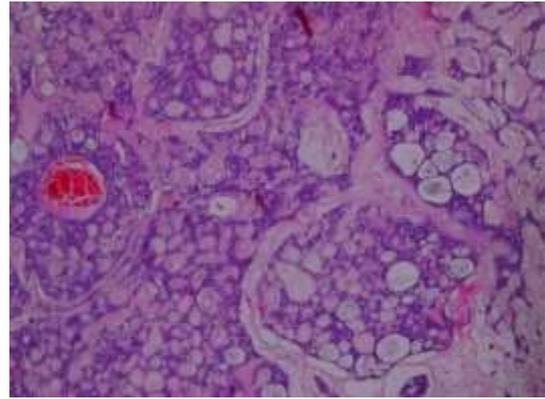


Fig. 1: Microphotograph of adenoid cystic carcinoma showing the cribriform pattern

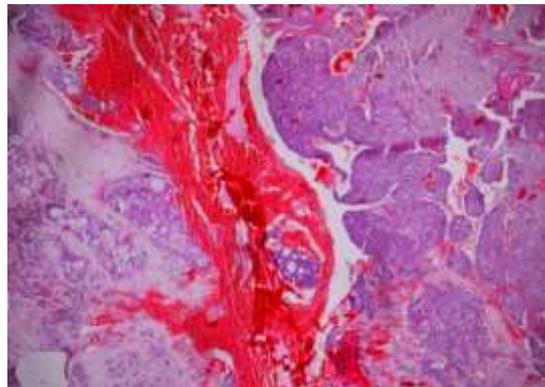


Fig. 2: Microphotograph showing basaloid and cribriform patterns

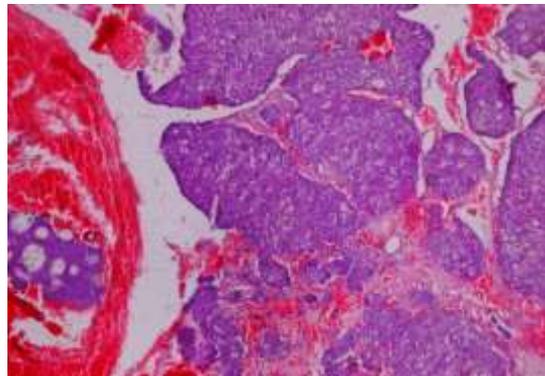


Fig. 3: Basaloid area in adenoid cystic carcinoma

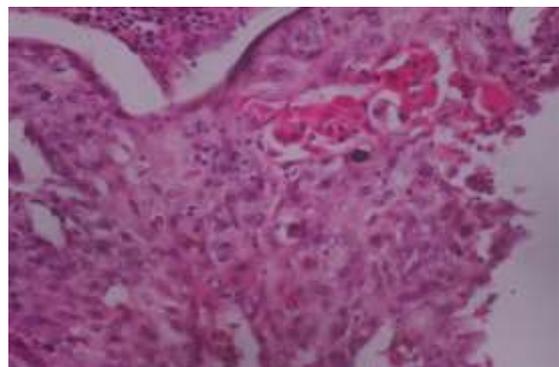


Fig. 4: Microphotograph showing moderately differentiated squamous cell carcinoma of the lacrimal gland

DISCUSSION

Lacrimal gland tumors are difficult to study because of their rare incidence and sparse information in the literature because of their rarity [1, 9]. Lacrimal gland tumors are divided into epithelial and non-epithelial tumors. Epithelial tumors are more common compared to the non-epithelial tumors [4]. In our study also, epithelial tumors were more common constituting 90% of all lacrimal gland tumors. Among the epithelial tumors, primary malignant tumors occurred less commonly compared to benign tumors, constituting 22.5% of all epithelial tumors (Table 3).

Table 3: Showing the distribution of epithelial tumors of lacrimal gland

Epithelial tumors	Wright et al 1992	Kohli et al	Our Study
Benign tumors	61%	71.1%	77.5%%
Malignant	38%	28.4%	22.5%

There were five female patients and four male patients in our study, with ages ranging from third to eighth decades. Comparing the ages of patients in our study, at the onset of symptoms, patients with adenoid cystic carcinoma were younger than the patients with malignant mixed tumor and squamous cell carcinoma. Similar observation was made in the study of John E Wright *et al.* [7]. The commonest symptoms were proptosis and globe displacement in seven of our cases. Patients with malignant lacrimal gland tumors have symptoms for a short period of time for about six months in case of adenoid cystic carcinoma and less than a year for other malignant tumors [2]. Most of our patients presented to the OPD within seven months of onset of symptoms. Pain is the cardinal symptom in adenoid cystic carcinoma [7]. In our study, only two cases (28.5%) of adenoid cystic carcinoma presented with pain, where as in the study of Sarah *et al.*, upto 80% have reported to have pain as presenting symptom. Early peripheral nerve and extraocular muscle invasion is thought to be the cause of the pain. Imaging is an important diagnostic tool in establishing the diagnosis of lacrimal gland malignancies. CT and MRI are the modalities of choice. MRI helps in evaluating the perineural spread in cases of adenoid cystic carcinoma [2].

Although preoperative diagnosis can be done based on the clinical and radiological features, the final diagnosis of malignant epithelial tumors can be established only after pathological evaluation of a biopsy. Adenoid cystic carcinoma is the commonest malignancy in our study, similar to the study of H.M. Alkatan *et al.* [1] and most other studies. Histologically, cribriform pattern is the commonest pattern of adenoid cystic carcinoma in our study similar to the study of Sarah *et al.* [2]. A combination of cribriform and tubular patterns was noted in two cases. The predominant growth pattern influences the biological

behavior and prognosis [2, 7]. Microscopically, one case of adenoid cystic carcinoma showed solid basaloid pattern in addition to the cribriform pattern. Higher mitotic activity was observed in the solid areas. To classify as a basaloid adenoid cystic carcinoma, at least half of the tumor in the biopsy material should consist of islands or larger aggregates of closely packed cells with hyperchromatic nuclei and scanty cytoplasm [7]. Solid pattern signifies a less well differentiated form and portends a worse prognosis compared to the cribriform and tubular patterns [7, 8]. Cribriform pattern carries a better than average prognosis according to one study. Tumor size at the time of diagnosis also correlates with prognosis. A report by Ahmad *et al.*, focusing on adenoid cystic carcinoma of lacrimal gland found that tumor size > 2.5 cm defines an unfavorable prognosis [12]. Adenoid cystic carcinomas recur for many years after initial treatment [7]. There is one case of recurrent adenoid cystic carcinoma in our study which recurred ten years after complete surgical resection and post radiation. The age of the patient was 19 years at the time of initial diagnosis. Radiotherapy is believed to delay recurrence in conjunction with surgical debulking, however it remains uncertain whether radiotherapy affects the outcome in these cases [7]. Adenoid cystic carcinoma is often slow to metastasize, but shows persistent invasive growth [2]. Metastases were not observed in any of our cases including the post RT recurrent case.

Carcinoma ex pleomorphic adenoma (CEPA) is a carcinoma that shows histological evidence of arising from a pleomorphic adenoma [2]. Histologic evidence of residual pleomorphic adenoma is usually seen. Most often the carcinomatous element is an adenocarcinoma (NOS). It was a poorly differentiated carcinoma in our case, which spread beyond the capsule into the surrounding tissues. The extent of invasion of the malignant component is an important prognostic factor [5] Primary squamous cell carcinoma of the lacrimal gland is a very rare tumor with very few case reports in literature. Primary from other sites should be ruled out before labelling it as primary squamous cell carcinoma of the lacrimal gland. Immunohistochemistry with antibodies to keratin and p63 were positive in our case.

The classification of lacrimal gland tumors is based on the 1991 WHO classification of salivary gland tumors, with an expanded classification in the 2006 AFIP monograph [5]. According to the histologic classification proposed by Ezekiel Weis *et al.*, based on their series and recently published series, minimally invasive CEPA is classified as low grade malignancy whereas adenoid cystic carcinoma (NOS), invasive CEPA and squamous cell carcinoma are high grade malignancies. Recently, a specific chromosomal translocation t(6;9) leading to fusion between the oncogene MYB and transcription factor gene

NFIB, with over expression of MYB was discovered in adenoid cystic carcinomas of head and neck region [2].

CONCLUSION

Primary malignant epithelial tumors of the lacrimal gland are very rare and difficult to study because of sparse literature on these tumors. Lacrimal gland may be considered as a minor salivary gland and the tumors of the lacrimal gland are classified like salivary gland tumors. However the use of a more diverse classification can be applied to epithelial lacrimal gland neoplasms. Adenoid cystic carcinoma of the lacrimal gland is the most common malignant neoplasm. Histologically, solid (basaloid) pattern portends a worse prognosis and tumor size greater than 2.5cm is associated with an unfavorable prognosis. Development of an inhibitor against MYB/NFIB fusion oncogene could be important in future in the treatment of adenoid cystic carcinoma. Primary malignant neoplasms of the lacrimal gland have a high morbidity and mortality. Recurrence after complete resection can occur making long term follow up imperative for these tumors. Primary squamous cell carcinoma of the lacrimal gland is a rare epithelial neoplasm with very few cases reported in literature.

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