Mucoepidermoid carcinoma ex pleomorphic adenoma of the lacrimal gland: A rare presentation

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Carcinoma ex pleomorphic adenoma in lacrimal gland is a rare entity unlike its salivary gland counterpart. This rare tumor poses a diagnostic challenge to clinicians as pre-operative diagnosis is difficult and diagnosis is only by careful pathological assessment. We report this uncommon lesion in a 62-year-old lady, wherein the malignant component was mucoepidermoid carcinoma. The elderly patient remained clinically and radiologically free of the tumor for two years after complete excision of the tumor but computed tomography at the end of two and a half years showed a recurrent lesion in the region of the lacrimal gland. This makes long term follow up of patients with these rare lacrimal tumors imperative with a minimum period of at least five years.

Key words: Carcinoma ex pleomorphic adenoma, lacrimal gland tumors, mucoepidermoid carcinoma

Pleomorphic adenoma (PA) or benign mixed tumor, the most common epithelial neoplasm of lacrimal gland arises from its epithelial and myoepithelial components. Carcinoma ex pleomorphic adenoma (CEPA) also called carcinoma in PA or malignant mixed tumor is defined as a carcinoma arising from a primary (de novo) or recurrent benign PA. Both benign and malignant components of the lesion are to be identified for a diagnosis of CEPA, the malignant components most
commonly being adenocarcinoma and the least common being mucoepidermoid.

Since lacrimal gland tumors are rare, the WHO classification of salivary gland tumors has been adapted to lacrimal gland tumors. According to this classification, lacrimal gland tumors are divided into epithelial, non-epithelial and tumor-like conditions. The epithelial neoplasms are classified as benign and malignant. The malignant epithelial tumors are sub-classified as low grade and high grade neoplasms. PA is classified as benign epithelial neoplasm and CEPA as a high grade malignant neoplasm. Armed Forces Institute of Pathology (AFIP) scoring system is an established and widely accepted grading system for mucoepidermoid carcinoma that objectively differentiates a low grade tumor from high grade carcinoma. The scoring system is based on five histologic features namely intracystic component, neural invasion, necrosis, mitotic activity and anaplasia. CEPA is sub-classified into non-invasive carcinoma or carcinoma in situ, minimally invasive (<1.5 mm of invasion from the capsule) and invasive carcinoma (>1.5 mm of invasion from the capsule). Computed tomography (CT) of the orbit may demonstrate features of both benign mixed tumor and invasive carcinoma. Bone erosion and calcification should raise the index of suspicion of malignancy in lacrimal gland tumors.

Case Report
A 62-year-old female presented with mild protrusion of the left eye associated with intermittent pain of 1 year duration. Orbital examination revealed the downward displacement of the left globe [Fig. 1]. There was a firm non-tender mass of 1.5 cm × 1.5 cm in the superolateral aspect of the orbit. Anterior segment of both eyes showed senile cortico nuclear cataracts with equally reacting pupils to direct and consensual light reflexes. The best corrected visual acuity in the right eye was 6/6 N6 and 6/18 N8 in the left eye. Abduction in the left eye was restricted. Intraocular pressure was within normal limits in either eye. Fundus examination of the right eye was normal, while the left eye showed normal disc and macula with dilated retinal veins [Fig. 2].

Figure 1: Pre-operative picture of the 62 year female patient showing downward displacement of left globe

Figure 2: Pre-operative fundus photographs of the patient. Note the dilated retinal veins in the left eye

Figure 3a and b: Showing a heterogenous lesion in the region of the left lacrimal gland with calcification

Figure 4: (a) Section showing pleomorphic adenoma with areas of hyalinization and a cellular tumor invading the capsular region (H and E, ×40). (b) Tumor cells are arranged in islands and composed predominantly of atypical squamoid cells, few mucin filled cells and intermediate cells with an area of calcification (white arrow) (H and E, ×100). (c) Individual cells show nuclear hyperchromasia, pleomorphism with moderate to scanty cytoplasm (H and E, ×200). (d) Islands of tumor cells with highly atypical cells showing perineural invasion (black arrow) (H and E, ×100)
Orbital CT showed a heterogeneous mass of $25 \times 18 \times 25 \text{ mm}^3$ in the superolateral aspect of the left orbit in the region of the lacrimal gland with calcification, inferiorly displacing the left lateral rectus [Fig. 3a and b]. The patient underwent lateral orbitotomy with total removal of the tumor. Histopathological examination of the lesion showed features of high grade mucoepidermoid carcinoma (AFIP score 9) with frequent mitotic figures of 5/10 HPF with perineural invasion and focal calcification showing in pleomorphic adenoma with a breach of more than 1.5 mm of capsule suggesting a final diagnosis of invasive mucoepidermoid carcinoma ex pleomorphic adenoma of the high grade type [Fig. 4a-d]. The patient refused further therapy. Postoperatively, there was no facial asymmetry [Fig. 5] and abduction was restored in the left eye.

Periodic follow up of the patient revealed no recurrence of the lacrimal lesion both clinically and radiologically for a period of 2 years. However, routine examination at the end of two and a half years, showed a minimal downward displacement of the eye [Fig. 6], a firm non-tender mass of $1 \text{ cm} \times 1 \text{ cm}$ in the superolateral aspect of the orbit, restriction of abduction with no regional lymphadenopathy. Contrast enhanced CT showed a mildly enhancing lesion $20 \times 14 \times 18 \text{ mm}^3$ just behind the region of the lacrimal gland without calcification but extending into intraconal space and infiltrating the lateral rectus, suggestive of a recurrent lacrimal lesion [Fig. 7a-f]. The patient declined any further treatment.

**Discussion**

According to the clinical series from the Wills Eye Hospital, lacrimal gland tumors represent almost 10% of orbital lesions, with inflammatory and lymphatic lesions together accounting for 80% and the epithelial lesions accounting for 20%. Of the epithelial lesions 45% were malignant with predominant lesion being adenoid cystic carcinoma and the least common being mucoepidermoid carcinoma. There is no mention of CEPA in their series. In a large series of 118 cases of epithelial gland tumors of the lacrimal gland, Rootman et al. described the most frequent diagnosis to be PA followed by adenoid cystic carcinoma and CEPA.
Of the nine cases of the latter, the malignant components included seven adenocarcinomas, one carcinosarcoma and one mucoepidermoid carcinoma.[5]

Management of CEPA is as that of PA when recognized as circumscribed or non-invasive carcinoma and that is by surgical excision. Significant infiltration and bony involvement necessitates removal of the bone with adjuvant radiation.[2,6,8] PA if left untreated can develop malignant changes within itself. Painful proptosis may portend malignant transformation or malignancy. Calcification in a lacrimal tumor of long duration can be a sign of malignancy in the elderly.[6,9] Calcification favors biopsy prior to excision as per the recommendation of Rose et al.[9] Non-invasive carcinoma carries excellent prognosis after complete excision. Minimally invasive and invasive carcinoma carries a grim prognosis despite complete excision and adjuvant radiotherapy.

Mucoepidermoid CEPA is a rare occurrence. This patient diagnosed to have a high grade CEPA of the invasive type with the malignant component being mucoepidermoid, arising de novo showed no clinical and radiological evidence of tumor at the end of 2 years. Radio imaging of orbits at the end of two and a half years showed signs of tumor recurrence even though she herself remained symptom free. Because of its rarity, the influence of therapy on the long term outcome of these tumors is difficult to assess. According to Wright et al., these tumors have high incidence of recurrence within 2 to 3 years of treatment.[10] Delay in treatment would adversely affect survival.[10] Pre-operative diagnosis of CEPA is difficult. Accurate histopathological assessment, appropriate classification, adequate treatment of CEPA and long term follow up in these patients with a minimum period of 5 years would increase survival rates.

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