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Case Report Open Access

Primary Ductal Adenocarcinoma of the Lacrimal Gland: Report of a Case and Review of Literature

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Abstract

Primary ductal adenocarcinoma is a rare subtype of adenocarcinoma. Literature review showed 13 cases of primary ductal adenocarcinoma of the lacrimal gland. We report a case of primary ductal adenocarcinoma of the lacrimal gland and review of literature highlighting its clinical presentation, histopathology including immunochemistry and overall outcome.

Keywords: Lacrimal gland; Ductal adenocarcinoma; Excision; Radiotherapy; Review

Introduction

Primary ductal adenocarcinoma of lacrimal gland (PDALG) has emerged as a distinct subtype of lacrimal gland adenocarcinoma [1] that accounts for 2% of all epithelial lacrimal gland tumors [2]. Microscopically, this neoplasm exhibits similar characteristics to ductal carcinoma of salivary gland and breast. It usually arise de novo and in only one case it was found as a malignant component of carcinoma ex pleomorphic adenoma [1,2]. Ductal adenocarcinomas are known to have highly malignant nature with only 13 cases reported of lacrimal gland. Out of the 13 published cases, only one has occurred in a female patient. To understand its biological behavior, management and prognosis, each case needs to be reported. We report a second case of PDALG in female and review of literature to describe the clinical, imaging and immunohistochemical features, management and prognosis of this malignancy.

Case Report

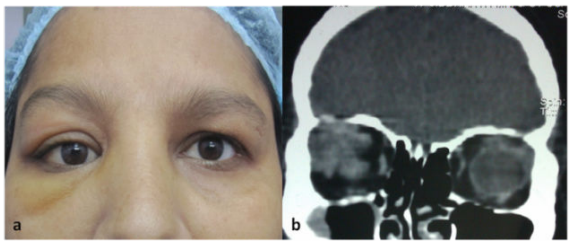

Figure 1: a: Clinical photograph showing fullness in right lacrimal gland region with inferior dystopia of eyeball. **b**: CT scan showing an irregular mass with diffuse enhancement in lacrimal gland fossa associated with erosion of roof of the orbit and no intracranial extension.

A 38-year-old female presented with painful mass in the right upper eyelid since 2 months. Visual acuity was 20/20 OU. Hertel exophthalmometry showed 2 mm proptosis with inferior dystopia OD (Figure 1a). Computed tomography showed a relatively well-defined mass with diffuse enhancement in lacrimal gland region associated with erosion of roof of the orbit (Figure 1b).

Patient underwent anterior orbitotomy. Thinning of the orbital roof was noted during surgery; however the tumor was excised in-toto along with periosteum. Histopathological examination revealed that tumor was comprised of duct like structures as main component and trabeculae, sheets, hyalinised stroma as infiltrative component (Figure 2a).

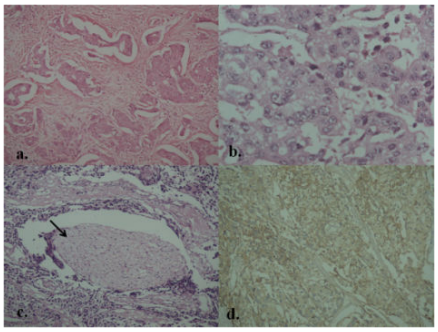

Figure 2: a: Microphotograph shows in situ duct like structures and infiltrative trabeculae, sheets with hyalinization and fibrosis in the stroma (H&E stain 100X). **b:** High power view shows marked pleomorphism , prominent nucleoli and mitotic figures (H&E stain 400X). **c:** Poorly differentiated component of the tumor with perineural invasion (arrow) (H&E stain 200X). **d:** Immunohistochemical staining showing positivity for epithelial membrane antigen (200X).

The tumor cells displayed varying degree of pleomorphism, numerous mitotic figures and prominent nucleoli (Figure 2b). Perineural and intravascular invasion was present (Figure 2c). Invasion into the orbital fat was present. Immunohistochemical

analysis showed positivity to cytokeratin-7, 10 and epithelial membrane antigen (Figure 2d). Stains for cytokeratin-20, S-100, proto-oncogene Her-2/neu, p-53 and estrogen receptor were negative. The diagnosis of primary ductal adenocarcinoma of the lacrimal gland was made.

Positron emission tomography scan revealed no systemic metastasis. Patient refused exenteration and was advised radiotherapy in view of invasion into the orbital fat. 8 weeks later, she developed local recurrence with intracranial and maxillary sinus involvement. Palliative radiotherapy was administered however, patient died of progressive disease after 6 months.

Discussion

Literature review revealed 13 de novo cases of PDALG, out of which 8 had been reported from Japan [4,7,9,11]. Mean age of presentation was 58.6 years (range: 39-78 years). Our patient presented at 38 years and is the youngest case of PDALG reported till date. All the reported cases were males, except two including the present case (M:F=12:1). Most common presentation was painless mass in the upper eyelid of less than 1 year duration. On imaging, 11 cases had irregular mass with ill-defined margins.

Associated bony destruction was seen in 3 cases [7,11] and bone remodeling without destruction was present in one case [5]. Five patients underwent tumor resection with globe-sparing surgery, orbital exenteration was done in 7 cases and post-operative radiotherapy was given in 7 cases (Table 1).

Reference	Age	Sex	Presentation	Duration	Management	Radiotherapy	Lymph nodes	Distant metastasis	Outcome
[3]	68	M	Painless mass	6 months	Fronto-temporal craniotomy and en-bloc orbitectomy with tumor resection	60 Gy RT given	No evidence	No evidence	Alive at 10 months
[4]	67	M	Painless mass	NA	En-bloc tumor resection with frontal craniotomy	40 Gy RT given to the subdural metastasis	No evidence	2 years post surgery, Subdural metastasis in temporal lobe, - resected	Alive at 2 years
[5]	46	M	Painless proptosis with neurofibromat-osis	2 years	Lid-sparing orbital exenteration	RT given	No evidence	No evidence	Alive at 19 months
[6]	59	M	Blepharoptosis with painless mass	15 years blepharo-ptosis	Lid-sparing orbital exenteration	RT planned	Parotid and cervical lymph nodes	No evidence	Alive at 6 months
[7]	67	M	Decreased vision and mass lesion	NA	En-bloc tumor resection	RT given	No evidence	Metastasis to Brain, liver, lungs, pancreas, common biliary duct	Died at 2 years 10 months
[8]	47	M	Mass in lacrimal gland region	NA	Orbital exenteration	RT given	Mediastinal nodes and skin lymphatics	Metastasis to spine, pelvis, femur, cerebellum 10 years after surgery	Died at 17 years
[9]	50	M	Non tender mass with low vision	2 years	Lateral orbitotomy with en-bloc tumor removal	Not given	No evidence	No evidence	Alive at 10 months
[10]	78	M	Painless palpable mass	NA	Lid-sparing exenteration	Not given	Parotid and cervical lymph nodes	No evidence	Died at 2 years
[11]	75	M	Swelling of upper eyelid	3 months	No surgery of orbital mass	Carbon ion radiotherapy 58 Gy	Submandib-ular lymph nodes	Metastasis to lung, chemotherapy given	Died at 2 years
	67	M	Swelling and ptosis of upper eyelid	6 months	Orbital exenteration with bone removal	No RT given	Submandib-ular lymph nodes	Multiple metastasis to bone and liver	Died at 1.3 years
	53	M	NA	18 months	Orbital exenteration	RT given 60 Gy	No evidence	Metastasis to spine, brain and liver	Died at 4.3 years
	39	M	NA	6	Orbital exenteration with bone removal	RT given 50 Gy	No evidence	Metastasis to lung and brain	Alive at 10 years

				months					
	46	F	NA	1month	Tumor resection with globe sparing surgery	Not given	No evidence	No evidence	Alive at 5.5 years
Our case	38	F	Painful swelling in upper eyelid	2 months	Tumor resection with globe sparing surgery	RT given 60 Gy after recurrence	No evidence	CNS metastasis	Died at 6 months

Table 1: Clinical data, management and outcomes of the published cases of primary ductal adenocarcinoma of the lacrimal gland (in chronological order).

The diagnosis was based on histopathology which depicts the in situ ductal component and infiltrative trabeculo-ductular component; the special stains and immunohistochemistry had confirmatory role. In all the reported cases, histopathology was consistent with PDALG except one which was hypothesized to be arising from pre-existing pleomorphic adenoma [12]. In most of the cases including the present case, on immunohistochemistry, tumor displayed strong positivity to cytokeratin-7, epithelial membrane antigen and carcinoembryonic antigen. In an only reported series of 5 patients11, authors also found androgen receptor positivity in all the cases (Table 2). There was a significant resemblance in the immunohistochemical pattern with salivary duct carcinoma, as this tumor was also found to be strongly reactive to cytokeratin-7, epithelial membrane antigen, carcinoembryonic antigen and androgen receptors similar to salivary duct carcinoma [13]. In contrast to the other histologic counterpart, duct carcinoma of the breast, immunoreactivity to estrogen and progesterone receptors was not found in any of the cases. Over expression of proto-oncogene Her-2/neu and p53 was seen in some cases [11], however it could not be correlated with distant metastasis and poorer prognosis unlike, in the breast cancer, where it is a significant predictor of overall survival [14].

Reference	Imaging	Size of mass	Positive Immunohistochemistry	Negative Immunohistochemistry
[3]	Irregular, nodular mass with lateral rectus involvement	4 × 2 × 1.5 cm	Keratin, B-72.3	HMB-45, NSE, S-100, CEA, PSA, Chromogrannin
[4]	Nodular, cystic mass compressing the optic nerve and eyeball	2.5 × 1.3 × 1 cm	EMA, CEA, Cytokeratin positive S-100 focally positive	Actin, estrogen receptor, Prostate specific antigen
[5]	Ill-defined large mass with homogenous enhancement with bony remodeling	NA	NA	Phospho Tungestic Acid Hematoxyline (PTAH)
[6]	Ill-defined mass with diffuse enhancement	1.5 × 1 × .3 cm	Cytokeratin-7, CEA, EMA, BRST-2, AE-1	PSA, Her-2/neu, p-53, estrogen receptor, S-100
[7]	Ill-defined mass with intralesional calcification present with bony erosion	3 cm	Cytokeratin-7, 18, 19, 34β E 12 Positive, Cytokeratin-10, 17 partially positive	S-100, Cytokeratin-20, α-smooth muscle actin
[8]	NA	NA	NA	NA
[9]	Homogenously enhancing, well defined, large ovoid mass in superolateral orbit	4 × 2.5 × 2 cm	Cytokeratin-7, 19, EMA	Cytokeratin- 20, estrogen receptor, progesterone receptor, C-erb-B2, S-100, α smooth muscle actin
[10]	Infiltrative mass with ill-defined margins with lateral rectus involvement	2.4 × 1.5 × 1 cm	Cytokeratin-7, MMP-2,9, 13, Her-2/neu	Cytokeratin-5, 20, p-53, prostate specific antigen, S-100, TTF
[11]	Irregular mass with bone destruction	2.8 cm	Androgen receptor, Her-2/neu, p53, Ki-67	Estrogen receptor, progesterone receptor
	Ill-defined mass with extension along superior rectus, calcification present	4 cm	Androgen receptor, p53, Ki-67	Estrogen receptor, progesterone receptor, Her-2/neu
	Diffuse irregular mass	3.7 cm	Androgen receptor, p53, Ki-67	Estrogen receptor, progesterone receptor, Her-2/neu
	Diffuse mass with bone destruction, calcification present	2.5 cm	Androgen receptor, p53, Ki-67, Her-2/neu	Estrogen receptor, progesterone receptor
	Irregular mass, calcification present	2.5 cm	Androgen receptor, p53, Ki-67, Her-2/neu	Estrogen receptor, progesterone receptor

Our case	Ill-defined mass with erosion of the orbital roof	3.5 × 2.5 × 2.5 cm	Cytokeratin-7, 10. Epithelial membrane antigen	S-100, Cytokeratin-20, Her-2/neu, p53, estrogen receptor

Table 2: Imaging and immunohistochemical features of the published cases of primary ductal adenocarcinoma of the lacrimal gland.

Out of 13 reported patients local recurrence was seen in one patient [7,5] patients developed lymph node metastasis and distant metastasis was seen in 7 patients (Table 1). The most common site for metastasis was brain [4,7,11]. Six of 13 patients succumbed to the disease albeit short follow up in most of the alive cases. The clinical behavior in our case was quiet aggressive as the history of illness was of 2 months and recurrence developed within span of 2 months after mass excision, followed by metastasis and death in 6 months. The present case differs from the previously published cases, being the youngest and the one with worst outcome owing to rapid progression of the disease. This report adds to the literature, the highly malignant nature of this lacrimal gland neoplasm and emphasizes on aggressive management to improve the prognosis and life salvage.

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