Lacrimal adenocarcinoma: a rare aggressive tumor of the eyelid

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ABSTRACT
Lacrimal gland adenocarcinoma (LGA) is a tumor representing 9% of the malignancies of this gland. Malignant lacrimal gland epithelial tumors form only 5% of all the orbital tumors with bone invasion and pain on presentation. LGA arise as a painful swelling from the lateral aspect of the upper eyelid manifesting as a mass causing pseudoptosis, exophthalmos and dystopia. Lacrimal gland malignancies are rare with poor prognosis. As aggressive treatment with lesser organ preservation is mandatory, psycho morphological counselling of the patient plays a vital role in post treatment rehabilitation.

Keywords: Adenocarcinoma, lacrimal gland, phthisis bulbi, orbital exenteration.

Introduction:
Lacrimal gland adenocarcinoma (LGA) is a tumor representing 9% of the malignancies of this gland. Malignant lacrimal gland epithelial tumors form only 5% of all the orbital tumors with bone invasion and pain on presentation. LGA arise as a painful swelling from the lateral aspect of the upper eyelid seen as a mass causing pseudoptosis, exophthalmos and dystopia with males predominantly affected. LGA present as palpable masses with soft tissue fullness, globe displacement and in advanced stages as abnormal ocular motility, reduced visual acuity, optic disc swelling, choroidal folds and diminished trigeminal nerve function. Malignant carcinoma arising within a pleomorphic adenoma as “pleomorphic adenocarcinoma” and if no prior history of pleomorphic adenoma (PA) surgery is present then it’s called “primary adenocarcinoma”. LGA presents in the 5th decade onwards with bone erosion seen in all cases while calcification is seen partially.

Case report:
A 70 year old woman with slowly progressive swelling in the right eye lid since 6 months was admitted with pain, diplopia and pseudoptosis. Pseudoptosis with mild exophthalmos and deviation of the eyeball and no bleeding or discharge was seen. She lost vision in the right eye with sinking in of the eyeball due to a trauma earlier, hence the eyelid swelling was not noticed for long. No history of smoking, drinking, diabetes mellitus, bronchial asthma, hypertension, tuberculosis was seen in the patient. Mass was 3×3 cm occupying the whole lid and on lid retraction, phthisis bulbi with no perception of light in the right eye with 6/60 vision in the left eye. Aspiration biopsy reported as adenocarcinoma of the lid with contrast enhanced CT of the orbit and the neck revealed a solid lesion of 2×3 cm of the right eyelid and phthisis bulbi.

Bone scan ⁹⁹ᵐ Tc pertechnate scan revealed solitary skeletal lesion seen in the body of the 11th vertebrae with osteoarthritis changes in the lumbar vertebrae and in the knee joint. Orbital exenteration of the right eye was done.

Fig.1: The rotation flap after orbital exenteration.
done with wide excision of the tumor. No periosteal invasion was seen. The defect was reconstructed with forehead rotation flap. (fig 1) Microscopy reported adenocarcinoma with myxoid and desmoplastic stroma with immune markers positive for cytokeratin and negative for epithelial membrane antigen (EMA), CK 7, CK20, CD3, CD31 and CD34. Orbital apex tissue, nerve bundles and skeletal muscles were free of the tumor. A final diagnosis of primary adenocarcinoma of the lacrimal gland or a skin adnexal origin was made. Post-operative 60 gy radiotherapy given with left eye sparing, wedge technique.

Discussion:

Lacrimal gland tumors form 10% (55% benign) of the orbital lesions while the epithelial tumors form 20%. PA forms the commonest benign tumor while adenoid cystic carcinoma (66%), carcinoma ex pleomorphic adenoma (18%), primary adenocarcinoma (9%) and mucoepidermoid carcinoma (3%) form the rest.1

These tumors go unnoticed or diagnosed in advanced stage as the malignancy infiltrates bones faster.2 LGA presents with blepharoptosis, dystopia, pseudoptosis, eyeball deviation, exophthalmos and diminision of vision in advanced stages.2 Blepharoptosis, ocular motility disturbance and diplopia reflect its malignant potential.8 Clinical staging should involve evaluation with history of symptom duration, pain, dysesthesia, globe distortion, assessing cervical lymph nodes, lungs and bone since metastasis are often overlooked.8 Aspiration cytology may miss disease at times as benign PA can have areas of cellular atypia without implying malignancy or have anaplasia, necrosis and increased mitotic activity indicating obvious malignancy.9

Looking for areas of carcinoma ex pleomorphic adenoma (CXPA) in PA is important and if found, capsular invasion should be searched10 for PA and noninvasive CXPA need only wide excision and observation while invasive CXPA needs radical surgery and adjuvant therapy has bad prognosis.10 Adenoid cystic carcinoma (ACC) gives worst prognosis with predominant solid(basaloid) pattern while tubular (ductal), cribriform (Swiss cheese) with perineural invasion, poor differentiation and positive surgical margins.11

Seen in patients below 30 years of age with CT bone erosion in 75%, bone destruction in 39% and soft tissue calcification in 22% of cases.3 Prognosis is worse with 50% recurrence in 2 years while only 50% survived 2.5 years after diagnosis with intracranial extension being major cause for mortality.12,13 LGA has a bad prognosis with fatality (50-80%) with average survival of 1.5 years.13 65% of the cases of primary LGA have recurrence in the first 5 years after treatment.13 Distinguishing it from low-grade polymorphous LGA or mucoepidermoid carcinoma (grades 1 and 2) is important as these fare better than LGA and ACC.13 Intraorbital exploration during wide excision is approached by lateral orbitotomy while orbital bone excision becomes necessary in cases of bony invasion, perineural and perivascular invasion.14

Markers for malignant epithelial tumor show cytokeratin (CK) 7 positivity whereas negative to CK 20.15 Pankeratin and CK-7 are expressed diffusely in all the variants of lacrimal ACC.16 Focal expression of p53 and Ki-67 in the basaloid variant of ACC appears to correlate with a poor prognosis.16 Primary ductal LGA overexpress androgen receptors and HER-2/neu protein while nuclear immunostaining for p53 ranged from 10% to 95% and that of Ki-67 from 20% to 70%.16

Contrast enhanced CT and MRI with high resolution, define the size, shape, extent, and invasion of adjacent structures including bone, marrow spaces, skull base and periorbital areas.8,9 They are round, ovoid, or elongated soft tissue mass with varying density and degree of infiltration, sometimes appear cystic with an irregular outline.8,9 Orbital exenteration and adjuvant therapy for advanced lesions, need a detailed patient counselling to balanced disease control, organ removal and loss of vision with adequate organ preservation.17,18

ACC being more aggressive with bone invasion in 50% and more, en bloc resection, exenteration and cranio-orbital resection with adjuvant radiotherapy are optimal.11 LGA, high grade mucopidermoid, invasive CXPA need radical excision and adjuvant radiotherapy while the low grade cases managed by wide excision and followup.12 The role of adjuvant radiotherapy and chemotherapy (cisplatin and doxorubicin) improving overall survival and reducing recurrence is yet to be well defined as the tumor incidence is low.19 The current management protocol stands at radical surgical excision of advanced lacrimal gland tumors with adjuvant radiation and chemotherapy with a multispeciality approach at rehabilitation.19

Conclusion:

Lacrimal gland malignancies are rare and with poor prognosis
with more morbidities. As aggressive treatment with lesser organ preservation is mandatory, psycho morphological counselling of the patient plays a vital role in post treatment rehabilitation.

References:


Selenium (Se) is an essential component of selenoproteins with primarily anti-oxidative functions. Humans acquire Se in foods such as fish, meat, eggs, cereals and seafood. Se concentration varies round the globe: it is low in China, while in other areas, such as in central parts of the US and in South America, the Se content in soils is higher, and residents in those areas acquire sufficient Se from vegetarian sources. The most common selenoprotein found in plasma is selenoprotein P (SePP) which constitutes about 50-60% of all Se in plasma in humans with a modest level of Se in the blood stream.

Low dietary Se intake and blood concentrations may have multiple effects on thyroid hormone synthesis and regulation. Firstly, Se is a necessary component within both the thioredoxin reductases and the glutathione peroxidase (GPx) family, which are powerful anti-oxidant enzymes. As the thyroid hormone metabolism causes an oxidative milieu within the thyroid gland, which is enhanced during thyrotoxicosis, GPxs and thioredoxin reductases are required to balance this oxidative stress. Secondly, thyroid hormone synthesis, mainly thyroxine, is converted within target cells by another group of selenoproteins, the deiodinases, to active triiodothyronine and inactive thyroxine metabolites. Thirdly, Se, as sodium selenite or selenomethionine, appears to influence the immune system by unknown mechanisms, as supplementation with Se decreases the levels of thyroid peroxidase auto-antibodies (TPO Ab) in autoimmune hypothyroidism.

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