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Original Article

Lacrimal gland Neoplasms: A 10 Year Retrospective Study

Authors
Dr Suguna Belur Venogopal[1], Dr Sneha Ashok Motwani[2], Dr Sruthi Prasad[3], Dr Geethamani V[4]
Department of Pathology, Kempegowda Institute of Medical Sciences, Bengaluru -560070
*Corresponding Author
Dr Sneha Ashok Motwani
Address: 439/A, 1st A Cross, 4th Block, Koramangala, Bengaluru – 560034, India

Abstract

Background: *The orbit is home to many tumors, but the lacrimal gland which anatomically is a part of the orbit is a rare site for both primary and secondary tumors. Incidence of lacrimal gland tumors is only 1 in 1 million people per year.[1] The tumors affecting the lacrimal gland can be broadly classified into epithelial, mesenchymal, lymphoid and metastatic.*

Objectives

- *To assess the histomorphological features of various lacrimal gland neoplasms.*
- *To classify them into benign and malignant neoplasms.*
- *To describe the age and sex distribution of various lacrimal gland neoplasms.*
- *To find out the frequency of various lacrimal gland neoplasms in our study population and compare it with the previous studies.*

Materials and Methods: *This retrospective study was carried out in a tertiary care hospital. A total of 37 lacrimal gland tumors were studied over a period of 10 years from January 2010 to October 2019. Tissues were fixed in formalin, routinely processed, stained with Hematoxylin and Eosin stain and studied for histomorphological features.*

Results: *The most common neoplasms in our study were epithelial neoplasms, of which, pleomorphic adenomas (benign) had the highest frequency followed by adenoid cystic carcinoma(malignant). These were followed by lymphoid tumors which included reactive lymphoid hyperplasia and malignant lymphomas. Mesenchymal tumors included neurofibromas and lymphangioma. There was one case of metastatic breast carcinoma.*

Conclusion: *Histopathology is critical in diagnosing and classifying neoplastic lesions of the lacrimal gland. Histopathology along with radiological findings provides an insight into the malignant potential and prognosis of the tumor. Thus, histopathological examination in addition to clinical and radiological findings aids in the accurate diagnosis and rational management of lacrimal gland neoplasms.*

Keywords: *Lacrimal gland, Neoplasms, Histomorphology.*

Introduction

The lacrimal gland is the only epithelial structure normally present in the orbit. It is an exocrine gland located in the superolateral part of the orbit. The gland is divided into a superficial, palpebral subconjunctival lobe and a deeper, orbital lobe by

the levatorpalpebrae aponeurosis.[2] The lacrimal gland is non-encapsulated and divided into lobules by thin fibrous septae. Histologically, the gland is composed predominantly of serous acini. Lymphocytes and plasma cells are commonly seen scattered between the acini of the lacrimal gland.[2]

Lesions of lacrimal glands account for 5-25% of all orbital masses.[3] These include inflammatory, structural and neoplastic disorders. Neoplastic disorders of the lacrimal glands are very rare, found only in one person per million people per year.[1] Lacrimal gland tumors are considered one of the challenging types of tumor.They are difficult to study because of their rare incidence (only 10% of the space occupying orbital lesions).[4] The WHO classification of salivary gland tumors has been adopted to lacrimal gland pathology.[5] Thus, these tumors can be broadly divided into epithelial, mesenchymal, lymphoid and metastatic. Rational clinical management of these tumors depends on their accurate histological typing. Radiological imaging also provides valuable information on the type of tumor and extent of invasion into the surrounding structures and thus aids in staging of malignant tumors.[4] Therefore histopathological examination along with radiological imaging plays a very important role in the diagnosis and management of these tumors.

Materials and Methods

The present study is a retrospective hospital based study, carried out over a period of 10 years from January 2010 to October 2019. Informed consent was taken from all the study subjects. A total of 37 neoplastic lesions of lacrimal gland were studied. The necessary clinical details and radiological findings were obtained.

The surgically resected specimens thus received in the department of Pathology were fixed in the 10% buffered formalin. Gross examination of the tissue fragments was done. The entire tissue was subjected to routine processing, followed by paraffin embedding. Sections, 3-4 micron thick were taken and stained with Haematoxylin & Eosin.

Histopathological examination was done, data was tabulated and descriptive analysis was used to study the cases.

Results

The study included 37 tumors of the lacrimal gland. The age of the patients in the study ranged from 9 to 70 years with a mean age of 42.18 years. The peak age of presentation (10 cases, 27%) was seen in the range of 31-40 years. Most (24/37, 64.86%) of the patients were in the age group of 31-60yrs (Table 1).

Table 1: Age distribution of lacrimal gland tumors

Age range	Epithelial tumors			Lymphoid tumors		Mesenchymaltumors	Metastatic tumors	Total no. of cases(%)
	Pleomorphic adenoma	Adenoid cystic carcinoma	Malignant mixed tumor	Reactive lymphoid hyperplasia	Lymphomas			
< 20 years	0	1	0	0	0	3	0	4(10.8%)
21-30 years	3	0	0	1	0	0	0	4(10.8%)
31-40 years	2	6	1	0	1	0	0	10(27.0%)
41-50 years	2	2	1	2	1	0	0	8(21.6%)
51-60 years	3	0	0	1	1	0	1	6(16.2%)
61-70 years	2	0	0	1	2	0	0	5(13.5%)
Peak incidence (years)	21-30 and 51-60	31-40	41-50	41-50	61-70	<20	51-60	31-40
Average age (years)	45.91	36.25	40.50	48.00	55.00	11.00	60.00	42.18

The study included 15(40.5%) males and 22(59.4%) female patients with a male: female ratio of 1:1.46.

Table 2: Sex distribution of lacrimal gland tumors

Classification	Type of tumor	Male (%)	Female (%)	Total no. (%)
Epithelial tumors	Pleomorphic adenoma	5(13.51%)	7(18.9%)	12(32.13%)
	Adenoid cystic carcinoma	2(5.40%)	7(18.9%)	9(24.32%)
	Malignant mixed tumor	1(2.70%)	1(2.70%)	2(5.40%)
Lymphoid tumors	Reactive lymphoid hyperplasia	3(8.10%)	2(5.40%)	5(13.51%)
	Lymphomas	4(10.81%)	1(2.70%)	5(13.51%)
Mesenchymaltumors		0(0.00%)	3(8.10%)	3(8.10%)
Metastatic tumors		0(0.00%)	1(2.70%)	1(2.70%)

On clinical examination, the left eye was involved in 19 patients (51.35%), right eye in 17 (45.94%) and a single patient (2.70%) showed bilateral eye involvement. The predominant symptom on presentation was proptosis and upper eyelid swelling (32 cases, 86.48%). Other symptoms in decreasing frequency included reduced lacrimation, ptosis, pain and reduced vision.

On histopathological examination, epithelial tumors (23, 62.16%) formed the majority, followed by lymphoid tumors (10, 27.02%) and mesenchymal tumors (3, 8.10%). There was a single case (2.70%) of metastasis (Table 2).

The epithelial neoplasms accounted for 23 out of 37 cases (62.16%). Of the 23 cases, 12 (52.17%) were benign, while 11 (47.82%) were malignant. All the benign epithelial tumors in our study were pleomorphic adenoma, presenting mostly in females (7/12, 58.33%) and with a mean age of 45.91 years. There was one case of a recurrent pleomorphic adenoma. Microscopically, all cases showed both epithelial and mesenchymal elements in varying proportions. Epithelial component was mostly seen in the form of ducts, with few in groups and sheets. Squamous metaplasia of the epithelium was seen in one case. The mesenchymal component in all cases was predominantly fibromyxoid with a minor chondromyxoid component. (Fig 1)

Of the 11 malignant epithelial tumors, adenoid cystic carcinoma was the majority (9/11, 81.81%) with malignant mixed tumors accounting for the remaining 2 cases (2/11,18.18%). Adenoid cystic carcinoma presented predominantly infemales (7/9, 77.77%) and at a mean age of 36.25 years. Two of the cases were that of a recurrent adenoid cystic carcinoma. Microscopically, they comprised of small basaloid cells arranged predominantly in cribriform pattern (7/9, 77.77%) followed by solid pattern (4/9, 44.44%), comedo (2/9, 22.22%), sclerosing (1/9, 11.11%) and tubular pattern (1/9, 11.11%). Perineural invasion was a characteristic finding in all the cases. Orbital soft tissue involvement was noted in all the cases (Fig 2)

Malignant mixed tumor (pleomorphic carcinoma) comprised of 2 cases, with a mean age of 40.5 years. Both genders were equally affected. Microscopically, in addition to features of pleomorphic adenoma, each of the cases showed adenocarcinoma in one, and that of adenoid cystic carcinoma in the other respectively.

Lymphoid tumors were seen in 10/ 37 cases (27.02%). Half of the cases were benign (reactive lymphoid hyperplasia) while the other half were malignant (lymphoma). Reactive lymphoid hyperplasia was found in 5 cases (13.51% of all neoplasms), and mostly in males (3/5, 60%) having a mean age of 48 years. Microscopically, there was effacement of lacrimal gland architecture by dense aggregates of lymphocytes, admixed with plasma cells and macrophages. Germinal centres were noted as well. Few ducts lined by epithelial cells were seen in the stroma. (Fig 3)

Lymphoma comprised 5 cases (13.51% of all neoplasms), all of which were of Non-Hodgkin's lymphoma. The patients were predominantly males (4/5, 80%), with a mean age of 55 years. Microscopically, all cases showed a monotonous population of atypical lymphoid cells with scant cytoplasm and hyperchromatic nuclei. Atypical mitosis were noted. On immunohistochemistry, 4 cases were proven to be Extranodal marginal zone

B-cell lymphoma (diffuse CD 20 positivity) and 1 case was Diffuse Large B-cell lymphoma (LCA and CD 20 positive) (Fig. 4)

There were 3 (8.10% of all neoplasms) mesenchymal tumors, of which 2 (5.40% of all neoplasms) were peripheral nerve sheath tumors and 1 (2.70% of all neoplasms) was lymphangioma. These tumors were found in young females with a mean age of 11 years. Both the peripheral nerve sheath tumors were cases of plexiformneurofibroma showing tortuous expanded nerve bundles with diffuse neurofibromatous component in between lobules of the lacrimal gland. (Fig 5) The case of lymphangioma, on microscopy showed a few dilated cystic spaces at the periphery of the lacrimal gland lobules.

A single case of metastasis to the orbit involving the lacrimal gland was encountered. This was seen in a 60 year old female with primary breast carcinoma. Microscopically, neoplastic cells were seen infiltrating the lacrimal gland. The cells were large with abundant pale to eosinophilic cytoplasm and smudged nuclei. Foci of lymphovascular invasion were noted (Fig 6)

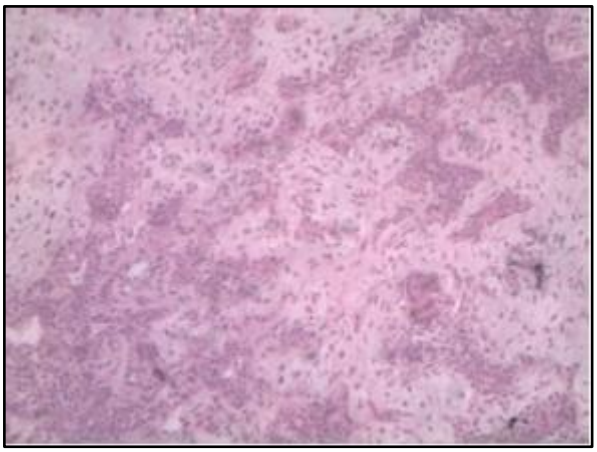


Fig. 1: Pleomorphic adenoma: Benign neoplasm showing epithelial and myoepithelial cells in groups, strands, tubular and glandular pattern. The stroma in between is fibromyxoid. (H&E, 100x)

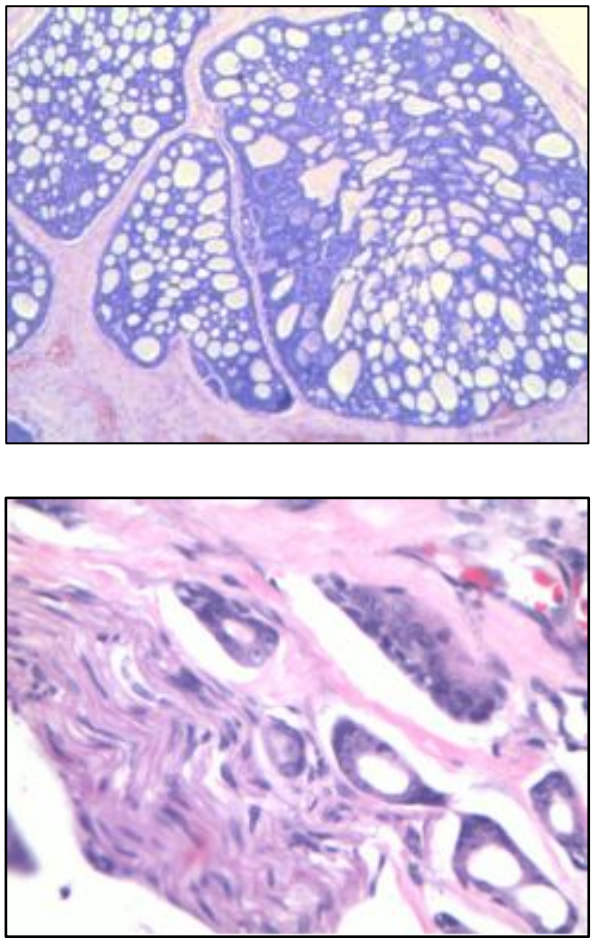


Fig. 2: A) Adenoid cystic carcinoma: Malignant neoplasm comprising of small basaloid cells arranged in cribriform pattern (H&E, 100x) B) Neoplastic cells showing perineural invasion (H&E,400x).

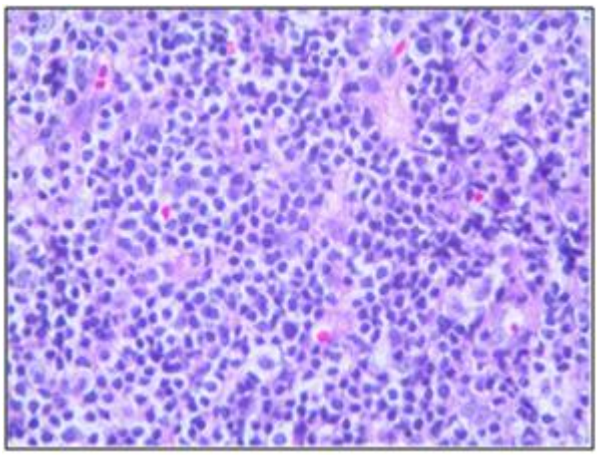


Fig.3: Reactive lymphoid hyperplasia: Diffuse proliferation of polymorphous lymphoid cells admixed with macrophages and few compressed ducts. (H&E,400x)

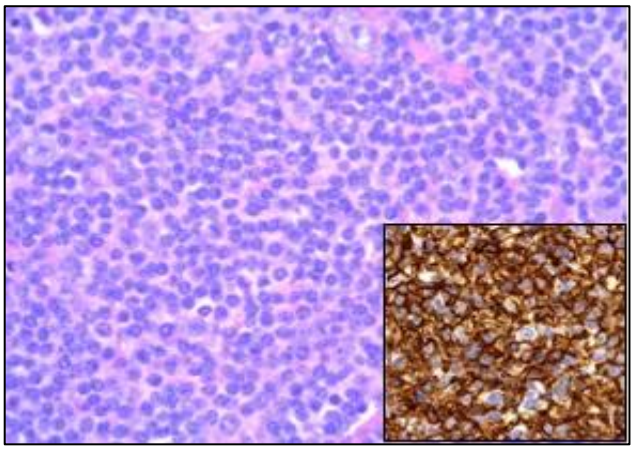


Fig. 4: Extranodal marginal zone B-cell Lymphoma: Malignant neoplasm comprising of sheets of monotonous atypical cells. Inset: CD20 positivity.(H&E,400x)

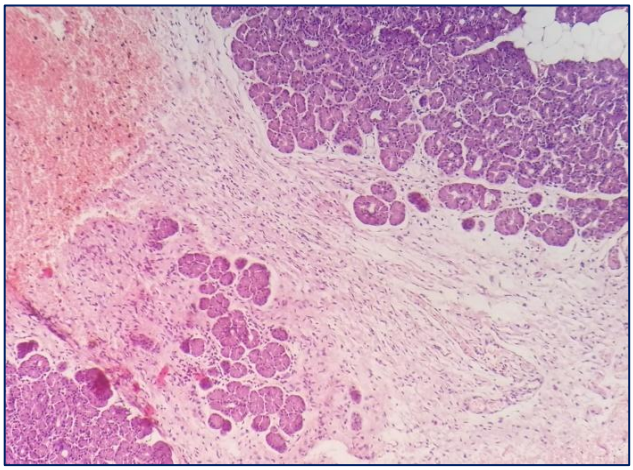
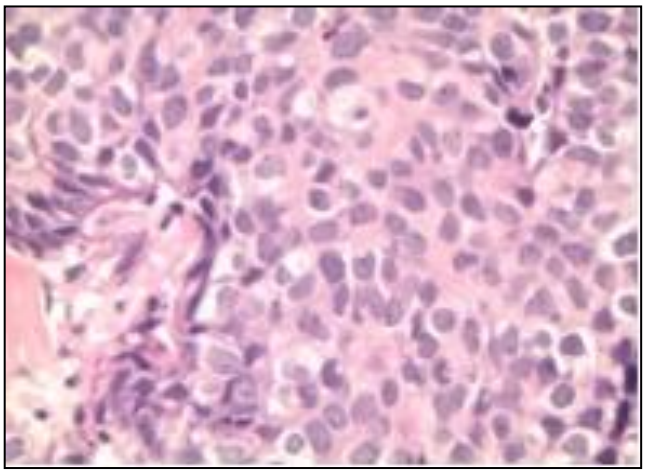


Fig. 5: Neurofibroma: Benign tumor comprising of interlacing tortuous fascicles of spindle cells with wavy nuclei (H&E,100x)



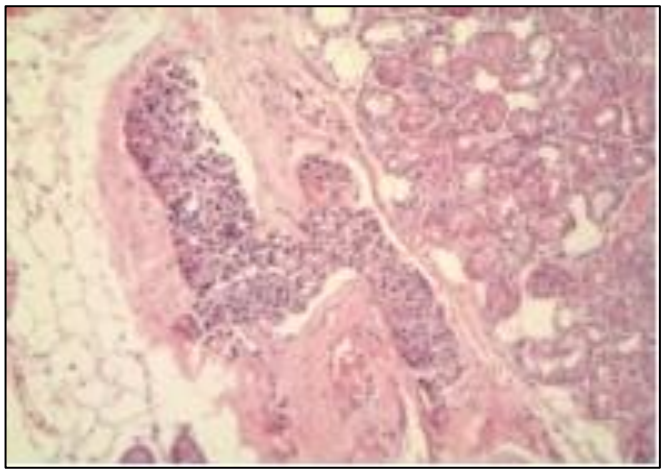


Fig. 6: Metastatic deposit in the lacrimal gland A)Sheets of pleomphorphic cells with high N:C ratio, anisonucleosis and scant eosinophilic cytoplasm. (H&E,400x) B) Lymphovascular invasion. (H&E,100x)

Discussion

Lacrimal gland presents with a spectrum of neoplasms having varying modes of presentation. The tumors can be broadly divided into epithelial, mesenchymal, lymphoid and metastatic. Epithelial tumors can be classified as benign or malignant, which can be further sub-classified as low grade or high grade. Clinically, benign tumors are usually painless, slow growing and indolent while malignant tumors are painful, rapidly growing and destructive. The commonest clinical symptom is proptosis which was the case even in the present study.[4]

The most common neoplasms in our study were benign epithelial tumors (pleomorphic adenoma), followed by malignant epithelial tumors, lymphoid tumors, mesenchymal tumors and metastatic tumors.

Epithelial tumors are account for 23-70 % of lacrimal gland tumors according to literature. [3] In our study, they accounted for 61.85% cases. The epithelial tumors encountered were pleomorphic adenoma, adenoid cystic carcinoma and malignant mixed tumors.

Pleomorphic adenoma (Benign mixed tumor)is the most common epithelial neoplasm of the lacrimal gland, as seen in the current study (52.17%).[5] The mean age of presentation was

45.91 years, which was comparable to study by Rose GE et al.[6] Though most studies do not show any gender preponderance, the present study showed a female preponderance similar to the findings by Kennedy et al.[7]A painless swelling in the upper lid present for a long duration (>12 months), without any symptoms and signs of inflammation is a pointer towards pleomorphic adenoma. On radiology, usually a well-defined lesion is seen and the surrounding bone is not involved.[8] Microscopically, typical pleomorphic adenoma has a biphasic appearance resulting from the intimate admixture of epithelial and mesenchymal elements. The mesenchymal component is predominantly myxoid in appearance, but occasionally osseous, chondroid and adipose tissue may be present.[9]In the present study we saw only fibromyxoid mesenchymal component in all cases. The mesenchymal elements are presumed to arise from the epithelial cells and represent modified myoepithelial cells. The tumor frequently recurs after incomplete excision resulting in tumor deposits within the orbit. Hence, complete excision of the tumor along with its pseudocapsule and an adequate rim of normal lacrimal gland tissue is the ideal management for this tumor.[8] Prognosis of pleomorphic adenoma depends on two factors- recurrence of the tumor after incomplete excision and malignant change. Malignant transformation is associated with age of the tumor which may be reflected by the extent of hyalinization on histology.[3]Specific molecular rearrangements have been analysed in cases of pleomorphic adenoma, corresponding to PLAG1 gene (pleomorphic adenoma gene 1) at chr8q12 and HMGA-2(high motility group protein) gene at chr12q14-15.[10]

Adenoid cystic carcinoma is the most common malignant tumor of the lacrimal gland, which is similar to that in the current study (9/11, 81.81%).[5] It comprised of 39.13% of all epithelial tumors similar to that reported by Forrest et al.[11]The mean age of presentation of adenoid cystic carcinoma in our study was 36.25 years comparable to the study by Ni et al (37 years).[12] Females were the predominantly affected gender (7/9, 58.33%) similar to the finding of Ni et al.[12]Clinically, they present as rapidly growing (duration<1 year), extremely painful, unilateral masses. On radiology, the tumor has irregular and serrated margins, quite often shows invasion and destruction of surrounding bone and occasionally shows calcification of the adjacent soft tissues.[8] Microscopically, small neoplastic cells with bland cytologic appearance are noted. Typical histopathologic patterns include the cribriform, solid, sclerosing, comedo and tubular subtypes.[9]These patterns influence the prognosis of the tumor. The predominant pattern of architecture in our study was cribriform (7/9, 77.77%) which is the pattern with highest frequency according to Gamel JW et al.[13] Other patterns observed were solid (4/9, 44.44%), comedo (2/9, 22.22%), sclerosing (1/9, 11.11%) and tubular pattern (1/9, 11.11%). Solid pattern is associated with a worse prognosis in both salivary and lacrimal gland tumors.[13] The absence of a cribriform pattern is also an indicator of poor prognosis.[3]The spread of the solid variant of the adenoid cystic carcinoma into the eyelid may mimic a primary basal cell carcinoma at this site.[9] Perineural invasion is a characteristic feature of adenoid cystic tumors of the lacrimal gland and results in pain and numbness.[8] All of the cases in the current study showed perineurial invasion and orbital soft tissue involvement. Other factors associated with poor prognosis include stage of the disease and increased bcl-2 expression.[14] Molecular analysis has revealed translocation t(6,9) specific to Adenoid cystic carcinomas irrespective of the site of the tumor. This translocation leads to the formation of MYB-NFIB fusion product which is associated with regulation of apoptosis and cell growth.[15] This fusion product may also serve as a potential molecular therapeutic target. C-kit over expression has also been noted in these tumors.[10] Management of adenoid cystic carcinomas includes surgery and radiotherapy.

Supplementation with intra-arterial cytoreductive chemotherapy can reduce recurrence and improve survival.[14]

Mixed malignant tumor also known as carcinoma ex pleomorphic adenoma is the malignant transformation of a primary or recurrent pleomorphic adenoma. In our study 2 cases (8.69%of all epithelial tumors) were of mixed malignant tumor comparable to the findings of Ni et al (9.00%).[12] The mean age of presentation in the current study was 40.5 years with no gender preponderance, both the findings comparable to that of Henderson et al.[16] Patients with malignant mixed tumor are known to be older than those with benign mixed tumor, which wasn't the case in the current study (mean age 40.5yrs and 45.91yrs respectively).[5] Clinically, the patients usually present with a painful, rapidly enlarging mass. This malignancy may develop de novo or secondary to a pleomorphic adenoma, which was incompletely excised or indolent. An enlarged lacrimal fossa accompanied by destruction of surrounding bone is indicative of a malignant tumor, on radiology.[8] The histologic variants of carcinoma include adenocarcinoma, adenoid cystic carcinoma, squamous cell carcinoma, undifferentiated carcinoma, sebaceous carcinoma and spindle cell sarcoma.[9]It is has been reported that the malignant regions of the tumors stained positively with androgen receptor, p53 and Her-2/neu on immunohistochemistry.[10] This tumor can be further classified based on extent of invasion into non-invasive/ minimally invasive tumors and invasive carcinomas. Non-invasive / minimally invasive tumors show invasion of <1.5mm from capsule and carry a remarkable prognosis with just complete surgical removal. Invasive carcinomas are aggressive tumors which show invasion of >1.5mm from capsule and are associated with a poor prognosis.[14]

Lymphoid lesions have a wide range of presentation from reactive lymphoid hyperplasia to malignant lymphomas, which pose a diagnostic challenge. The lacrimal gland often contains intrinsic lymphoid tissue, which form a part of the mucosa-associated lymphoid tissue (MALT). Lymphoproliferative lesions of the lacrimal gland are typically painless tumors with insidious onset. They are seen usually seen in patients of older age groups and may often have bilateral presentation.[8] WHO states that there is a higher incidence of reactive lymphoid hyperplasia in females especially in a setting of autoimmune disease.[16] However, in our study we found reactive lymphoid hyperplasia to occur predominantly in middle aged men with a mean age of 48 years. These findings were comparable with that of Farmer et al.[17]Radiologic findings of lymphoid tumors are characterized by non-erosive lesions that mould around the orbital structures.[8] Polyclonal proliferation of the intrinsic lymphoid cells of the lacrimal glands results in reactive lymphoid hyperplasia. Apart from differentiated lymphocytes, occasional plasma cells, macrophages, eosinophils, reactive germinal follicles may also be seen. Stroma usually contains scant fibrous tissue. On microscopy, all the cases in the current study also showed a polymorphous population of lymphocytes admixed with plasma cells and macrophages. [9]

Ocular adnexal lymphomas account for 2% of all extranodal lymphomas of which lacrimal gland lymphomas constitute 7-26%.[18]Lymphomas affecting the lacrimal gland are primary or secondary. Primary malignant lymphomas are neoplasms that show clonal proliferation of the intrinsic lacrimal lymphoid cells, while secondary lymphomas occur as a part of disseminated Non-Hodgkin's lymphoma. In the present study, the mean age of patients with lymphoma was 55 years which was slightly lower compared to other studies where the mean age of presentation was in the 7th decade.[17,18] The male preponderance of our cases, differed from the findings by Farmer et al and Rasmussen et al.[17,18] The most frequent type of lymphomas are of B cell type, with the commonest being extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (MALT lymphoma). Extranodal marginal zone B

cell lymphoma was the most common subtype (4/5, 80%) found in our study, which is comparable to literature.[5]

Mesenchymal tumors arise more frequently from tissues surrounding the lacrimal gland rather than the gland itself. Very few cases have been reported in literature and include hemangioma, hemangiopericytoma, lipoma solitary fibrous tumor, lymphangioma, neurofibroma and schwannoma.[5]

Neurofibromas are peripheral nerve sheath tumors which are well recognized in the orbit but have a very low incidence in the lacrimal gland. A bimodal pattern of age distribution is noted. Those associated with von Recklinghausen's disease usually present in childhood, while solitary neurofibromas present in middle-aged adults.[19]In our study, we encountered 2 cases of plexiform neurofibroma, both occurring in childhood and associated with neurofibromatosis.

Lymphangiomas are vascular tumors that may present in the orbit as a mass lesion. They are usually reported in the first few decades of life. We encountered a single case of lymphangioma in a 10 year old child.

Metastasis to lacrimal gland is very rare (less than 1% of the lacrimal gland malignant tumors) and has been reported in patients with carcinoma breast, lung and kidney. The spread is predominantly haematogenous.[5]The current study, showed a single case of metastatic breast carcinoma to the lacrimal gland.

Conclusion

The lacrimal gland is a tiny structure encompassing a wide spectrum of neoplasms. The classification of these neoplasms is similar to salivary gland neoplasms and includes epithelial, lymphoid, mesenchymal and metastatic neoplasms. Each of these neoplasms have their own unique histopathological features. A combination of histomorphologic typing and radiologic imaging is crucial in differentiating the various neoplastic lesions of the lacrimal gland, thus aiding in their rational clinical management.

Sources – Nil

References

1. https://www.cancer.net/cancer-types/lacrimal-gland-tumor/statistics
2. Klintworth GK, Cummings TJ. Normal eye and ocular adnexa. In: Stacey E Mills. Histology for Pathologists.4th ed. Philadelphia: Lippincott Williams & Wilkins; 2012.p.394-397
3. Weis E, Rootman J, Joly TJ, et al. Epithelial Lacrimal Gland Tumors: Pathologic Classification and Current Understanding. Arch Ophthalmol. 2009;127(8):1016–1028.
4. Alkatan HM, Al-Harkan DH, Al-Mutlaq M, Maktabi A, Elkhamary SM. Epithelial lacrimal gland tumors: A comprehensive clinicopathologic review of 26 lesions with radiologic correlation. Saudi J Ophthalmol. 2014;28(1):49–57.
5. Ramon L. Font MD, J.OscarCroxatto MD, Narsing A. Rao. MD. Tumors of the eye and ocular adnexa- AFIP Atlas of tumor pathology- Series 4.p.223-242.
6. Rose G, Wright J. Pleomorphic adenoma of the lacrimal gland. British Journal of Ophthalmology. 1992;76(7):395-400.
7. Kennedy R E. An evaluation of 820 orbital cases. Trans Am Ophthalmol 1984; 82:134-157
8. Duck Kim Y. Lacrimal gland tumors. In:Karcioglu ZA. Orbital Tumors, Diagnosis and Treatment. New York: Springer, 2005:204-220.
9. Klintworth GK, Cummings TJ. The eye and ocular adnexa. In: Stacey E Mills Sternberg's Diagnostic Surgical Pathology, 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.p989-990.
10. Von Holstein S, Coupland S, Briscoe D, Le Tourneau C, Heegaard S. Epithelial tumours of the lacrimal gland: a clinical, histopathological, surgical and oncological

survey. Acta Ophthalmologica. 2012;91(3):195-206.
11. Forrest AW. Epithelial lacrimal gland tumors: pathology as a guide to prognosis. Trans Am AcadOpthalmol. 1954;58:848.
12. Ni C, Cheng SC, Dryja TP, et al. Lacrimal gland tumors: a clinicopathologic analysis of 160 cases. Int Ophthalmol Clin 1982;22:99–120.
13. Gamel JW, Font RL. Adenoid cystic carcinoma of the lacrimal gland: the clinical significance of a basaloid histologic pattern. Hum Pathol 1982;13: 219–225.
14. Bernardini FP, Devoto MH, Croxatto JO. Epithelial tumors of the lacrimal gland: an update. Curr Opin Ophthalmol. 2008;19(5):409-13.
15. Persson M, Andren Y, Mark J, Horlings HM, Persson F &Stenman G (2009): Recurrent fusion of MYB and NFIB transcription factor genes in carcinomas of the breast and head and neck. Proc Natl Acad Sci USA 106: 18740– 18744.
16. Andrew NH, Coupland SE, Pirbhai A, Selva D. Lymphoid hyperplasia of the orbit and ocular adnexa: A clinical pathologic review. Surv Ophthalmol. 2016;61(6):778-790
17. Farmer JP, Lamba M, Lamba WR, et al. Lymphoproliferative lesions of the lacrimal gland: clinicopathological, immunohistochemical and molecular genetic analysis. Can J Ophthalmol. 2005;40(2):151-160.
18. Rasmussen P, Ralfkiaer E, Prause JU, Sjö LD, Siersma VD, Heegaard S. Malignant Lymphoma of the Lacrimal Gland: A Nation-Based Study. Arch Ophthalmol. 2011;129(10):1275–1280
19. McDonald P, Jakobiec F, Hornblass A, Iwamoto T. Benign Peripheral Nerve Sheath Tumors (Neurofibromas) of the Lacrimal Gland. Ophthalmology. 1983;90(12):1403-1413.