Original Article

Clinicopathological Characteristics and Predictive Clinical Features of Lacrimal Gland Lesions

Yossi Eriska[1], Raja Erinda[2], Trilaksana Nugroho[2]

[1]Ophthalmology Resident, Ophthalmology Department, Diponegoro University, Semarang, Indonesia

[2]Reconstructive Oculoplastic dan Oncology, Ophthalmology Department, Diponegoro University, Semarang, Indonesia

Corresponding email: yossieriska.sc@gmail.com

ABSTRACT

Introduction: Lacrimal gland tumors encompass a wide spectrum of benign, malignant and inflammatory conditions. Understanding the clinico-demographic profile and histopathological findings is crucial for early detection, determining appropriate treatment strategies and improving patient outcomes. **Methods:** This was a retrospective observational study of patient with lacrimal gland lesions diagnosed at the Reconstructive Oculoplastic and Oncology department at a tertiary care hospital in Central Java. Thirty-nine patients with biopsy-proven lesions between January 2021 and December 2024 were included. Clinical characteristics including age, sex, laterality, symptom duration, proptosis, lagophthalmos, and ocular motility restriction were evaluated. Histopathological diagnoses were categorized into benign, malignant, and inflammatory lesions. Statistical analyses were performed to assess associations between clinical variables, sex, and tumor classification. **Results:** A total 47 eyes of 39 patients were retrospectively reviewed. The mean age of patients was 46.15 ± 20.27 years (range 2–76), with 48.7% male and 51.3% female. Malignant tumors were more frequent in patients older than 60 years (69.2%), while benign tumors were more common in patients aged 40–59 years (60.0%). Histopathological analysis demonstrated that lymphoid and inflammatory disorders were the most common lesions. Inflammatory disorders consisted of dacryoadenitis and systemic inflammatory disease (sarcoidosis). Proptosis and shorter symptom duration were significantly associated with malignancy, whereas bilateral involvement was significantly associated with inflammatory disorders. No statistically significant difference in tumor classification was observed between male and female patients. **Conclusion:** Lymphoid and inflammatory disorders were the most prevalent lacrimal gland lesions. Identifying clinical markers such as proptosis, symptom duration, laterality can assist in early malignancy detection and guide management decisions effectively. This study is limited by its retrospective design, single-center setting, and small sample size, which may introduce selection bias and limit generaizability.

Introduction

Tumors of the lacrimal gland have an incidence of 1 case per 1,000,000 persons per year and constitute approximately one quarter of orbital space-occupying lesions with the majority being benign.[1] Lesions of the lacrimal gland may be considered in five distinct groups: inflammations, lymphoproliferative disorders, epithelial tumors, metastatic tumors, and cystic lesions. Together, they constitute approximately 5% to 10% of all orbital masses.[2] The diagnosis depends on the histopathological findings which helps in the choice of treatment and the prognosis.[3]

Lacrimal gland tumors are usually grouped into two types: epithelial and non-epithelial. Most cases are non-epithelial, making up about 70–80% of solid lacrimal gland masses. The most common cause is non-specific inflammation, known as dacryoadenitis.[4] After that, lymphoma is the next most common non-epithelial tumor, making up around 37% of malignant cases. For epithelial tumors, the most common benign type is pleomorphic adenoma, while the most common malignant type is adenoid cystic carcinoma (ACC), which accounts for about 60% of malignant epithelial tumors.[5]

Although the epidemiology and histopathological patterns of lacrimal gland tumors have been described in several studies, there is a paucity of data from Indonesia, particularly Central Java, where published reports are scarce. The lack of regional data limits understanding of local disease patterns and may affect clinical decision-making. Therefore, this study aims to evaluate the clinico-demographic characteristics, clinical presentation, and histopathological spectrum of lacrimal gland tumors treated at a tertiary care hospital in Central Java.

Method

A retrospective observational study was conducted on 47 eyes of 39 patients diagnosed with lacrimal gland tumors and managed over a 4-year period from January 2021 to December 2024 at the Reconstructive Oculoplastic and Oncology Department of Kariadi Hospital in Semarang. Only cases with a clearly documented diagnosis of lacrimal gland tumor in the medical records were included. All cases underwent histopathological examination, which served as the basis for final classification.

Data collected included patient demographics, clinical presentations, imaging findings, and histopathological diagnoses. Orbital imaging (computed tomography and/or magnetic resonance imaging) was reviewed in all cases as part of the diagnostic work-up. Clinical characteristics analyzed included patient age, sex, laterality, duration of symptoms, presence of proptosis, lagophthalmos, ocular motility restriction, and metastatic features. Histopathological diagnoses were categorized into benign tumors, malignant tumors, and inflammatory disorders. Inflammatory disorders were defined as histopathologically confirmed dacryoadenitis or lacrimal gland involvement secondary to systemic inflammatory disease, including sarcoidosis.

Patients with incomplete medical records or those who had received prior interventions (such as chemotherapy or radiotherapy) that could influence histopathological interpretation were excluded. Data were analyzed using SPSS version 21. Descriptive statistics, including mean ± standard deviation, median, and frequency (%), were calculated. The chi-squared test or Fisher's exact test was used to assess associations between categorical variables. A p-value of < 0.05 was considered

statistically significant. **This** study had the ethical approval from the Ethics committee of the hospital.

Results and Discussion

Table 1. Sociodemographic and Clinical Presentation.

Variabel	Frekuensi	%	Mean ± SD	Median (Min-Max)
Age (years)			46,15 ± 20,27	49 (2 – 76)
0 – 18	3	7,7		
19 – 36	13	33,3		
40 – 59	10	25,6		
> 60	13	33,3		
Sex				
Males	19	48,7		
Females	20	51,3		
Laterality				
Unilateral	28	71,8		
Bilateral	11	28,2		
Duration of symptom (year)				
< 1	20	51,3		
> 1	19	48,7		
Protrusion of eyeball				
Yes	15	38,5		
No	24	61,5		
Lagoftalmos				
Yes	9	28		
No	30	76,9		
Restricted Ocular Movement				
Yes	10	25,6		
No	29	74,4		

The study included 47 eyes with a mean age of 46,15 ± 20,27 (range, 2-76) years with a median of 49 years, age distribution showed that 7.7% of patients were aged 0–18 years, 33.3% were 19–36 years, 25.6% were 40–59 years, and 33.3% were over 60 years old. 20 (51.3%) were females and 19 (48.7%) were males. Unilateral involvement was seen in 28 patients (71.8%), Bilateral involvement occurred in 11 patients (28.2%). The duration of symptoms was less than 1 year in 20 cases (51.3%), more than 1 year in 19 cases (48.7%). The patient presented with proptosis (eyeball protrusion) was present in 15 patients (38.5%), Lagophthalmos was found in 9 patients (23.1%), Restricted ocular movement was noted in 10 cases (25.6%). (Table 1)
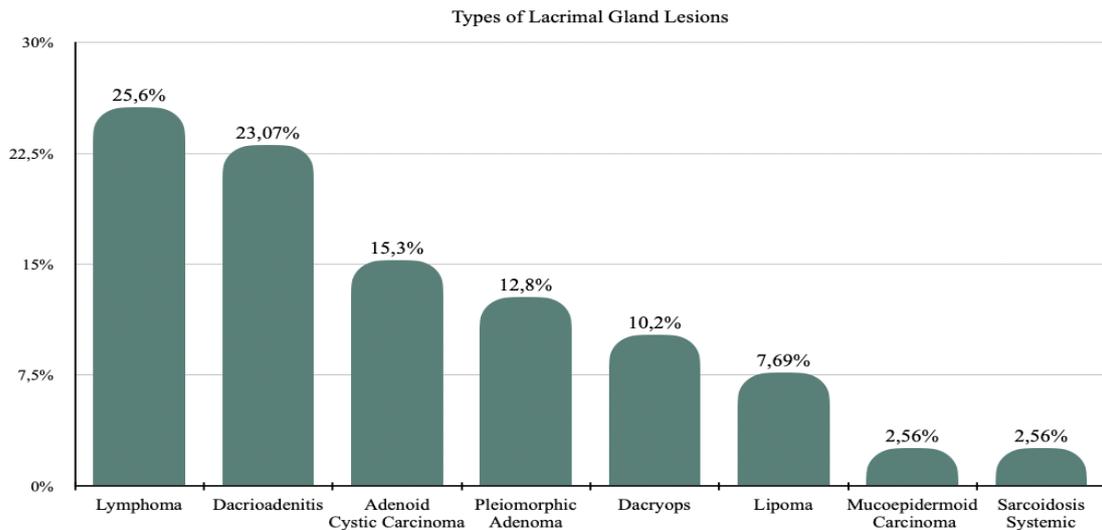
Types of Lacrimal Gland Lesions

Figure 1. Types of lacrimal gland lesions

Histopathological analysis based on patients revealed **lymphoma in 10 (25.64%)** as the most common lesion, followed by **dacryoadenitis in 9 (23.07%), adenoid cystic carcinoma in 6 (15.38%), pleomorphic adenoma in 5 (12.82%), dacryops in 4 patients (10.25%), lipoma in 3 (7.69%), mucoepidermoid carcinoma in 1 (2.56%),** and **systemic sarcoidosis in 1 (2.56%).** Based on histopathological findings, lesions were broadly classified as tumor lesions (benign and malignant) and non-tumor lesions (inflammatory and cystic). Non-tumor lesions accounted for a substantial proportion of cases, predominantly inflammatory disorders. (Figure 1).

Table 2. Sex and tumor classification

Sex	Tumor Classification						P
	Benign		Malignant		Inflammatory		
Female	n	%	n	%	n	%	
Male	6	31,6	8	42,1	5	26,3	0,612

Although a slight female predominance was observed overall, no statistically significant association was found between sex and tumor classification (p > 0.05), suggesting that lacrimal gland lesions in this study affected both sexes similarly. (Table 2)

Table 3. Age group and tumor classification

Age (years)	Tumor Classification						P
	Benign		Malignant		Inflammatory		
	n	%	n	%	n	%	
0 – 18	2	66,7	0	0	1	33,3	
19 – 36	4	30,8	5	38,5	4	30,8	0,098
40 – 59	6	60	3	30	1	10,0	
> 60	1	7,7	9	69,2	3	23,1	

The relationship between age group and tumor classification was analyzed (Table 3). Although variations were observed across age categories, the association did not reach statistical significance (p = 0.098). In the 0–18 years group, the majority of cases (66.7%) were benign, and 33.3% were classified as inflammatory; no malignant tumors were found. Among individuals aged 19–36 years, 38.5% had malignant tumors, while 30.8% had benign tumors and 30.8% had inflammatory disorders. In the 40–59 years group, 60.0% had benign tumors, 30.0% had malignant tumors, and 10.0% had inflammatory lesions. Patients aged over 60 years most frequently had malignant tumors (69.2%), followed by inflammatory (23.1%) and benign tumors (7.7%). While malignant lesions were more commonly observed in older age groups—particularly in those over 60 years—the association was not statistically significant based on the Chi-Square test (p > 0.05)

Table 4. Clinical Presentation and Tumor Classification

Variable	Tumor Classification						P
	Beningn		Malignant		Inflammatory		
	n	%	n	%	n	%	
Proptosis (Protrusion of eyeball)							
Yes	5	33,3	10	66,7	0	0	0,014
No	8	33,3	7	29,2	9	37,5	
Restricted Ocular Movement							
Yes	4	40,0	6	60,0	0	0	0,128
No	9	31,0	11	37,9	9	31,0	
Metastase							
Yes	1	16,7	4	66,7	1	16,7	0,453
No	12	36,4	13	39,4	8	24,2	
Duration of symptom (1 year)							
Yes	3	15,0	12	60,0	5	25,0	0,034
No	10	52,6	5	26,3	4	21,1	

The analysis assessed the relationship between clinical variables and tumor classification. Proptosis (protrusion of eyeball) showed a significant association with tumor classification (p = 0.014). Among patients with proptosis, 66.7% had malignant tumors, while 33.3% had benign tumors. Notably, none of the patients with proptosis had inflammatory disorder. In contrast, among those without proptosis, 33.3% had benign tumors, 29.2% had malignant tumors, and 37.5% had inflammatory disorder. Similarly, symptom duration was significantly associated with tumor classification (p = 0.034). In patients with symptoms for less than one year, 60.0% had malignant tumors, while 15.0% were benign and 25.0% were inflammatory. In contrast, among those with symptoms for more than one year, 52.6% had benign tumors, 26.3% malignant, and 21.1% inflammatory disorder. These findings, supported by Chi-Square test results with p-values below 0.05 for both variables, indicate that proptosis and shorter symptom duration are significantly associated with malignant tumor classification. (Table 4)

The relationship between inflammatory disorders and lesion laterality was analyzed, revealing a significant association (p = 0.001). Among patients diagnosed with inflammatory disorders, 77.8% had bilateral involvement, while only 22.2% had unilateral lesions. Conversely, in patients without inflammatory disorders, the majority (86.7%) had unilateral lesions, and only 13.3% had bilateral involvement. These results suggest that bilateral presentation is strongly associated with inflammatory lacrimal gland lesions, whereas non-inflammatory lesions are more commonly unilateral.

Discussion

This study analyzed 47 eyes from 39 patients with lacrimal gland lesions, providing valuable insights into their clinical presentation, histopathology, and potential diagnostic indicators. Our study showed the mean age of diagnosis 46,15 ± 20,27 years, similar to another study (41.67 years). Although there was a female predominance in our study, a greater number of males presented with malignant tumors similar to another study.[6] Other studies showed no gender preference.[7]

The most frequently identified lesions in our study were lymphomas (25.6%) and dacryoadenitis (23.1%), followed by adenoid cystic carcinoma (15.4%) and pleomorphic adenoma (12.8%). These findings align with global literature indicating that non-epithelial lesions, especially lymphoproliferative and inflammatory disorders, account for the majority of lacrimal gland masses.[8,9] A study by Qian et al. analyzing 582 lacrimal gland biopsies found similar trends, with lymphoid and inflammatory conditions comprising the largest categories.[10] Although age was not statistically associated with tumor classification (p = 0.098), notable trends were observed. Malignant tumors predominated in patients over 60 years, whereas benign lesions were more frequent among those aged 40–59 years. This age-related trend has been documented in previous literature, where malignancies like adenoid cystic carcinoma and orbital lymphomas have a predilection for older adults.[11,12]

The age distribution varies among these various conditions. Infection of the lacrimal gland is more common in children, whereas noninfectious inflammations occur frequently in young and middle-aged populations. Lymphoma is frequent in the sixth decade of life but may occur at all ages. Epithelial tumors may also occur in patients of all ages but are primarily a disease of middle-aged adults. PA, the most common primary lacrimal gland solid tumor, presents at a mean age of 40 years, with a range from 8 to 80 years. Adenoid cystic carcinoma (ACC), the most common lacrimal gland epithelial malignancy, has a bimodal age distribution, with most patients diagnosed in their 40s and a smaller peak in the teenage years.[2]

Significant associations were found between proptosis and shorter symptom duration (<1 year) with malignant tumor classification (p = 0.014 and p = 0.034, respectively). These findings are consistent with previous studies that noted proptosis, globe displacement, and rapid onset as key clinical indicators of malignancy, particularly in adenoid cystic carcinoma and lymphoma.[13] Proptosis often indicates rapid orbital expansion, which is more characteristic of high-grade tumors or invasive lesions, such as adenoid cystic carcinoma or orbital

lymphoma. In contrast, benign and inflammatory lesions tended to present with slower progression and less pronounced ocular displacement, making history-taking and symptom duration equally important in differentiating the lesion type.

Laterality has long been recognized as a clinically relevant parameter in the evaluation of orbital diseases, particularly lacrimal gland pathologies. In this study, we found a significant association between bilateral involvement and inflammatory lacrimal gland disorders (p = 0.001). Among patients with histopathologically confirmed inflammatory lesions, 77.8% presented with bilateral disease, whereas 86.7% of patients without inflammatory disorders exhibited unilateral lesions. This finding strongly supports the hypothesis that bilateral lacrimal gland involvement is a hallmark of inflammatory rather than neoplastic processes. Our results align closely with findings from recent international studies. Plaza et al. (2020) and Ramos et al. (2023) both emphasized the diagnostic value of bilaterality as a clinical clue toward inflammation, particularly in IgG4-related disease and chronic dacryoadenitis. In those studies, bilateral gland involvement was reported in more than 70% of inflammatory cases, consistent with our observed rate of 77.8%.[15,16]

The lacrimal glands are frequently affected in systemic inflammatory and autoimmune diseases, such as IgG4-related disease (IgG4-RD), sarcoidosis, Sjögren's syndrome, and idiopathic orbital inflammation (IOI). These conditions often exhibit symmetrical and chronic involvement of the lacrimal glands, leading to bilateral swelling that is often painless and progressive.[2]

In contrast, neoplastic processes—whether benign (e.g., pleomorphic adenoma) or malignant (e.g., adenoid cystic carcinoma, lymphoma)—tend to be localized and unilateral due to their focal origin within glandular or lymphoid tissue. While bilateral orbital lymphoma does occur, it remains relatively uncommon compared to the bilateral presentation seen in inflammatory diseases.[2]

This study is limited by its retrospective nature, small sample size, and single-center setting, which may reduce the generalizability of the results. The lack of radiologic and immunohistochemical data reduces diagnostic depth and accuracy. Additionally, the absence of follow-up data limits the ability to evaluate treatment outcomes.

Conclusion

This study highlights the varied clinical and histopathological presentations of lacrimal gland lesions, with lymphomas and inflammatory disorders emerging as the most prevalent types. While age group was not statistically associated with lesion classification, malignancies were more commonly observed in older individuals. Notably, clinical signs such as proptosis and shorter symptom duration showed a significant relationship with malignant lesions, whereas bilateral involvement was more indicative of inflammatory conditions. These results indicate that certain clinical features can serve as important diagnostic indicators in differentiating lacrimal gland disorders. These findings may assist clinicians in early risk stratification prior to biopsy. Careful assessment of these signs may facilitate earlier detection, minimize delays in

diagnosis, and support more effective treatment planning.

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