Section: Miscellaneous

Original Research Article

HISTOPATHOLOGICAL AND CLINICAL CORRELATION OF PTERYGIUM CASES IN A TERTIARY CARE CENTRE IN SOUTH INDIA

Divya P[1], Annie Rose L[2], Anupriya A[3], Ragavi Venkataramanan[4]

[1]Assistant Professor, Department of Ophthalmology, St Peter's Medical College, Hospital and Research Institute, Hosur, Krishnagiri, Tamil Nadu, India.
[2]Assistant Professor, Department of Pathology, St Peter's Medical College, Hospital and Research Institute, Hosur, Krishnagiri, Tamil Nadu, India.
[3,4]Assistant Professor, Department of Ophthalmology, St Peter's Medical College, Hospital and Research Institute, Hosur, Krishnagiri, Tamil Nadu, India.

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Corresponding Author:
Dr. Divya P,
Assistant Professor, Department of Ophthalmology, St Peter's Medical College, Hospital and Research Institute, Hosur, Krishnagiri, Tamil Nadu, India.
Email: divyapalaksha04@gmail.com

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ABSTRACT

Background: To determine the correlation between clinical and histopathological changes in pterygium patients and to investigate its relevance in recurrence of the pterygium.

Material and Methods: A total of 50 patients with pterygium who underwent excision with conjunctival auto graft, were subjected to histopathological study and the results were correlated to clinical findings prospectively. Prior to surgery, clinical features of pterygium such as redness, fleshiness, extent over the cornea was recorded and grading was done using slit lamp biomicroscopy. Post operatively the pterygium specimens were investigated by haematoxylin-eosin(H&E) and (VVG) Verhoeff's- van Gieson's elastic stain to look for epithelial and stromal changes. All the patients were followed up clinically post operatively for 3 months to look for recurrence of pterygium and their histopathological relevance were studied.

Results: This study examined 50 patients (88% female, mean age 51±12.4) undergoing pterygium surgery. Indications for surgery included cosmetic concerns (56%), astigmatism >2D (30%), recurrent redness/pain (10%), and pre-cataract surgery (4%). Pterygium severity: 16% grade 1, 70% grade 2, 14% grade 3, with a mean length of 3.32±1.26 mm and width of 3.92±1.15 mm. Redness was observed in 22% (grade 1), 64% (grade 2), and 16% (grade 3); fleshiness in 18% (grade 1), 52% (grade 2), and 30% (grade 3). Significant correlations were found between pterygium grade, redness, fleshiness, and astigmatism >2D ($p<0.01$, $p=0.03$). Histopathology revealed epithelial hyperplasia (94%), atrophy (38%), pigmentation (58%), and goblet cell hyperplasia (12%). Vascular density averaged 8.30±2.09 vessels/HPF. Stromal inflammation, hemorrhage, elastosis, and elastotic degeneration were prevalent (82%, 100%, 98%, and 96%, respectively). One recurrence occurred after 2 months.

Conclusion: Our study highlights the significant clinical and histopathological findings associated with pterygium, emphasizing the correlation between features such as redness, fleshiness, and vascularity with histopathological changes like stromal inflammation and elastosis. The non-carcinogenic nature of pterygium was confirmed, as no dysplasia was observed. Moreover, histopathological evaluation of excised tissues is crucial, as it may reveal underlying ocular surface squamous neoplasia or concurrent malignancies. These findings underscore the importance of tailored treatment strategies and ongoing surveillance for improved management of pterygium.

Keywords: Pterygium, Eye Disorders.

INTRODUCTION

Pterygium is a conjunctival disorder with a global prevalence of 12%.[1]

It is a fleshy, triangular, wing shaped fold of conjunctiva encroaching on the cornea. It is an active benign proliferative lesion with inflammatory process associated with cellular proliferation, angiogenesis, connective tissue remodeling, fibrinoid change etc.

Ocular surface inflammation is broadly accepted to play a prominent role in the initial pterygium pathogenesis and in its recurrence.[2]

It is most commonly seen in hot climatic regions and long term exposure of the ocular surface for solar UV irradiation is found to be a common risk factor for its development.[3,4] This postulation is supported by increased numbers of pterygium cases in populations living in tropical regions.[5]

The treatment includes surgical excision with conjunctival auto graft to prevent it from causing astigmatism, obscuration of visual axis, diplopia, recurrent inflammation, restriction of eye motility and for cosmetic purposes.

Our present study will determine the correlation between histopathological changes and clinical findings in pterygium cases. This might help in providing better interpretation of the pathogenesis and management guidelines,[6] to reduce recurrence, inflammation, vascularization,[7] etc.

MATERIALS AND METHODS

A total of 50 patients undergoing pterygium excision with conjunctival auto graft reconstruction of the bare sclera were subjected to histopathological evaluation in the year 2024, in accordance with international agreements and declaration of Helsinki (2013). The study was approved by institutional ethical committee and informed consent was obtained from all patients before data collection, surgery and pathological evaluation.

Patients with the following conditions that can individually cause histopathological changes were excluded from the study:

1. Recurrent pterygium cases
2. Previous ocular trauma
3. Previous ocular surgery
4. Chronic cicatricial conjunctival diseases, chronic dry eye.
5. Patient who are on long term topical eye medications.

All the patients posted for surgery underwent a complete ocular examination by slit lamp biomicroscopy. Morphological clinical features of the pterygium including redness, fleshiness, extent, dimensions were recorded and photographs were taken. The dimensions included length (distance from the apex of the pterygium to the limbus) and width (distance between two opposite edges intersecting the limbus). All patients underwent retinoscopy and the level of astigmatism was categorized as less than or more than 2D.

Extent of the pterygium was graded as Grade 1: between limbus and point midway between limbus and pupillary area, Grade 2: till pupillary area, Grade 3: crossing pupillary area.[8]

Redness of the pterygium was graded as, Grade I: no redness or faint pinkish hue, Grade II: scattered areas with moderate redness, Grade III: significant diffuse redness.[9]

Fleshiness of the pterygium was graded based on Tan's classification:,[10]

T1: Atrophic - Episcleral vessels visible beneath the body of the pterygium.

T2: Intermediate - Episcleral vessels partially visible beneath the body of the pterygium

T3: Fleshy – Episcleral blood vessels obscured

All the patients were admitted and surgery was done on an inpatient basis and discharged the next day.

Surgical Procedure

Under all aseptic precautions, under local anaesthesia, eye was painted and draped, speculum put, pterygium head was peeled from the cornea and excised along with the subconjunctival fibrous tissue. Conjunctival auto graft was taken from the superior conjunctiva and fixed to the bare sclera using 8-0 vicryl suture. Pad and bandage was put for a day and patient was evaluated in slit lamp next day before discharge. All the patients withstood the procedure well. Prophylactic oral and topical antibiotics with topical steroids and lubricants application was advised post operatively. Patients were followed up 1 week, 1 month, 3 months post operatively and any recurrence of the pterygium was documented.

The excised tissue was fixed in 10% buffered neutral formalin immediately, processed and embedded in paraffin tissue blocks. Two sets of sections of 5 mm thickness were made for each block. One section was stained with H&E and another section stained with VVG stain (Verhoeff-van Gieson's elastic stain). The sections were evaluated by one pathologist and cross verified by another; both of them were masked to the clinical data of the cases.

The sections were observed for the following histopathological parameters

Epithelial hyperplasia was termed when epithelium with more than six layers thickness was noted and epithelial atrophy when less than three layers thickness seen. Goblet cell density was determined by averaging the total number of goblet cells in 10 consecutive visual fields of high magnification (400x) and was graded as absent, present or increased (hyperplasia is >20 cells).

Epithelial pigmentation was categorized as present or absent based on the presence of pigments in the basal or suprabasal keratinocytes. Some authors even consider this as primary acquired melanosis,[11] and few others as conjunctival hypermelanosis.[12]

To study the stromal vascular density, the whole tissue was examined and three densely vascular high-power fields (400x) were selected and the number of vessels was counted in all three fields and the average was taken. Vascular spaces with endothelial lining and red blood cells within the lumen were considered for counting.

Stromal inflammation was documented as presence of leucocytic infiltration in the stroma and the type of leucocytes (lymphocytes or mixed- lymphocyte with neutrophil) was noted. The stromal inflammation was graded as Grade 0: Absent or very few leucocytes, Grade 1: Mild or patchy leucocytic infiltrate and Grade 2: Moderate to dense or diffuse infiltrates.

Stromal hemorrhage was graded as; Nil: No obvious hemorrhage, Mild: hemorrhage in one or two high power fields (400x), dense: hemorrhage involving more than two high power fields (400x).

Stromal elastosis were documented as present or absent when observed on H&E and VVG stained sections. Elastotic degeneration of collagen were reported as present or absent, observed on H&E and VVG stained sections showed wavy vermiform appearance of fibres.

Statistical Analysis

It was calculated by considering the study - Prevalence and associated factors for pterygium in rural agrarian central India done by Nangia et al,[13] Using open epi version 3.01, with confidence interval (1-α) of 95% with prevalence of 12.9% and absolute precision of 10%, total cases to be studied was 48.

Data Collection: the data will be collected using standard questionnaire for basic demographic data. Details of the morphology will be noted using slit lamp biomicroscope and histopathological findings of the pterygium will be noted using lab reports.

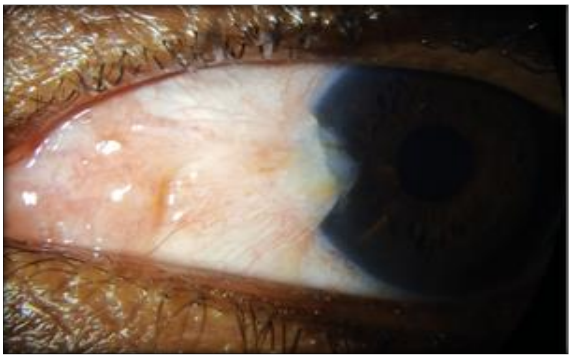
The data will be entered in the Microsoft excel sheet version 2010. After data coding, editing and data cleaning, it will be transferred to SPSS version 24 for analysis. To test the association between the groups, Chi- Square test will be used. Any p <0.05 will be considered statistically significant. To test the mean difference student-t test will be used.

RESULTS

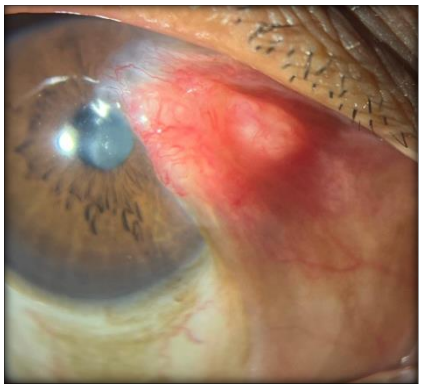
Of the 50 patients in the study; 44 patients (88%) were females and 6 patients (12%) were males. The age ranged from 25 to 73 years (mean age 51±12.4). 56% of the patients underwent surgery for cosmetic complaints, 30% had a decreased vision due to astigmatism of >2D, 10% due to recurrent redness and pain and 4% had excision of pterygium as a pre requisite prior to cataract surgery.

The pterygium extent over the cornea was grade 1 in 8 patients (16%), grade 2 in 35 patients (70%) and grade 3 in 7 patients (14%). The mean length was 3.32±1.26 mm (range from 1.5 mm – 6.2mm) over the cornea and the mean width was 3.92±1.15 mm (range from 2.5mm to 7.1 mm).

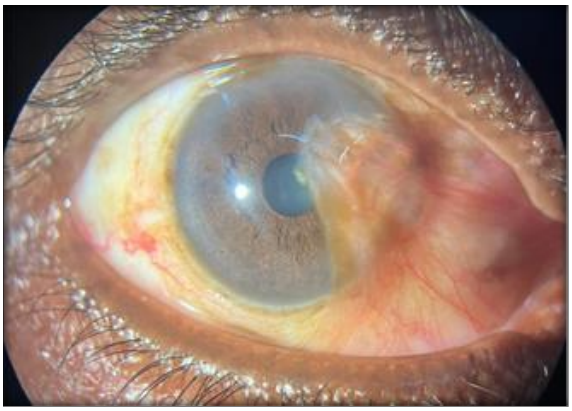
The pterygium redness with grade 1 was seen in 11 patients (22%), grade 2 in 32 patients (64%), and grade 3 in 8 patients (16%). Fleshiness of the pterygium with grade 1 (T1) was noted in 9 patients (18%), grade 2(T2) in 26 patients (52%) and grade 3 (T3) in (15%). A significant correlation was seen between the grade of redness and fleshiness (p value - <0.001) (Table 1). 34% had an astigmatic refractive error of <2 D and 16% had >2D.



Grade 1: Redness



Grade 3: Redness and fleshiness and extent of pterygium

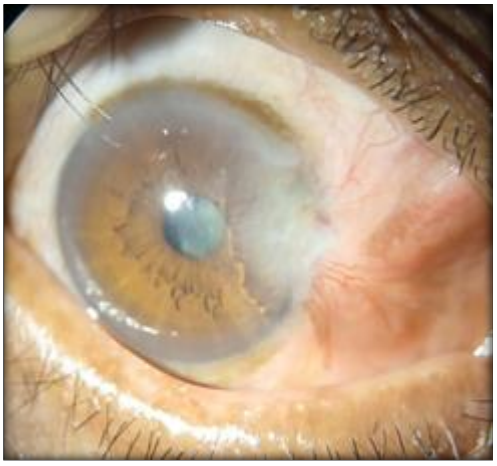


Grade 3: Extent of pterygium

On retinoscopy, 34% had an astigmatic refractive error of <2 D and 16% had >2D power. There was also statistically significant positive correlation between the higher grades of pterygium with respect to extent (p value <0.01), fleshiness (p value <0.01),

redness (p value 0.03) and >2D of astigmatic power. [Table 2]

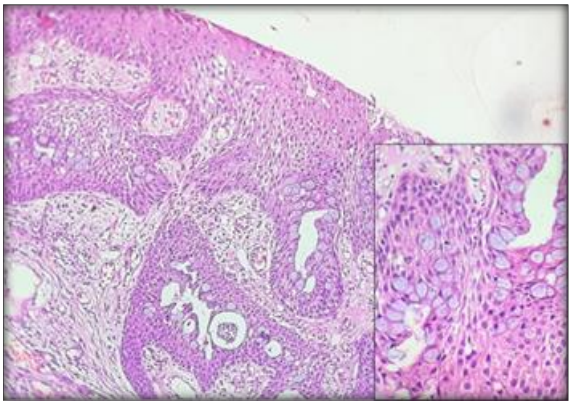
Recurrence of the pterygium was seen in 1 patient with a grade 3 pterygium after 2 months of surgery, epithelial hyperplasia and grade 2 stromal inflammation was noted on histopathology.



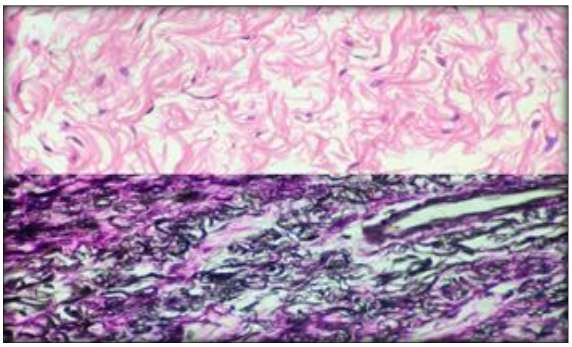
Histopathological epithelial changes like epithelial hyperplasia was seen in 94% of the patients, 38% had epithelial atrophy; squamous metaplasia was seen in 20%, reactive epithelial atypia was seen in 22%. Epithelial pigmentation was noted in 58% of patients.

Goblet cell hyperplasia (>20 cells) was noted in 12%. Mean vascular density was 8.30±2.09 (range 4- 12) vessel /HPF.

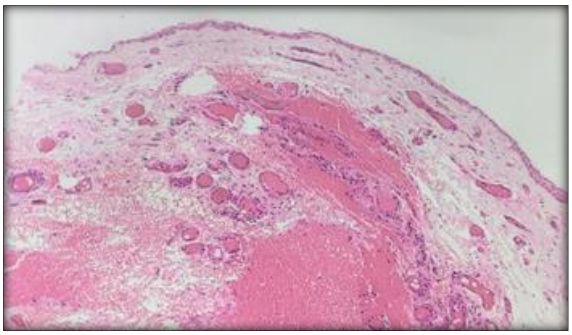
Stromal changes like stromal inflammation with leuckocytic infiltration was seen in 41 patients (82%) where in 31 had grade 1(mild) inflammation and 4 patients had grade 2 (significant) inflammation. Significant number of patients had stromal changes like; stromal hemorrhage seen in all patients (100%), stromal elastosis was seen in 49 patients (98%) and elastotic degeneration was noted in 96% of the patients.



H&E stain (400x magnification: Epithelial hyperplasia, Squamous metaplasia with Goblet ell hyperplasia (right)



Elastotic degeneration 400x magnification:
H&E stain (Top), Verhoeff-van Gieson's elastic stain (Bottom)



H&E 40x magnification: Increased stromal vascular density and stromal hemorrhage

These histological findings were correlated with the grade of redness and fleshiness of pterygium. [Table 3 and 4]

Table 1

Sl.no	Clinical Findings	Grade – 1 n	%	Grade – 2 n	%	Grade – 3 n	%	P- value
1.	Redness of pterygium	8	16	34	68	8	16	<0.001
	Fleshiness of pterygium	9	18	26	52	15	30	

Table 2

Sl.no	Degree of astigmatism	Grade – 1 n	Grade – 2 n	Grade – 3 n	P- value
1.	Extent of pterygium				
	<2D	8	29	0	<0.01
	>2D	0	5	8	
2.	Fleshiness of pterygium				

	<2D	9	22	6	<0.01
	>2D	0	4	9	
3.	Redness of pterygium				
	<2D	8	30	0	0.03
	>2D	0	4	8	

Table 3: Redness

Sl. No		Grade of redness						P - value
		Grade 1 (n=8)		Grade 2 (n=34)		Grade 3 (n=8)		
		n	%	n	%	n	%	
1.	Epithelial hyperplasia	7	87.5	32	94	8	100	0.302
2.	Goblet cell hyperplasia	4	50	13	38.2	3	37.5	1.000
3.	Reactive atypia	1	12.5	7	20.5	1	12.5	1.000
4.	Squamous metaplasia	1	12.5	9	26.4	1	12.5	0.542
5.	Sub-epithelial fibrosis	6	75	22	64.7	7	87.5	1.000
6.	Stromal inflammation i. Grade 1 ii. Grade 2	 3 0	 37.5 0	 24 4	 70.5 11.7	 8 0	 100 0	0.645
7.	Fragmented basement membrane	8	100	34	100	8	100	1.000
8.	Stromal elastosis	7	87.5	33	97	8	100	1.000
9.	Elastotic degeneration	7	87.5	32	94	8	100	1.000
10.	Epithelial pigmentation	5	62.5	17	50	6	75	1.000
11.	Calcification	1	12.5	4	11.7	0	0	0.415

Table 4: Fleshiness

Sl. No		Grade of fleshiness (TAN's classification)						P - value
		Grade 1 (n=9)		Grade 2 (n=26)		Grade 3 (n=15)		
		n	%	n	%	n	%	
1.	Epithelial hyperplasia	9	100	23	88.4	15	100	0.244
2.	Goblet cell hyperplasia	3	33.3	11	42.3	7	46.6	0.831
3.	Reactive atypia	0	0	6	23	5	33.3	0.876
4.	Squamous metaplasia	2	22.2	6	23	2	13.3	0.263
5.	Sub-epithelial fibrosis	7	77.7	17	65.4	11	73.3	0.926
6.	Stromal inflammation i. Grade 1 ii. Grade 2	 2 0	 22.2 0	 19 2	 73 7.6	 14 2	 93.3 13.3	0.224
7.	Fragmented basement membrane	9	100	26	100	15	100	1.000
8.	Stromal elastosis	8	88.8	25	96	15	100	0.432
9.	Elastotic degeneration	8	88.8	24	92	15	100	0.586
10.	Epithelial pigmentation	5	55.5	13	50	10	66.6	0.563
11.	Calcification	1	11.1	3	11.5	1	6.6	0.686

DISCUSSION

Pterygium, being a very common ocular condition has been studied to look for the correlation between the clinical features and histopathological findings which might aid in the understanding of pathogenesis of the disease. It might also give insights regarding the treatment modalities- pre, intra and post operatively to decrease the inflammation, vascularity, recurrence etc.

In our study the number of female patients who underwent pterygium excision was higher (88%) compared to males in contrast to other studies. Of these patients 56% had cosmetic complaints, 34% had recurrent inflammation and the rest 10% had a visual disturbance indicating surgical excision. The mean age of the patients was 51±2.4 years and 42 patients were older than 40 years, which is similar to the studies done by Qadi R et al,[14] and Bueno et al,[15] showing higher prevalence in older than 40 years age.

A statistically significant positive correlation was seen between the degree of redness and fleshiness of the pterygium (p value-<0.001) similar to multiple other studies.[9,16,17]

22% of the patients in our study had reactive atypia, squamous metaplasia was seen in 20%, and none had dysplasia suggesting the non carcinogenic nature of pterygium in accordance with van acker et al.[4,18] Epithelial pigmentation was noted in 58% of patients. Goblet cell hyperplasia (>20 cells) was noted in 12% of the patients which was lesser in number compared to other studies.

Stromal elastosis was seen in 98% and elastotic degeneration of collagen stained with VVG stain and H&E were noted in 96% of our cases as pterygium is aptly described as degenerative disorder.[19]

A significant stromal inflammation with leukocytes was noted in 82% of the cases and the mean vascular density was 8.30±2.09 (range 4- 12) vessel /HPF. There was a significant correlation between redness, fleshiness and leukocytic infiltration, suggesting that preoperative use of topical steroids would help in decreasing the inflammation and

vascularity hence reducing the intraoperative bleed and discomfort.

This also gives insights into the new modality of treatment of decreasing the redness, size, extent and symptoms, by injecting sub conjunctival anti Vegf (vascular endothelial growth factor) as mentioned in the study by pathania et al.[20]

Recurrence was seen in 1 patient who had a pterygium of grade 3 fleshiness, redness and epithelial hyperplasia with higher vascularity on histopathology in accordance with the findings of the study done by shweta et al.[21]

We would also want to propose that all the excised pterygium tissues should be evaluated histopathologically, as there is a possibility of unsuspected and (ocular surface squamous neoplasia) in patients with pterygium as described by Lomeli-Linares D,[22] and also concurrent carcinoma in situ, Squamous cell carcinoma was seen in 17 and 12% of patients with pterygium in a study done by Sevel D et al.[23]

CONCLUSION

Our study highlights the significant clinical and histopathological findings associated with pterygium, emphasizing the correlation between features such as redness, fleshiness, and vascularity with histopathological changes like stromal inflammation and elastosis. The non-carcinogenic nature of pterygium was confirmed, as no dysplasia was observed. Moreover, histopathological evaluation of excised tissues is crucial, as it may reveal underlying ocular surface squamous neoplasia or concurrent malignancies. These findings underscore the importance of tailored treatment strategies and ongoing surveillance for improved management of pterygium.

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