

## OCULAR ADNEXAL LYMPHOMAS- A CLINICOPATHOLOGIC AND HISTOMORPHOLOGIC ANALYSIS

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### ABSTRACT

#### BACKGROUND

Ocular adnexal lymphomas are mainly Non-Hodgkin's lymphomas distributed in the conjunctiva, orbit and eyelids. These lymphomas are the commonest of the ocular adnexal lymphoid proliferations. In this study, ten cases of ocular adnexal lymphomas were analysed over a three year period.

#### MATERIALS AND METHODS

Comparison of clinicopathologic and histomorphologic features was done in ten cases of ocular adnexal lymphomas. Immunohistochemical confirmation was obtained in six cases.

#### RESULTS

Of ten cases, equal incidence (40% each) was found in conjunctiva and orbit with eyelid forming 20%. Most common presentation of intraocular lymphoma was found to be decreased vision with non-resolving uveitis. Orbital tumours presented as proptosis with visible conjunctival mass. The commonest histologic type of intraocular NHL is extra nodal marginal zone lymphoma (MALT lymphoma). Primary intraocular lymphomas are unilateral and 75% cases become bilateral with central nervous system involvement and death.

#### CONCLUSION

The present study is a retrospective analysis of ten cases of ocular adnexal lymphomas over a period of three years. Clinicopathologic and histomorphologic analysis was done in detail. Immunohistochemical confirmation was obtained in 6 cases.

#### KEYWORDS

Ocular Adnexa, Clinicopathologic and Histomorphologic Study, MALT Lymphoma, Immunohistochemistry.

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#### BACKGROUND

Ocular adnexal lymphomas are the commonest of the ocular adnexal lymphoid proliferations. The commonest type is Non-Hodgkin's lymphoma, intraocular Hodgkin's lymphoma being rare. The most common presentation of intraocular lymphoma is decreased vision with non-resolving uveitis. Orbital tumours usually present as proptosis and visible conjunctival mass.

The commonest histological type of intraocular NHL is extranodal marginal zone lymphoma.<sup>1</sup> (MALT lymphoma). Primary intraocular malignant lymphomas are unilateral and 75% cases become bilateral with central nervous system involvement and death.<sup>2</sup> The present study is a retrospective

analysis of ten cases of ocular adnexal lymphomas over a period of three years.

#### MATERIALS AND METHODS

A retrospective analysis from March 2007 to March 2010 was conducted which included ten cases that were diagnosed as ocular Non-Hodgkin's lymphoma. The ocular adnexal area was divided into conjunctiva, orbit and eyelids. Parameters analysed included clinical presentation, correlation with clinical diagnosis, radiological and peroperative findings and pathological investigations (peripheral smear examination, cytology, macroscopy and histopathology).

Diagnosis was based on histomorphologic and immunophenotypic characters. All the cases had H & E stained sections available for evaluation. Immunohistochemical confirmation was obtained in six cases and typing was according to the REAL classification. Comparison of various parameters studied and detailed histopathological examination was done in all cases.

#### Inclusion Criteria

All cases of ocular Non-Hodgkin's lymphoma diagnosed by clinical examination and histopathologic confirmation over a three year period.

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**Exclusion Criteria**

All cases of ocular lymphoid proliferations other than Non-Hodgkin’s lymphoma.

**OBSERVATIONS AND RESULTS**

The ten cases analysed were found at three specific sites – four conjunctival, four orbital and two eyelid tumours. Of these one tumour at each site was bilateral. (Table 1)

Site	Number	Unilateral	Bilateral
Conjunctival	4	3	1
Orbital	4	3	1
Eyelid	2	1	1

**Table 1. Site of Involvement with Incidence of Bilateral Tumours**

The age and sex distribution of the patients are shown in Table 2. There were 8 males and 2 females.

Age (Years)	M	F
10 – 20	1	0
21 – 30	0	0
31 – 40	1	0
41 – 50	2	1
51 – 60	1	1
61 – 70	3	0
<b>Total</b>	<b>8</b>	<b>2</b>

**Table 2. Age and Sex Distribution**

Majority were in 61- 70 age group.

All ten cases presented clinically as mass lesions. One conjunctival and two orbital tumours also presented with proptosis with one orbital tumour showing lateral extension into the conjunctiva. One conjunctival and one orbital tumour had short duration of presentation of less than three

months. Restrictive myopathy and optic neuropathy was associated in an orbital lymphoma.

One case of orbital lymphoma had history of similar swelling fourteen years ago also diagnosed as NHL. One eyelid lymphoma had a previous lung biopsy reported as mantle cell lymphoma.

Clinical diagnosis was lymphoma in all cases except for one conjunctival tumour diagnosed as lymphoma / haemangioma.

Radiological diagnosis suggested NHL/other malignancies e.g.: metastasis, neuroendocrine tumour in majority of cases. Exceptions were one orbital tumour in which CT was suggestive of inflammatory pseudotumour and one eyelid tumour suggestive of preseptal cellulitis. The radiological findings in the orbital tumours included both homogenous hyperdense masses and homogenous hypochoic areas.

Peripheral smear examination showed atypical lymphocytes in one orbital and one eyelid lymphoma. Fine needle aspiration cytology was done in four cases and were diagnosed as NHL. One conjunctival and one orbital lymphoma had other previous FNAC’s suggestive of inflammatory pseudotumour.

Macroscopic appearance was characteristic in one orbital tumour showing homogenous creamy white appearance on cut section. Peroperatively one conjunctival mass showed episcleral erosion while one orbital mass was seen infiltrating into the superior oblique tendon.

Histopathological features of tumours are given in Table 3.

Histopathological diagnosis given with available IHC confirmation is given in Table 4.

Sl. No.	Conjunctival Tumours		Orbital Tumours		Eyelid Tumours	
	Histopathologic Diagnosis	IHC Confirmation	Histopathologic Diagnosis	IHC Confirmation	Histopathologic Diagnosis	IHC Confirmation
1.	Small round cell neoplasm possibly NHL	MALT lymphoma (CD 20 +ve, CD 5 -ve, BD 6 -ve)	Lymphoproliferative disease s/o NHL of B cell origin.	MALT lymphoma	Malignant small round cell neoplasm – NHL	Malignant lymphoma possibly lymphoblastic lymphoma (Tdt +ve, CD 20, mib, sig inconclusive)
2.	S/o NHL low grade possibly B cell origin	-	NHL possibly low grade	MALT lymphoma	-	-
3.	Lympho-proliferative disease possibility NHL of B cell origin	-	Lympho-proliferative disease possibly NHL	S/o malignant lymphoma small cell B phenotype CCD2 0+ve cyclin D1, CD 23 CD5 – in conclusive	-	-
4.	Histo pathology suggestive of lympho-proliferative disease	Malignant lymphoma B cell consistent with MALT (CD 20 +ve CD5 -ve CD 23 -ve)	NHL IHC is recommended	-	-	-

**Table 4. Histopathologic Diagnosis with IHC Confirmation**

## DISCUSSION

Majority of tumours in our study were in the conjunctiva and orbit (40% each) with eyelid constituting 20%. A study of 82 ocular lymphomas showed majority of cases to be orbital (58%) followed by the conjunctiva (35%) and then eyelid (9%).

Lymphoid tumours are the commonest primary orbital malignancies. Most of the orbital tumours had long duration of presentation ranging from 8 months to 4 years. Orbital lymphoma is described to present as slowly enlarging lesions arising from orbit, eyelid, lacrimal gland or conjunctiva.<sup>3</sup> Lower risk of death is seen in patients with symptom duration more than 12 months and probably represents low grade histology.

Lymphoid infiltrates of the conjunctiva are associated with lower incidence of extraocular lymphoma (20%) than of orbit and eyelid (35% and 67%). None of the cases in the present study showed any evidence of extraocular lymphoma.

One tumour each at all 3 sites was bilateral. Incidence of bilateral orbital lymphoma was found to be 20% in a study compared to 10% in our study. A bilateral MALT lymphoma of the orbit has been reported in a 80 year old male<sup>4</sup> Bilaterality is associated with significantly increased risk of dissemination and significantly reduced disease specific survival.

Median age of presentation of ocular lymphoma is found to be more than 60 years.<sup>5</sup> as the present study also showed. Sex distribution is found to be variable in various studies.<sup>5</sup> with majority showing male predominance as in our study.

The present study showed mass lesion to be the commonest clinical presentation (100%) followed by proptosis (20%). A similar study showed periorbital swelling (41%) as the commonest presentation with palpable mass (28%) followed by proptosis and conjunctival mass.

Both hyperechoic masses and hypoechoic areas were found in the orbital lesions in radiology in our study. The characteristic feature described in CT scan of orbital lymphoma is well defined, lobulated or nodular homogenous masses of relatively high density and sharp margins. Hypoechoic areas have also been described in radiology.<sup>6</sup>

Two cases in the present study showed atypical lymphocytes in the peripheral smear. An unusual case of bilateral orbital MALT lymphoma with marginal zone lymphoma cells in the peripheral blood has been reported.

MALT lymphoma was the commonest histologic and immunohistochemical type in our study (40%). The commonest type of ocular adnexal lymphoma is found to be MALT lymphoma in several studies All four cases showed the characteristic histopathology with round, monocytoid, centrocyte like, plasmacytoid and few large cells. A case has been reported with similar morphologic features and poorly formed follicles.

Primary intraocular MALT lymphoma presents as localized disease and has a better outcome compared to

other types. Since small percentage recur prolonged follow up is required. A study of 15 cases of orbital lymphoma showed all cases to be low grade MALT lymphoma associated with good prognosis.

One case of lymphoblastic lymphoma was obtained in an eyelid tumour. This type along with other high grade tumours like large cell lymphoma and Burkitt's lymphoma has been described in the orbit also.

A case of small lymphocyte lymphoma in the orbit was obtained. These are less often associated with extraocular lymphoma (27%).<sup>7</sup> An unusual case of composite lymphoma of the orbit has been described in an 82 year female.

The extent of disease at the time of presentation is said to be the most important prognostic factor. Lesions of the conjunctiva are reported to have the highest overall survival rate followed by the orbit and then eyelid.

## CONCLUSION

Detailed clinicopathologic study of ocular lymphomas were done. All the cases were subjected to comparison of histopathological features. Cases diagnosed as NHL were confirmed immunohistochemically in selected cases and typed as per the REAL classification. MALT lymphoma was confirmed to be the commonest histologic subtype with best prognosis.

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