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Conjunctival Lymphoma Masquerading as Conjunctival Inflammatory Disorders

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Abstract

Aim: To diagnose conjunctival lymphoma through clinical features and correlating histopathology.

Methods: It is a retrospective case study between January 2014 - December 2019 in a tertiary eye hospital. 15 patients (5 male, 10 female) aged 30-60 years presenting with redness irritation watering of conjunctiva in both eyes treated as inflammatory lesion not resolving with topical medications. All patients underwent S/L evaluation and subjected to HPE and advised USG abdomen to look for visceral involvement.

Results: Out of 15 patients who were advised HPE only 8patient underwent HPE out of which 4 showed revealed sub epithelial focal sheets of lymphoid cells with follicle formation suggestive of atypical lymphoid hyperplasia. Other 2 patients showed B-cell NHL, 1 small cell lymphoma and 1 MALToma. None of the 15 patients had systemic involvement.

Conclusion: Conjunctival lymphomas should be included in differential diagnosis of non-resolving conjunctival inflammatory lesions. Though 7 HPE results were still awaited still all the 15 cases clinical picture is pathognomonic for diagnosing conjunctival lymphoma though HPE is confirmatory. Yearly follow up is important to look for any local recurrence and systemic involvement..

Keywords: Conjunctival Lymphoma; Masquerade; Inflamed Pterygium; Inflamed Pinguecula

Abbreviations

M: Male; F: Female; RE: Right Eye; LE: Left Eye; USG: Ultrasound; MALT: Mucosa Associated Lymphoid Tissue; HP: Histopathological; NHL: Non Hodgkins Lymphoma; EMZL: Extranodal Marginal Zone Lymphoma; DLBCL: Diffuse Large B-cell Lymphoma; HPE: Histopathological Examination; EBRT: External Beam Radiotherapy; OCT: Ocular Coherence Tomography; UBM: Ultrasound Bio- Microscopy.

Introduction

Conjunctival Lymphoma is an ocular surface tumour that usually presents as painless, mobile, 'salmon pink' nodular lesions in upper/ lower fornices and bulbar conjunctiva. These lesions are usually primary extra-nodal B-cell neoplasms, although 10 to 30 percent are secondary tumours in patients with disseminated lymphoma. They are primary Non-Hodgkin extra nodal B-cell lymphoma [1], out of which

Extranodal marginal zone lymphoma (EMZL) or MALToma (Mucosa associated Lymphoid Tissue) is most prevalent subtype followed by follicular and Diffuse Large B-cell Lymphoma (DLBCL) [2,3]. EMZL is slightly more common in female patients and typically presents in the 6th decade [4-6]. Follicular lymphoma is 2nd most common type seen in 7th decade [4,7]. DLBCL are less common and faster-growing lymphomas with equal sex preponderance, most often occur in their seventies [4,8]. Causative factor includes infectious (*Chlamydia psittaci* [9,10], *Helicobacter pylori* [11,12], *Borrelia*, Hepatitis C), Autoimmune (thyroid orbitopathy, Hashimoto thyroiditis, Sjogren syndrome, and celiac disease) [13]. The lesions normally present either in an isolated fashion in conjunctiva or in association with anteriorly located orbital lymphoid tumours [14]. They typically have indolent course and higher five-year survival rate. About 20% of patients present with bilateral involvement [15]. Lymph nodes palpation and abdominal ultrasound should be done to rule out systemic involvement and complete hemogram to rule out leukemia. The clinical and histopathological examination (HPE) helps in differentiation of benign reactive lymphoid hyperplasia from malignant lymphoid proliferations. Differential diagnosis includes Pterygium, Pinguecula, Chronic conjunctivitis Episcleritis/scleritis, Papilloma, Pyogenic granuloma, Squamous cell carcinoma, Melanoma [14]. Treatment includes excision biopsy, External Beam Radiotherapy (EBRT), intralesional injections of interferon alfa-2b, systemic rituximab, brachytherapy, cryotherapy and observation [16,17]. Here we report 15 cases of conjunctival lymphoma with clinical and HPE features who underwent conjunctival biopsy for evaluation unresponsive to various medical treatment methods.

Materials and Methods

A retrospective study was conducted on patients of conjunctival lymphoma who presented between January 2014 to December 2019 at a tertiary eye hospital. Data were retrieved and analysed from patient records stored in hospital electronic medical record system.

Results

Out of total 15 cases analysed in our study 5(33.33%) were male and 10(66.67%) were female. Demographic and clinical data of patients are detailed in Table 1. Age of our patients ranged between 30-60 years, with mean age 46.86 years. Age distribution details are summarised in Table 2. Visual Acuity (VA) at presentation ranged from 6/6 to HM, which is detailed in Table 3. Lesions in all cases appeared as pink, red sub epithelial lesion as seen in Figure 1. Among 15 cases, 14(93.33%) were found in bulbar conjunctiva and 1(6.67%) in inferior fornix. Bilateral eye involvement was seen in 11 cases (73.33%), whereas right eye and left eye involvement were 1(6.67%) and 3(20%) cases respectively. All patients were previously evaluated and treated elsewhere prior to presenting us, whose previous treatment details are summarised in Table 4. All our cases were advised excision biopsy and ultrasound abdomen. Systemic involvement was not found in any of our patients. Among all patients, 8 cases underwent excision biopsy and histopathological examination (HPE).Histopathological types of these cases are detailed in Table 5. Clinical and histopathological images of two cases are provided in Figure-1(a-d). Active treatment was given in 2 cases (13.33%) whereas 13 cases (86.67%) were kept under observation.

Case No	Age	Sex	Vision	Slit Lamp Finding	Previous Diagnosis and Treatment	Procedure Advised
1	62	M	RE-6/12, LE-5/60	Nasal and temporal conjunctival mass resembling salmon patch appearance with Immature cataract- in both eyes	Inflamed pinguecula treated with steroids	LE Phacoemulsification+ LE Excision biopsy and USG abdomen
2	48	F	RE- 6/9, LE- 6/9	Nasal and temporal conjunctival mass resembling salmon patch appearance + Posterior subcapsular cataract- in both eyes	Inflamed pterygium treated with steroids	RE Phacoemulsification+ RE Excision biopsy and USG abdomen
3	31	M	RE -6/6, LE -6/6	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	Inflamed pterygium treated with steroids	Excision biopsy and USG abdomen

4	34	F	RE -6/6, LE -6/6	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	Inflamed pinguecula treated with steroids	Excision biopsy and USG abdomen
5	39	F	RE-6/6, LE-6/6	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	Inflamed pinguecula treated with steroids	Excision biopsy and USG abdomen
6	36	F	RE-6/6, LE-6/6	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	Inflamed pinguecula treated with steroids.	Excision biopsy and USG abdomen
7	55	F	RE-6/6, LE-6/6	Nasal and temporal conjunctival mass resembling salmon patch appearance+ RE Inferior fornix- in right eye only	Inclusion cyst	Excision biopsy and USG abdomen
8	60	M	RE-6/6, LE-6/36	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	Inflamed pinguecula treated with steroids	Excision biopsy and USG abdomen
9	55	M	RE-6/6, LE-6/60	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	MALToma	Excision biopsy and USG abdomen
10	50	F	RE-6/6, LE-6/6	Nasal and temporal conjunctival mass resembling salmon patch appearance in left eye	Episcleritis treated with steroids	Excision biopsy and USG abdomen
11	29	M	RE-6/12, LE-6/6	Nasal and temporal conjunctival mass resembling salmon patch appearance in left eye	Episcleritis treated with steroids	Excision biopsy and USG abdomen
12	51	F	RE-6/6P, LE-6/6P	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	Vernal keratoconjunctivitis treated with steroids	Excision biopsy and USG abdomen
13	52	F	RE-6/6, LE-1/2/60	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	Inflamed pterygium treated with steroids	Excision biopsy and USG abdomen
14	37	F	RE-6/6, LE-6/6	Nasal and temporal conjunctival mass resembling salmon patch appearance in both eyes	Inflamed pterygium treated with steroids	Excision biopsy and USG abdomen
15	50	F	RE-6/6, LE-HM	Nasal and temporal conjunctival mass resembling salmon patch appearance in left eye	Inflamed pinguecula treated with steroids	Excision biopsy and USG abdomen

Table 1: Demographic and clinical details of patients.

Age Range (in years)	No of Patients (Percentage)
<30	1 (6.67%)
30-39	4 (26.67%)
40-49	2 (13.33%)
50-59	6 (40%)
≥60	2 (13.33%)

Table 2: Age distribution of patients.

VA (Visual Acuity)	No of Patients (Percentage)
06-Jun	6 (40%)
6/9-6/36	5 (33.33%)
≤6/60	4 (26.67%)

Table 3: Patient categorisation according to visual acuity at presentation.

Treated Before as	No. of Patients (percentage)
Inflamed pinguecula	6 (40%)
Inflamed pterygium	4 (26.67%)
Inclusion cyst	1 (6.67%)
Vernal Kerato-Conjunctivitis	1 (6.67%)
Episcleritis	2 (13.33%)
MALToma	1 (6.67%)

Table 4: Details of previous diagnosis and treatment received.

Histopathological Features	No of Patients (Percentage)
B-cell NHL	2 (25%)
Small cell lymphoma	1 (12.5%)
MALToma	1 (12.5%)
Atypical lymphoid hyperplasia	4 (50%)

Table 5: Histopathological types found in patients with HP study.

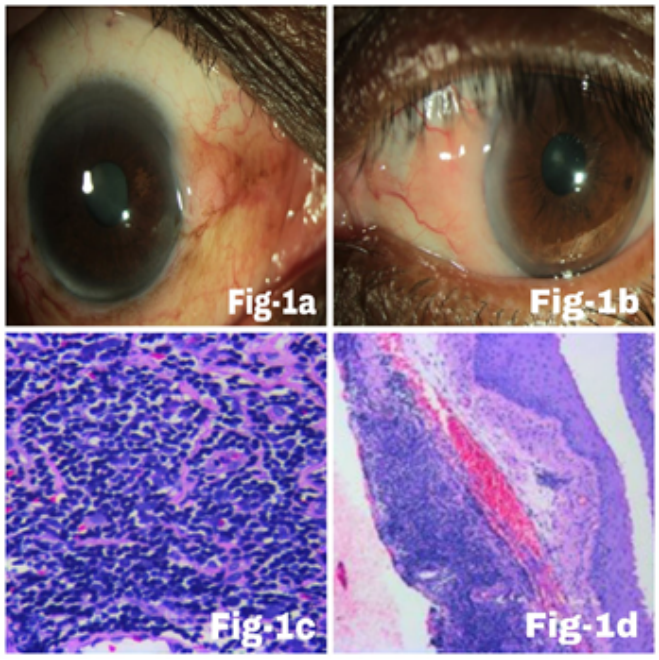

Figure 1: Shows clinical and histopathological cases of conjunctival lymphoma.

Discussion

The conjunctiva is common site of extra-nodal lymphoma development, which comprises 25-30% of all lymphomatous disease [18,19]. It classically presents as a chronic, sessile, pink-coloured sub-epithelial conjunctival mass, typically described as a “salmon patch” [20,21]. It may also present as chronic follicular conjunctivitis [22]. Patients may have no

significant symptoms or non-specific symptoms like ocular irritation, redness and rarely, ptosis or exophthalmos (where significant orbital involvement is present) [21,23,24].

There are various methods to arrive at diagnosis of conjunctival lymphoma. Clinical examination, slit lamp examination, fundoscopy, ocular coherence tomography (OCT), ultrasound bio- microscopy (UBM) play vital roles in initial steps of evaluation. Histopathological examination (HPE) or biopsy is done to confirm the diagnosis. Our study emphasizes both clinical and histopathological findings are important. Out of 15 cases only 8 cases underwent excision biopsy in our study.

The incidence of systemic disease is less frequent with low-grade subtypes than with high-grade subtypes. According to a study by Shields CL, et al. [25], out of 117 patients with lymphoid tumors of the conjunctiva, 17% of patients with unilateral conjunctival involvement at the time of diagnosis had systemic lymphoma, while this number rose to 47% for those with bilateral conjunctival involvement. Our patients presented with apparently localized lesions and underwent thorough systemic work-up. None of our cases had distant metastasis/systemic involvement at presentation and treated with excision alone. Our cases were only observed thereafter with no further treatment.

Treatment of conjunctival lymphoma is decided by the extent of disease involvement; whether it is localized to the conjunctiva or disseminated to other parts of the body. Localised conjunctival lymphoma is treated by External Beam Radiotherapy, intralesional Interferon alfa-2b, intralesional Rituximab or observation [16,17,26,27]. In case of disseminated disease/systemic involvement, a number of single agents (including chemotherapy and immunotherapy) as well as combination chemotherapy regimens are commonly used. Among systemic therapies, Rituximab, Doxycycline, radioimmunotherapy and multi-agent chemotherapy regimen (cyclophosphamide, Adriamycin, vincristine, prednisolone) are generally used [16,17,28].

Prognosis of conjunctival lymphomas depends on the pathological type and stage of presentation of the disease. Over-all 5-year survival rate ranging between 50 and 94% [29,30]. In our study, on follow-up of all 15 cases, 1 had recurrent lesion (6.67%), 7patients had no recurrence (46.67%), 5 patients had same size lesion who did not underwent biopsy (33.33%) and 2 patients lost to follow up (13.33%).

Conclusion

Bilateral conjunctival focal elevated nodular pinkish lesions of varying should be evaluated to rule out potentially malignant conditions. Patient with disseminated disease can be referred to Oncologists. Team consisting of ophthalmologists, radiotherapists and haematologist are required for better management and thereby minimizing untoward results. A number of important criteria must be considered: 1) The histopathologic subtype of lymphoma, 2) Extent of the lymphoma, 3) Patient and disease related prognostic factors, and 4) The effect on the eye and visual function. Proper evaluation of patient can prevent misdiagnosing a case of NHL for allergic conjunctivitis and other conjunctival inflammatory lesions.

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