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REVIEW ARTICLE

# Ocular Adnexal Lymphomas: Report of 2 Cases of Mantle Cell Lymphomas and Short Review of Literature

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**Abstract** Mantle cell lymphoma in ocular region is a rare phenomenon which can be either primary or secondary. Most of these cases are usually diagnosed after excisional biopsy of the involved area with first visit being in the Ophthalmology OPD. We share our experience of two such cases being referred from Ophthalmology OPD. 1st case is about a 52-year-old man who came for complaints of redness of left eye with excessive lacrimation. Examination revealed congestion of left temporal bulbar conjunctiva and a small pinkish outgrowth 2 × 2 cm adherent to temporal bulbar conjunctiva. 2nd case is a 55-year-old gentlemen who presented with complaints for 8 months duration of swelling left eyelid. Excisional biopsy and histopathological examination in both the cases were done to confirm the diagnosis. CECT head and neck were done at baseline and during follow up. These cases are being presented due to the rarity and dramatic response to chemotherapy.

**Keywords** Ocular adnexal lymphomas · Mantle cell lymphomas · Cyclin D1

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## Introduction

Mantle cell lymphoma (MCL) comprises around 3–10 % of non-Hodgkin lymphomas [1]. Waldeyer's ring and the gastrointestinal tract are common extra nodal sites of involvement by MCL. Only case reports exist describing involvement of the ocular adnexa by this entity. Ocular adnexal lymphomas involve the orbit, eyelid, lacrimal gland, and conjunctiva. However, MCLs in the ocular adnexa, primary or secondary, are extremely rare, and only a few cases have been reported in the English literature. Herein, we report two rare cases of orbital MCL.

### Case Report 1

A 52 year old man visited to ophthalmology OPD for complaints of redness of left eye with excessive lacrimation. There was no history of diminished vision, photopsia, floaters or diplopia. Clinical examination revealed congestion of left temporal bulbar conjunctiva and a small pinkish outgrowth 2 × 2 cm adherent to temporal bulbar conjunctiva (Fig. 1a, c) with no hepatosplenomegaly and lymphadenopathy noted elsewhere in the body. Fundus (Fig. 1b) and slit lamp examination of patient was essentially normal. PET CT scan showed faint FDG uptake in the thin sheet of soft tissue in the lateral aspect of the globe of left eye with no abnormal hyper metabolism noted anywhere in the body (Fig. 2c, d). CECT orbit and base of

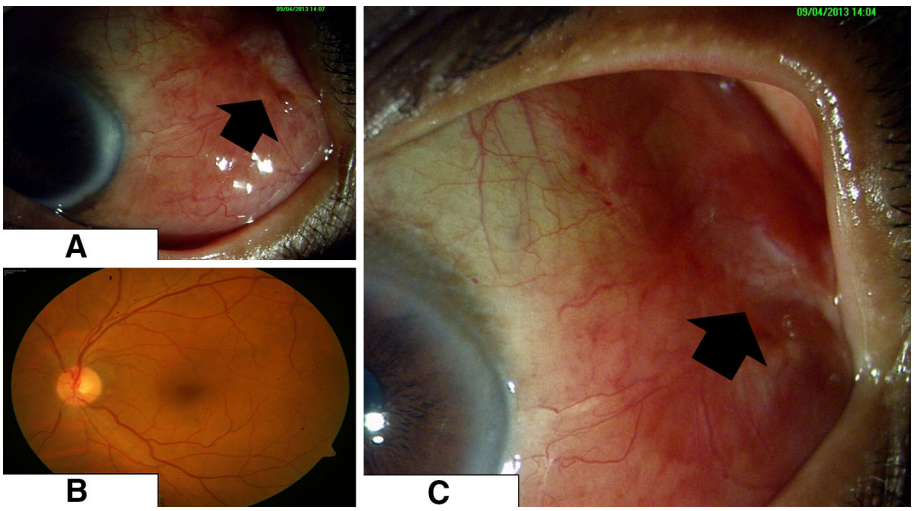


**Fig. 1** **a, c** Congestion of left temporal bulbar conjunctiva and a small *pinkish* outgrowth 2 × 2 cm adherent to temporal bulbar conjunctiva, **b** fundus of the involved eye with no evidence of tumor invasion. (Color figure online)

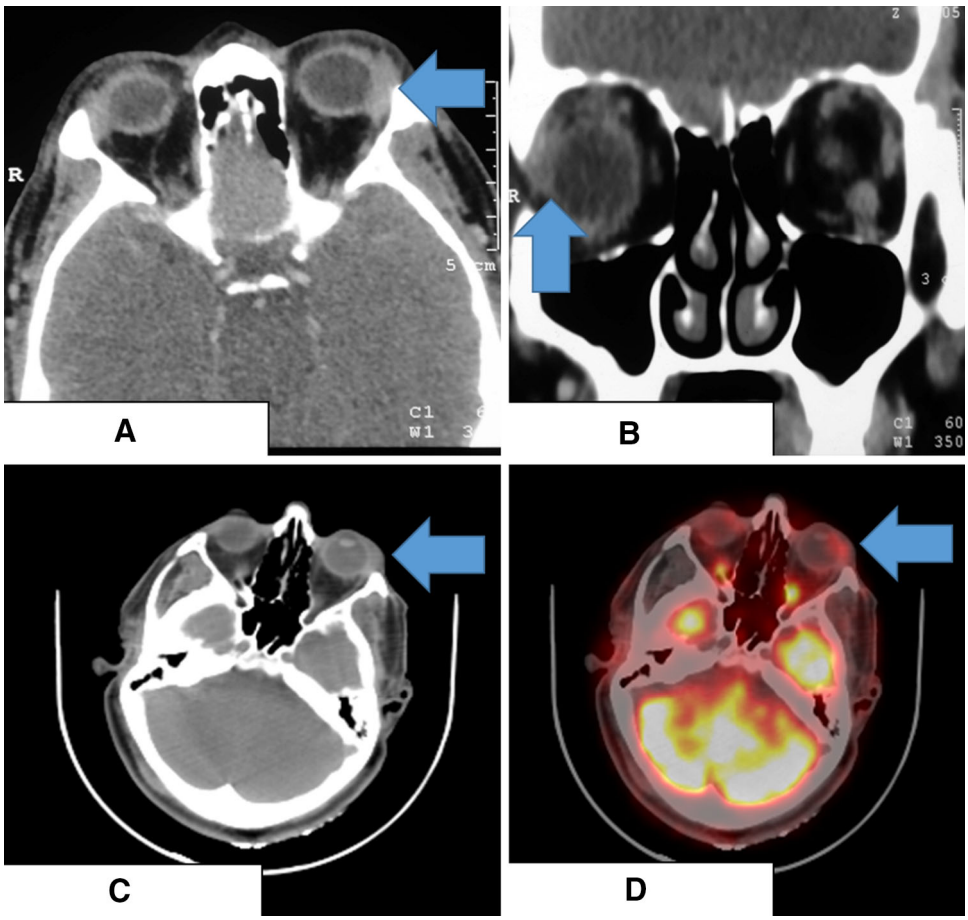


**Fig. 2** **a, b** CECT orbit in both transverse (Fig. 1a) and sagittal view (Fig. 1b) showed well defined hyper dense lesion 3.4 × 3.3 cm involving intraconal as well as extraconal compartments of the left orbit, **c, d** PET−CT showing increased FDG uptake in left supero-medial orbit (SUV = 5.2)

skull was also done to access the orbital extent of tumor which showed a small homogenously enhancing soft tissue lesion measuring 10 × 6 mm in the intraconal compartment of left orbit, just lateral to left inferior rectus (Fig. 2a, b). Excisional biopsy of the soft tissue mass was done under local anesthesia and histopathological examination showed sub epithelium with lymphoid tissue showing abundant follicles having germinal centres (Fig. 3a). Mantle zones of follicles showed predominant population of cells with size of 1–2 times the size of mature lymphocytes with angulated nuclei and clumped chromatin and reticulin stain highlighting the nodular pattern (Fig. 3b). Immunostain for cyclin D 1 highlighted these cells in the inner mantle zones with infiltration into germinal centre

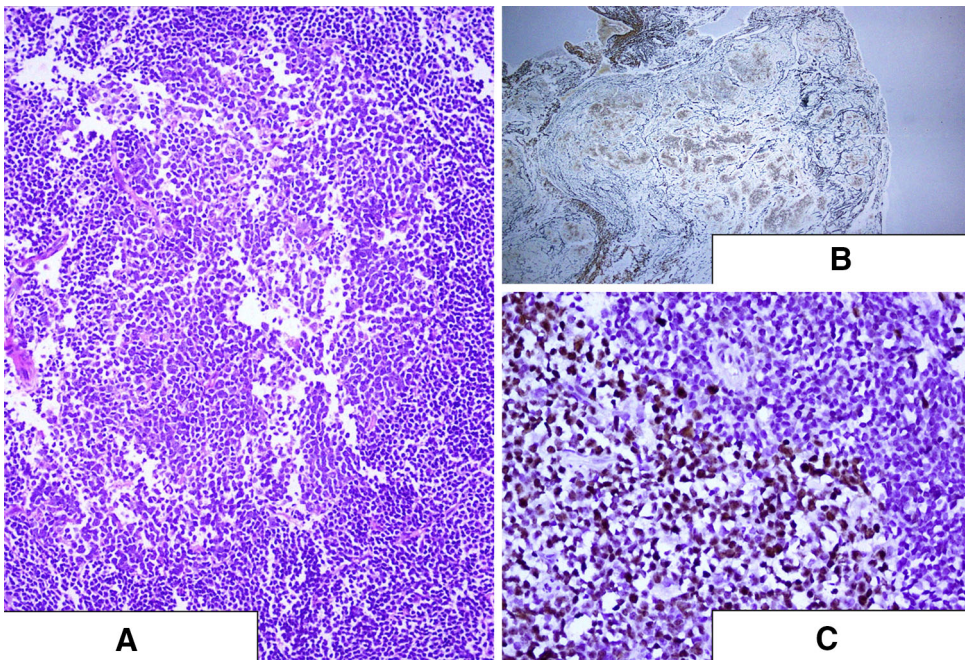


**Fig. 3** **a** Nodular infiltration by small lymphocytes with a prominent germinal centre (Magnification ×20), **b** reticulin stain highlighting the nodular pattern (Magnification ×10), **c** cyclin D1 nuclear staining in the germinal centre and mantle zone (Magnification ×40)

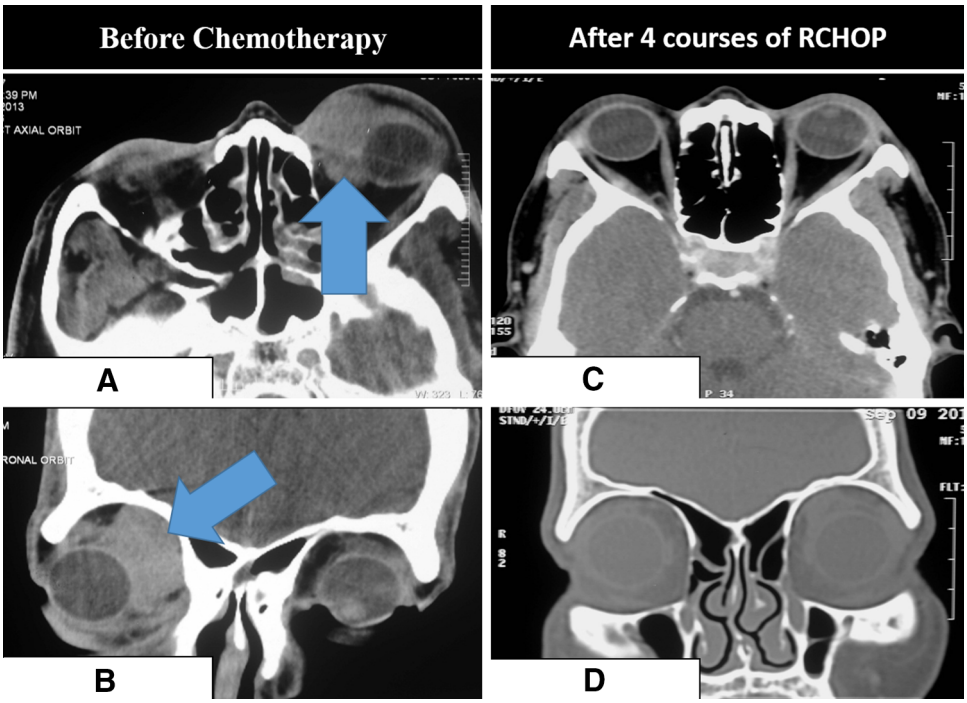


**Fig. 4** **a, b** CECT orbit in both transverse (Fig. 4a) and sagittal view (Fig. 4b) showed well defined hyper dense lesion 3.4 × 3.3 cm involving intraconal as well as extraconal compartments of the left orbit, **c, d** reassessment for response was done by repeat CECT orbit which showed significant improvement

with positivity for CD 20 and negativity for Bcl-2 and CD3 (Fig. 3c). Bone marrow trephine biopsy was normal. Hence, a diagnosis of MCL stage IA was made. He is being started on RCVP (rituximab, cyclophosphamide, vincristine, and prednisolone) chemotherapy, 2 cycles of which was received by patient at the time of writing this manuscript.

Case Report 2

A-55-year-old gentlemen presented with complaints for 8 months duration of swelling left eyelid that was not associated with diplopia, ptosis, and lacrimation and diminished vision. The right eye was normal. No B symptoms were noted. Examination showed mild swelling

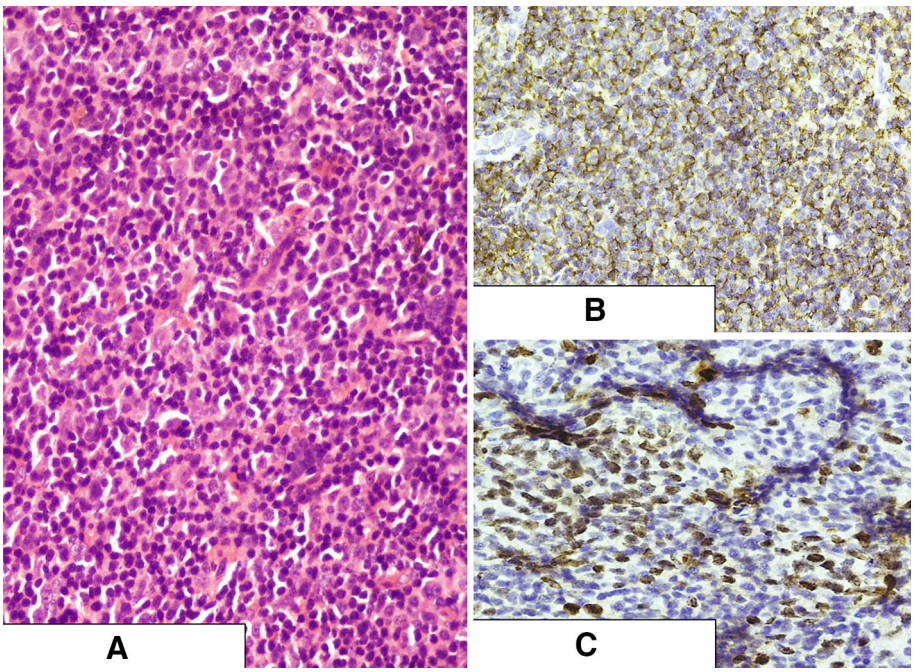


**Fig. 5** **a** Sheet-like infiltration by small lymphocytes (Magnification ×20), **b** CD20 diffuse positivity (Magnification ×20), **c** cyclin D1 nuclear staining in many of the cells (Magnification ×40)

noted over supraorbital ridge and upper eyelid. CECT orbit in both transverse (Fig. 4a) and sagittal view (Fig. 4b) showed well defined hyper dense lesion 3.4 × 3.3 cm involving intraconal as well as extraconal compartments of the left orbit. The lesion is displacing the orbit infer laterally. Other lab parameters including hemogram, liver function tests, renal function tests, serum LDH levels, B2 microglobulin levels and bone marrow examination were normal. FNAC specimen from swelling when subjected to histopathological examination with immunocytochemistry showed sheet-like infiltration by small lymphocytes (Fig. 5a). Immunohistochemistry showed CD20 diffuse positivity (Fig. 5b) and cyclin D1 (Fig. 5c) nuclear staining in many of the cells. He was subsequently started on RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy, four cycles of which were received by the patient till now, following which swelling disappeared almost completely. Reassessment for response was done by repeat CECT orbit (Fig. 4c, d) which showed significant improvement. He is being planned to receive two more courses of RCHOP.

## Discussion

About 80–90 % of primary ocular adnexal lymphomas are extra nodal marginal zone B cell lymphomas of mucosa-associated lymphoid tissue (MALT) and second most common lymphoma being diffuse large B cell lymphoma [2]. The primary involvement of the conjunctiva by lymphoma, comprises about one third of ocular adnexal lymphoma. MCL is a relatively rare lymphoma, accounting for less than 10 % of all lymphomas. In the ocular adnexal region, including rare cases of conjunctiva, MCL accounts for between 1–5 [3] and 9 % [4] of the lymphomas. A special feature of ocular MCLs is their advanced stage at diagnosis, aggressive behavior, male predominance with advanced age at time of diagnosis [5]. Jenkins et al. [6] reported that of the ocular adnexal MCL, 80 % present in stage III/IV and the median overall survival to be only 57 months. Our 1st case is 52 year old male but with early Stage (IA).

A PubMed search using the term "ocular adnexal MCL" revealed 16 publications with one being a case series of 353 cases of lymphomas involving ocular adnexa done by Ferry et al. [7] which showed 19 out of 353 case being diagnosed as MCL constituting just 5 %. However they did not specify the categorical location of tumor within orbit. One of oldest studies by Medeiros et al. [8] of 99 cases of lymphoid infiltrates of orbit and conjunctiva found no case of MCL. Cahill et al. [2] reported one case of secondary MCL involving right conjunctiva of a 57 year old patient when they retrospectively analyzed 20 cases of ocular adnexal lymphomas (Table 1).

Another large study in which the patients were identified through the Danish Ocular Lymphoma Database covering the years 1980–2005 was done by P Rasmussen et al. and they reported 21 patients with MCL in the orbital and adnexal region comprising 9 % (21/230) of all lymphoma in the ocular region most common site being the orbit and eyelid. Another important aspect which this study highlighted was difference in behavior pattern between primary

**Table 1** Studies, authors, year of publication, number of OALs studied and their further sub categorisation

| Number of OALs | Rasmussen et al. [4] | Ferry et al. [7] | Rootman et al. [11] | Nola et al. [16] | Nakata et al. [14] | Cahill et al. [2] | Haedrich et al. [12] | Oh DE et al. [15] | Looi et al. [5] | McKelvie et al. [17] | Sharara et al. [18] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| OAL(n) | 230 | 353 | 122 | 24 | 77 | 20 | 53 | 128 | NA | 70 | 17 |
| MCLs | 21 | 19 | 1 | 1 | 2 | 1 | 2 | 4 | 10 | 2 | 2 |
| Orbit | 13 | NA | NA | NA | 0 | 0 | 0 | NA | 9 | 1 | 0 |
| Eyelids | 13 | NA | NA | NA | 2 | 0 | 1 | NA | 5 | 0 | 1 |
| Conjunctiva | 6 | NA | NA | NA | 0 | 1 | NA | NA | 0 | 0 | 1 |
| Lacrimal gland | 2 | NA | NA | NA | 0 | 0 | 0 | NA | 5 | 1 | 0 |
| Lacrimal sac | 2 | NA | NA | NA | 0 | 0 | 0 | NA | 2 | 0 | 0 |

**Table 2** Orbital/adnexal MCLs and their demography

| Author | OAL(n) | Conjunctival cases | Male | Female | Mean age | Primary | Secondary | Age/sex |
|---|---|---|---|---|---|---|---|---|
| Ferry et al. [7] | 19 | NA | 13 | 6 | 51–91 | 7 | 12 | – |
| Rasmussen et al. [4] | 21 | 6 | 18 | 3 | 60–90 | 14 | 7 | – |
| Khanlari et al. [13] | 1 | 1 | – | – | – | 1 | 0 | 64/m |
| Cahill et al. [2] | 1 | 1 | – | – | – | 0 | 1 | 57/- |
| Haedrich et al. [12] | 2 | 1 | – | – | – | 1 | 1 | – |
| Looi et al. [5] | 10 | 0 | 9 | 1 | 32–84 | 8 | 2 | – |
| McKelvie et al. [17] | 2 | 0 | 1 | 1 | 64–80 | 2 | 0 | – |
| Sharara et al. [18] | 2 | 1 | 1 | 1 | 53–70 | 2 | 0 | – |

and secondary adnexal MCLs and they reported that patients with involvement of the orbital and adnexal region as first presenting symptom had more frequently bilateral eye and bone marrow involvement, and inferior overall survival as opposed to patients with secondary ocular adnexal MCL [4]. However, Ferreri et al. [9] and Shields et al. [10] analyzed in their studies that patients with lymphoma of conjunctival localization had better outcome than lymphomas of other areas of the eye considering both local and systemic relapse. Rootman and colleagues [11] studied 122 patients of primary unilateral ocular adnexal lymphomas and found only one case of histologically proven MCL. Auw Haedrich et al. [12] did conventional and immunohistology on representative sections of 53 specimens of 46 patients with ocular adnexal lymphoma and found that most common site involved by OAL was in the orbit (22 cases) followed by conjunctiva [13], eyelid [14], lacrimal sac [1], and sclera (n = 1) with only two cases of immunohistologically proven MCL involving conjunctiva and eyelid respectively (Table 2).

Oh and Kim [15] did a study in South Korea on 128 patients of ocular adnexal lymphomas and reported four cases (3.1 %) of MCL although they did not specified the site of involvement within the orbit. Looi et al. [5] studied ten patients of ocular MCL and found predominantly male predominance (9:1) with 90 % of patients having more than one site of involvement with 80 % cases having primary ocular involvement and the rest two cases had primary in tonsil and prostate respectively. Also, eight out of ten patients demonstrated stage III/IV disease at presentation and bone marrow involvement was observed in seven patients (70 %), with 6 (60 %) also showing atypical cells in the peripheral blood smear. Lymphocytosis was not observed in any patient, and only one patient had an elevated serum lactate dehydrogenase levels. Our patient had no infiltration of bone marrow with stage I disease with normal peripheral blood smear and serum LDH of 257.00 IU/L. Nola et al. [16] reported single case out of 20 ocular adnexal lymphomas. Also Nakata et al. [14] reported two cases of MCLs involving eyelid and/or conjunctiva out of 77 cases of ocular adnexal lymphomas they studied. Isolated rare case have been of conjunctival MCL have been reported in past [13]. McKelvie et al. [17] reported only two cases of MCLs out of 70 cases of OALs he studied with orbit and lacrimal gland being the site of involvement.

## Conclusion

These two cases are rare entity among ocular adnexal lymphomas and also its uncommon to involve eyelid and conjunctiva. Upon therapy both of our patient have shown

dramatic response clinically and radiologically. Importance lies in the fact that entities such as ocular adnexal MCL are much more clinically aggressive than the more common entity of extranodal marginal zone lymphoma (EMZL) and hence knowledge of histopathological diagnosis helps in prognosis.

**Conflict of interest** None.

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