Conclusion

We present a very rare case of unilateral isolated foveal hypoplasia diagnosed in a 9-year-old male. Our case shows persistence of inner retinal layers with a shallow foveal depression, which, based on the above classification, constitutes grade 1 isolated unilateral foveal hypoplasia.

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References

1. Oliver MD, Dotan SA, Chemke J, Abraham FA. Isolated foveal hypoplasia. *Br J Ophthalmol*. 1987;71:926-30.
2. Katagiri S, Yokoi T, Mikami M, Nishina S, Azuma N. Outer retinal deformity detected by optical coherence tomography in eyes with foveal hypoplasia. *Graefes Arch Clin Exp Ophthalmol*. 2016;254:2197-201.
3. Karaca EE, Mehmet O. Isolated foveal hypoplasia: clinical presentation and imaging findings. *Optom Vis Sci*. 2014;91:61-5.
4. Asakawa K, Ishikawa H. Electroretinography and pupillography in unilateral foveal hypoplasia. *J Pediatr Ophthalmol Strabismus*. 2016;53:e26-8.
5. Dubis AM, Hansen BR, Cooper RF, Beringer J, Dubra A, Carroll J. Relationship between the foveal avascular zone and foveal pit morphology. *Invest Ophthalmol Vis Sci*. 2016;53:1628-36.
6. Thomas MG, Kumar A, Mohammad S, et al. Structural grading of foveal hypoplasia using spectral-domain optical coherence tomography. *Ophthalmology*. 2011;118:1653-60.
7. Marmor M, Choi SS, Zawadzki RJ, Werner JS. Visual insignificance of the foveal pit: reassessment of foveal hypoplasia as fovea plana. *Arch Ophthalmol*. 2008;126:907-13.
8. Holmström G, Eriksson U, Hellgren K, Larsson E. Optical coherence tomography is helpful in the diagnosis of foveal hypoplasia. *Acta Ophthalmol*. 2008;88:439-42.
9. El-Dairi MA, Asrani SG, Enyedi LB, Freedman SF. Optical coherence tomography in the eyes of normal children. *Arch Ophthalmol*. 2009;127:50-8.
10. Noval S, Freedman SF, Asrani S, El-Dairi MA. Incidence of fovea plana in normal children. *J AAPOS*. 2014;18:471-5.

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Mantle cell lymphoma: conjunctival mass in a female patient

Mantle cell lymphoma (MCL) is a rare neoplasm in the ocular adnexa, accounting for 3%–5% of conjunctival B-cell non-Hodgkin lymphomas (NHL).[1,2] Conjunctival MCL typically presents in male patients in the eighth decade and is often advanced at the time of presentation.[3] Treatment typically consists of chemotherapy or radiation, although the prognosis is poor.[4] The authors present a rare case of conjunctival MCL in a female patient. Collection and evaluation of protected patient health information complied with the Health Insurance Portability and Accountability Act.

Case Report

A 61-year-old female presented with a painless, salmon-colored conjunctival lesion approximately 8 × 5 mm in size in the medial canthal region of the right eye (Fig. 1). The mass had been present for 2 weeks, and at her follow-up visit 1 month later it appeared to have grown. She had no visual symptoms or complaints in the right eye, although she had been experiencing flashes and floaters in the left eye, which was found to be a posterior vitreous detachment. Ophthalmic examination was otherwise within normal limits. No palpable or visible posterior extension could be appreciated. Patient denied B-symptoms such as fever, night sweats, or lymphadenopathy. She had no history of malignancy.

There was high clinical suspicion of lymphoma, and the patient subsequently underwent biopsy of the right conjunctival lesion. Histopathology showed soft tissue infiltration of fairly uniform atypical lymphocytes with slightly irregular nuclear membranes and focally vesicular chromatin without prominent nucleoli. Occasional mitoses were

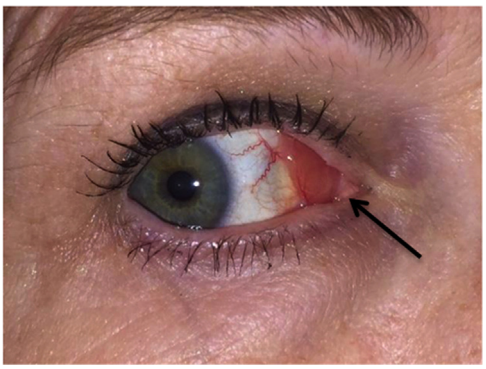

Fig. 1—Right eye in abduction showing a salmon-colored conjunctival lesion near the medial canthus, approximately 8 × 5 mm in size.

identified. Immunohistochemical staining showed CD20+, CD5+, Bcl-2+, CyclinD1+, CD10−, CD23−, and 50% Ki-67 proliferation consistent with MCL. Computed tomography (CT) of orbits showed no other ocular involvement. Staging positron emission tomography (PET) and CT showed multiple small, mildly hypermetabolic axillary, mediastinal, hilar, retroperitoneal, mesenteric, and external iliac lymph nodes as well as splenomegaly. Bone marrow biopsy showed 10% MCL involvement.

She subsequently started rituximab, bendamustine, and cytarabine for stage IV MCL but was switched to rituximab and bendamustine after severe cytopenias after the second cycle. PET/CT showed complete remission with resolution of lymphadenopathy and splenomegaly after the third cycle. Remission was maintained after completion of 6 cycles. She did not require maintenance therapy. Marrow biopsy after completion of chemotherapy was normocellular. She subsequently developed rituximab-induced delayed neutropenia, which resolved with filgrastim. As of 10 months after completion of chemotherapy, she continues to be in remission.

Discussion

MCL is a rare type of B-cell NHL that accounts for approximately 3%–5% of conjunctival lymphomas.[1,2] It is a high-grade, aggressive lymphoma that typically presents in the eighth decade. Males are 6 times more likely to be diagnosed with ocular adnexal MCL than females.[3] Although female patients with conjunctival MCL have been reported in the literature,[3,5–7] these have mostly represented minor percentages within larger conjunctival lymphoma studies[3,7] with the exception of one prior case report.[6] Conjunctival MCL in a female patient is a rare presentation that warrants attention from clinicians.

Conjunctival MCL presents as a painless "salmon-colored" mass[3] that tends grow rapidly and is more often bilateral than unilateral.[5] Patients typically seek medical treatment soon after the appearance of the mass.[3] When there is clinical suspicion, a full ophthalmologic examination along with tissue histopathology is necessary to make the diagnosis.[3] At the genetic level, MCL is characterized by the t(11;14)(q13;32) translocation, which causes overexpression of cyclin D-1 and subsequent cellular proliferation and dysregulation.[3] Occult disease is present in approximately 80% of patients who initially present with ocular adnexal MCL.[8] Thus, staging with PET and CT/magnetic resonance imaging as well as bone marrow biopsy is warranted upon diagnosis.[3,5] Nodal involvement and splenomegaly, as noted in this patient, are often present.[9]

The mainstay of treatment for MCL is chemotherapy, usually involving R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone), although a combination of rituximab, bendamustine, and cytarabine is a valid alternative for older patients.[10] The prognosis is typically poor for advanced MCL, with a 5-year overall survival of 40%.[4] However, a different study showed that patients who receive rituximab-containing regimens have a 3-year survival rate of 57% compared to 40% for patients who received regimens without rituximab.[11] For patients younger than 65 years, allogeneic hematopoietic stem cell transplant is a potentially curative option.[4]

Although conjunctival MCL overwhelmingly present in male patients, female sex does not necessarily preclude MCL from the differential diagnosis of conjunctival lymphomas.

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References

1. Coupland SE, Hellmich M, Auw-Haedrich C, Lee WR, Stein H. Prognostic value of cell-cycle markers in ocular adnexal lymphoma: an assessment of 230 cases. *Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol*. 2004;242:130-45.
2. Ferry JA, Fung CY, Zukerberg L, et al. Lymphoma of the ocular adnexa: a study of 353 cases. *Am J Surg Pathol*. 2007;31:170-84.
3. Kirkegaard MM, Coupland SE, Prause JU, Heegaard S. Malignant lymphoma of the conjunctiva. *Surv Ophthalmol*. 2015;60:444-58.
4. Chandran R, Gardiner SK, Simon M, Spurgeon SE. Survival trends in mantle cell lymphoma in the United States over 16 years 1992–2007. *Leuk Lymphoma*. 2012;53:1488-93.
5. Rasmussen P, Sjö LD, Prause JU, Ralfkiaer E, Heegaard S. Mantle cell lymphoma in the orbital and adnexal region. *Br J Ophthalmol*. 2009;93:1047-51.
6. Choi CJ, Stagner AM, Jakobiec FA, Lee NG. Limbal mantle cell lymphoma of the conjunctiva. *Ophthalmology*. 2016;123:377.
7. Kirkegaard MM, Rasmussen PK, Coupland SE, et al. Conjunctival lymphoma—an international multicenter retrospective study. *JAMA Ophthalmol*. 2016;134:406-14.
8. Ferrer A, Salaverria I, Bosch F, et al. Leukemic involvement is a common feature in mantle cell lymphoma. *Cancer*. 2007;109:2473-80.

9. Vali Khojeini E, Durham BH, Chen M. Mantle cell lymphoma and involvement of the orbit and ocular adnexa. *Case Rep Pathol.* 2013;2013:e581856.
10. Visco C, Finotto S, Zambello R, et al. Combination of rituximab, bendamustine, and cytarabine for patients with mantle-cell non-Hodgkin lymphoma ineligible for intensive regimens or autologous transplantation. *J Clin Oncol Off J Am Soc Clin Oncol.* 2013;31:1442-9.
11. Abrahamsson A, Albertsson-Lindblad A, Brown PN, et al. Real world data on primary treatment for mantle cell lymphoma: a Nordic Lymphoma Group observational study. *Blood.* 2014;124:1288-95.

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Conjunctival Kaposi's sarcoma with orbital extension in an HIV-negative man

Kaposi's sarcoma (KS) is a vascular tumour whose development requires infection by human herpesvirus 8 (HHV-8). Although most commonly found in immunosuppressed patients, such as those AIDS, in the United States, classic KS is often found in older-aged men of European or Mediterranean ancestry without immunosuppression. Involvement of the skin of one's extremities in classic KS is typically more common than that of viscera or mucocutaneous surfaces.

There are few cases in the literature regarding ocular KS in HIV-negative patients. Involvement of the conjunctiva in an HIV-negative, immunocompetent patient has been previously described.[1,2] Disseminated forms of KS with facial involvement have also been reported to involve the eye.[3] Here we present a very unusual case of KS of the conjunctiva extending into the orbital space in an HIV-negative patient.

Case Report

A 93-year-old Caucasian male presented with a nodule in the left eye (Fig. 1A). Two violaceous lesions of approximately 5 mm in diameter were also found on the left forearm (Fig. 1B). He has a remote history of a gastrointestinal stromal tumour that was treated with imatinib mesylate (Gleevec, Novartis). All laboratory tests were negative, including HIV. There was no history of acquired or iatrogenic immunosuppression. On examination, best-corrected visual acuity was 20/25 OU. Intraocular pressures were 11 mm Hg in the right eye and 10 mm Hg in the left eye. Fundoscopy was normal in both eyes. Slit-lamp examination findings were within normal limits in the right eye. In the left eye, there was conjunctival hyperemia with a nodule in the inferior fornix. The patient underwent computed tomography of the orbits, which confirmed the conjunctival nodule and showed lateral extension to the orbit (Fig. 1C).

Total excision of the nodule was performed, and the specimen was sent for histopathological analysis. At low magnification (20×), a fragment of conjunctiva with a subepithelial tumour was seen (Fig. 1D). The tumour was composed of dilated blood vessels with numerous spindle cells between them. There were also extensive areas of hemorrhage. At high magnification (40×), the intervascular tissue was composed of atypical spindle cells with spindle and hyperchromatic nuclei. Several extravasated red blood cells were observed. Immunohistochemistry for HHV-8 was positive with nuclear expression, which confirmed the diagnosis of KS.

Discussion

HHV-8, or KS-associated herpesvirus, is a dsDNA virus of the gammaherpesvirus family, commonly spread via saliva and blood.[4] The virus is associated with multiple neoplastic diseases—not only vascular tumours, such as KS, but also B-cell proliferative syndromes, such as primary effusion lymphoma and the plasmablastic variant of multicentric Castleman disease.[5] The virus enters host cells via the endocytic pathway and is able to infect endothelial cells and immune cells. HHV-8 then expresses multiple viral proteins that help evade innate and adaptive immune responses, allowing long-term latency, primarily inside B cells. Of note, the latency-associated nuclear antigen (LANA) protein is associated with both immune evasion and tumourigenesis, the latter via direct inactivation of *p53* and retinoblastoma (*Rb*) genes.[6] LANA is thus commonly used for histologic diagnosis of KS, as with the case of our patient.[7] HHV-8 further promotes tumourigenesis via upregulation of vascular endothelial grown factor–derived and platelet-derived growth factor–derived angiogenesis, as well as activation of the PI3K/Akt/mTOR signalling pathway by expression of human protein homologues, such as viral G-protein-coupled receptor protein and viral IL-6.[6]

KS of the eye may have an appearance similar to vascular lesions, such as hemangiomas, arteriovenous fistulas, pyogenic granulomas, malignant blue nevi, bacterial angiomatosis, and any other vascular malformations.[2] Immunohistochemistry is a valuable tool for confirming the diagnosis for all forms of KS, especially in the case of patients without a history of HIV or any other form of immunosuppression. As in our patient, KS shows a characteristic feature of spindle-shaped, endothelium-derived tumour cells around vascular slits, often with evidence of extravasation such as hemosiderin, red blood cells, and fibrosis. Immunohistochemistry for CD34 can identify proliferation of endothelial cells,[8] and LANA-1,