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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,

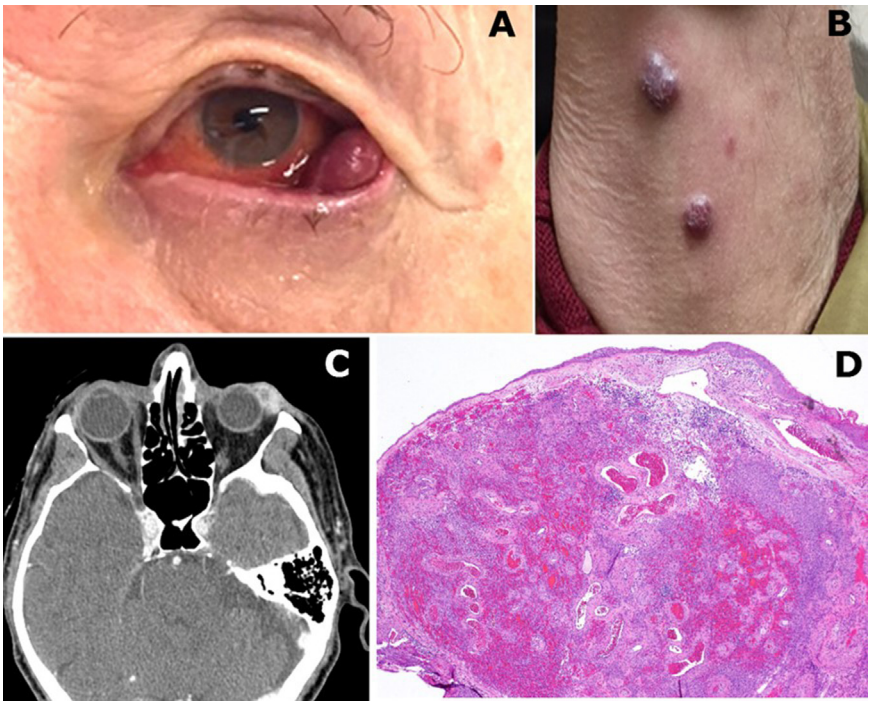

Fig. 1—(A) Solid mass at lateral canthus of left eye causing mild ectropion of the lower eyelid. (B) Cutaneous lesions on left forearm found at time of diagnosis. (C) Computed tomography scan of orbit showing invasion of left temporal orbital space. (D) Low magnification (20) showing well-circumscribed tumour with dilated vessels and extravasation.

which is found uniformly in the nucleus of virtually all HHV-8–infected cells, has been shown to be useful for distinguishing tumours with similar histologic features.[7,9]

In an HIV-positive patient, ocular KS typically regresses with HAART alone.[10] For HIV-negative patients, current treatment options include surgical excision, cryotherapy/laser ablation, radiotherapy, and intralesional chemotherapy. Because the virus establishes residence in the immune system, none of the therapies listed eliminate the possibility of tumour re-emerging elsewhere in the body. For our patient, surgical excision was preferred because the tumour was extending into the orbital space. Because the tumour was well delineated, complete removal of the tumour was performed and there was no need for adjunctive laser or cryotherapy.

KS is typically very sensitive to radiotherapy, but radiation to the ocular space may incur very well-known side effects, such as dry eyes and secondary tumour formation. If patients are on immunosuppression for organ transplant, sirolimus, an mTOR inhibitor, has been shown to be very effective in controlling various cutaneous KS lesions,[11] but subconjunctival/intravitreal injection of sirolimus for ocular diseases currently remains in the clinical trial stages.[12,13]

Conclusions

Although KS is much more common in HIV-positive males, our case report is a reminder that elderly HIV-negative men can be affected. Despite the conjunctiva being the most affected ocular structure in KS, it is always important to rule out orbital extension. Careful history taking and histopathology can confirm the diagnosis of ocular KS. The treatment level should be appropriate for the stage of disease. New therapies for KS have a potential to be used in the ocular space in the future.

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Bilateral disc edema in hypertensive emergency

Bilateral optic disc edema can be a result of several etiologies and deserves a thorough work-up. Neuroimaging and laboratory studies should be performed to rule out neoplastic, vascular, infectious, ischemic, or inflammatory etiologies, and a lumbar puncture (LP) should be performed to measure intracranial pressure (ICP) if necessary after performing the appropriate imaging studies. Patients with papilledema should be evaluated for alternative causes of increased ICP. We present the case of a patient who presented with bilateral optic disc edema and was found to have increased ICP. Although it is true that the systemic blood pressure (BP) should be checked in every case of bilateral optic disc edema to exclude hypertensive emergency, the presence of severe hypertension does not obviate the need for either neuroimaging or evaluation for increased ICP-related papilledema (i.e., LP).

Case

A 35-year-old obese African American male (body mass index of 35.9 kg/m^2) presented with bilateral optic disc edema and vision loss. He had a history of multiple hypertensive emergency episodes and uncontrolled essential hypertension complicated by congestive heart failure (with an ejection fraction of 20%). He had chronic kidney disease and focal segmental glomerular sclerosis. The patient did not have a history of sickle cell disease or obstructive sleep apnea. Medications included hydrochlorothiazide and lisinopril. Family history included hypertension in his father. All other histories were noncontributory. He was not taking any medications that could produce increased ICP.

He presented to the emergency department with acute loss of vision OD. He was found to have a systolic BP of 230/146 mm Hg. Visual acuity was hand-motion OD and 20/40 OS. Funduscopic examination showed Friesen grade IV optic edema OD with hemorrhages and cotton wool spots contiguous to the nerve and grade III–IV optic edema OS (Fig. 1). He was subsequently diagnosed with hypertensive emergency and admitted for BP control. The BP improved but did not normalize on medical therapy. Three weeks later he presented to the neuro-ophthalmology clinic with bilateral vision loss. He also reported headaches and tinnitus, but denied nausea, vomiting, or weakness. BP measurements at home had remained over 200 mm Hg systolic since discharge despite multiagent antihypertensive therapy with carvedilol, hydralazine, and isosorbide dinitrate.

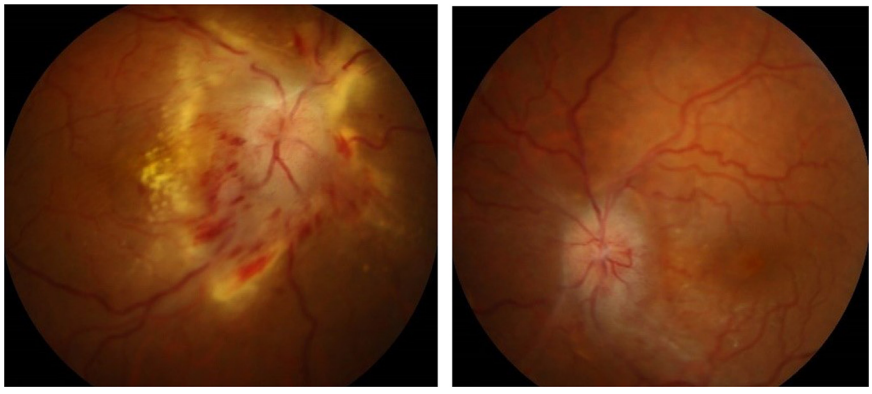

Fig. 1—Fundus photos OU showing marked disc edema, peripapillary flame shaped hemorrhages, and cotton wool spots.