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Case Report

Ocular Manifestations of Kaposi Sarcoma: Insights from an HIV-Positive Patient and an Immunocompetent HIV-Negative Patient

Kaposi Sarkomunun Göz Bulguları: HIV Pozitif Bir Hasta ve Immunocompetent HIV Negatif Bir Hastada Sonuçlar

Ebubekir DURMUŞ[1], Esma Ecem ERSOY[1], Ulviyya ASKEROVA[1], Fatma YILMAZER[2]

[1]İstanbul Medeniyet University Faculty of Medicine, Department of Ophthalmology, İstanbul, Turkey
[2]İstanbul Medeniyet University Faculty of Medicine, Department of Pathology, İstanbul, Turkey

ABSTRACT

Kaposi sarcoma (KS) is a vascular neoplasm caused by human herpes virus-8 and is commonly associated with immunocompromised states such as acquired immunodeficiency syndrome. While ocular involvement is rare and typically occurs in human immunodeficiency virus (HIV)-positive patients, it can exceptionally present in HIV-negative, immunocompetent individuals. This report presents two cases of conjunctival KS: One in an HIV-positive patient and another in an HIV-negative patient. The patients were diagnosed and followed up at İstanbul Medeniyet University Göztepe Prof. Dr. Süleyman Yalçın City Hospital. Written informed consent was obtained from the patients for the preparation of this case report. A 35-year-old HIV-positive male with a history of cutaneous and genital KS presented with a painless, reddish, hemorrhagic mass on the left inferior fornix and a firm mass on the lower eyelid. Surgical excision with adjuvant cryotherapy and amniotic membrane transplantation was performed. One year postoperatively, no recurrence or new lesions were observed. A 76-year-old immunocompetent female presented with a painless, progressively enlarging mass in the left inferior fornix. She underwent surgical excision, adjuvant cryotherapy, and amniotic membrane transplantation. Histopathology confirmed the diagnosis of KS, and at the 1-year follow-up, no recurrence or new lesions were observed. Ocular KS, though rare, can occur in both immunocompromised and immunocompetent individuals. This report highlights the importance of considering KS in the differential diagnosis of subconjunctival hemorrhage, even in patients without underlying immunosuppressive conditions. Both cases were successfully managed with surgical excision, adjuvant cryotherapy, and amniotic membrane transplantation, with no recurrence during follow-up.

Keywords: Ocular kaposi sarcoma, subconjunctival hemorrhage, HIV positive patient, HIV negative patient

ÖZ

Kaposi sarkomu (KS), insan herpes virüsü-8 tarafından oluşturulan vasküler bir neoplazm olup, genellikle edinilmiş bağışıklık yetersizliği sendromu gibi immun yetmezlik durumlarıyla ilişkilidir. Oküler tutulumu nadir olmakla birlikte, genellikle insan bağışıklık yetmezliği virüsü (HIV)-pozitif hastalarda görülürken, nadiren HIV-negatif, immun kompetan bireylerde de ortaya çıkabilir. Bu olgu sunumu, bir HIV-pozitif hasta ve bir HIV-negatif hasta olmak üzere iki konjunktival KS olgusunu sunmaktadır. Hastalar İstanbul Medeniyet Üniversitesi Göztepe Prof. Dr. Süleyman Yalçın Şehir Hastanesi'nde tanı almış ve takip edilmiştir. Bu olgu raporunun hazırlanması için hastalardan yazılı bilgilendirilmiş onam alınmıştır. Olgu sunumları: Olgu 1: Otuz beş yaşındaki HIV-pozitif erkek hasta, cilt ve genital KS öyküsü ile birlikte sol inferior fornikste ağrısız, kırmızı, kanamalı bir kitle ve alt göz kapağında sert bir kitle ile başvurdu. Cerrahi eksizyon, adjuvan kriyoterapi ve amniyotik membran transplantasyonu yapıldı. Operasyondan bir yıl sonra, nüks veya yeni lezyonlar gözlemlenmedi. Olgu 2: Yetmiş altı yaşındaki immun kompetan kadın hasta, sol inferior fornikste ağrısız, giderek büyüyen bir kitle ile başvurdu. Cerrahi eksizyon, adjuvan kriyoterapi ve amniyotik membran transplantasyonu gerçekleştirildi. Histopatolojik inceleme KS tanısını doğruladı ve bir yıl sonraki takipte nüks veya yeni lezyonlar gözlemlenmedi. Oküler KS, nadir olmasına rağmen, hem immun yetmezlik durumunda hem de immun kompetan bireylerde görülebilir. Bu rapor, subkonjunktival kanama durumunda KS'yi ayırıcı tanıda göz önünde bulundurmanın önemini vurgulamaktadır; bu, immun baskılayıcı durumları olmayan hastalarda bile geçerlidir. Her iki vaka da cerrahi eksizyon, adjuvan kriyoterapi ve amniyotik membran transplantasyonu ile başarılı bir şekilde yönetilmiş ve takip sırasında nüks gözlemlenmemiştir.

Anahtar kelimeler: Oküler kaposi sarkomu, subkonjonktival kanama, HIV pozitif hasta, HIV negatif hasta

Address for Correspondence: E. E. Ersoy, İstanbul Medeniyet University Faculty of Medicine, Department of Ophthalmology, İstanbul, Turkey
E-mail: esmaecemersoy@gmail.com **ORCID ID:** orcid.org/0000-0002-9563-1846

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INTRODUCTION

Kaposi sarcoma (KS) is a vascular neoplasm caused by human herpes virus 8 (HHV-8), regarded as an acquired immunodeficiency syndrome (AIDS)-defining illness due to its opportunistic nature and frequent occurrence in immunocompromised individuals. It commonly presents in patients with a CD4+ lymphocyte count below 500 cells/µl, particularly under 200 cells/µL[1]. Clinically, KS manifests as a spectrum ranging from indolent, low-grade lesions to purplish-red tumors, which may affect various body regions and develop into fatal, multisystemic angioproliferative malignancies[2]. The global incidence of KS has risen, paralleling the increasing prevalence of AIDS[3]. In addition, KS has been observed in patients undergoing immunosuppressive therapy following organ transplantation[4]. Ocular involvement in KS is rare and primarily associated with AIDS[5]. Between 4% and 12% of AIDS-related KS cases involve ocular manifestations, most commonly affecting the conjunctiva and eyelids[6]. However, ocular KS in human immunodeficiency virus (HIV)-seronegative individuals is exceedingly rare[7].

In this report, we present two cases of conjunctival KS: One in an HIV-seropositive patient with concurrent skin, eyelid, and conjunctival involvement, and another in an HIV-seronegative patient with recurrent conjunctival KS. The HIV-seronegative case is particularly notable, as it represents KS in an immunocompetent individual without any underlying immunosuppressive condition. Both patients underwent surgical excision, cryotherapy, and amniotic membrane transplantation. At the 1-year postoperative follow-up, no recurrence was observed in either patient.

CASE REPORT

Case 1

A 35-year-old HIV-positive bisexual male presented with a three-month history of a mass on his left lower eyelid. Prior to this, he had lesions on his nose and genital area, diagnosed as KS via biopsy. At presentation, his CD4 cell count was 93 cells/mL, CD8 cell count was 1825 cells/mL, CD4/CD8 ratio was 0,050 and HIV polymerase chain reaction was 61 copies/mL; he was also receiving anti-retroviral therapy with a combination of bictegravir, emtricitabine, and tenofovir. Visual acuity was 6/6 in both eyes. Examination revealed a firm, immobile mass measuring approximately 4x4 mm on the left lower eyelid, extending to the ciliary margin, and a hemorrhagic vascular lesion measuring 8x3 mm on the palpebral conjunctiva wtih the patient reporting no pain. Surgical excision of conjunctival lesions, along with cryotherapy and amniotic membrane transplantation, and cryotheraphy for the lower eyelid was recommended. The surgery was performed under local anesthesia. The vascularized conjunctival mass was excised with a 3 mm margin, and cryotherapy was applied to the conjunctival margins and eyelid mass. The conjunctival defect was covered with an amniotic membrane graft secured with 10/0 nylon sutures. Histopathological examination confirmed conjunctival KS with positive staining for HHV-8, CD31, and CD34, and approximately 5-15% of cells were positive for Ki67 (Figure 1). At the 1-year postoperative follow-up, the palpebral conjunctiva appeared normal, with regression of the lower eyelid mass. There was no recurrence or new ocular lesions, and systemic involvement was ruled out with biannual positron emission tomography-computed tomography (PET-CT) scans. Figure 2 illustrates the clinical appearance of KS in the palpebral conjunctiva and eyelid, along with the postoperative outcome.

Case 2

A 76-year-old female with a history of glaucoma presented with a progressively enlarging mass in her left lower eyelid, which had been present for approximately one month. Slit-lamp examination revealed a hemorrhagic, raised lesion measuring about 10x3 mm in

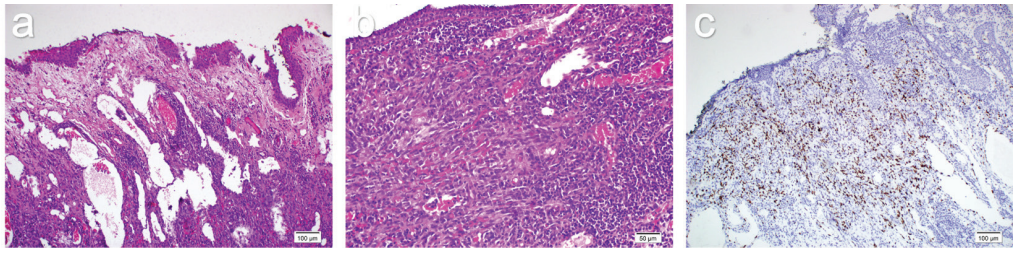

Figure 1. This is the pathology slide of the patient with positive HIV serology. Hematoxylin and eosin staining at x10 magnification (a). Hematoxylin and eosin staining at x20 magnification revealed widespread extravasated erythrocytes outside the vessels. Lymphocytic infiltrates containing plasma cells are present within and around the lesion in most cases (b). Positive nuclear expression was observed in HHV-8 immunohistochemical analysis (c).

HIV: Human immunodeficiency virus, HHV-8: Human herpes virus 8

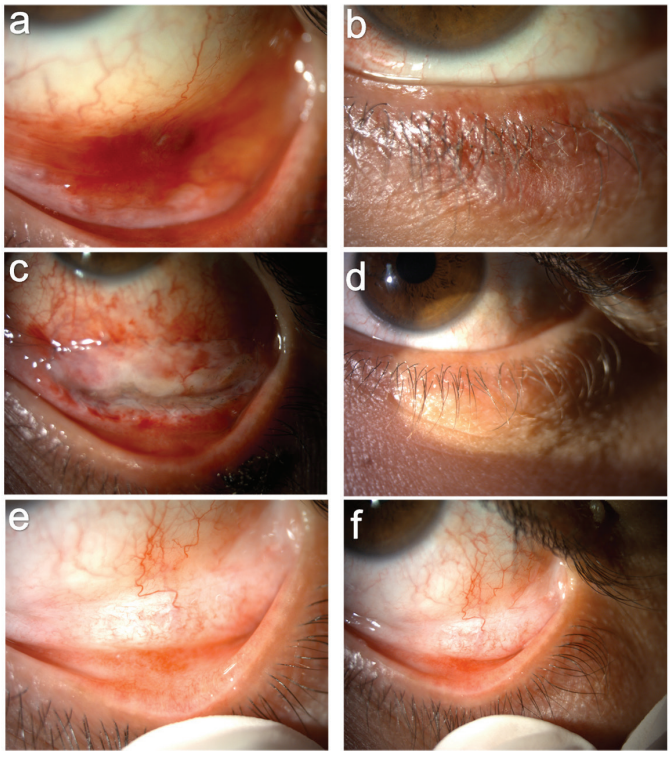

Figure 2. The clinical appearance of KS in the palpebral conjunctiva and eyelid is characterized by a painless, reddish lesion resembling a subconjunctival hemorrhage, flat with a nodular component in the lower fornix (a), and a vascularized, immobile, and rigid mass at the eyelid margin in same patient (b). The conjunctival lesion was surgically excised, followed by cryotherapy and amniotic membrane transplantation (c). The eyelid lesion was treated with cryotherapy alone. Following cryotherapy, the eyelid lesion showed regression of vascularization and shrinkage (d). No recurrence or new lesions were observed at either of the postoperative follow-ups within the first year (e,f).

the left inferior fornix. The patient reported no history of immunosuppressive therapy, high-risk sexual behavior, or intravenous drug use. Hematological and biochemical tests were within normal limits, with no evidence of immunosuppression. Both B- and T-cell counts were normal, and repeated HIV tests were negative. Other serological markers, including anti-hepatitis C virus and HBsAg, were also seronegative. A systemic scan was conducted, during which a chest X-ray revealed early signs of chronic obstructive pulmonary disease. In 2020, the patient underwent a punch biopsy for angiomatous lesions in the umbilical region, diagnosed as hemangioma. In 2019, an excisional biopsy of a similar hemorrhagic lesion in the left conjunctiva confirmed the diagnosis of KS. Contrast-enhanced orbital magnetic resonance imaging (MRI) indicated that the conjunctival lesion was localized without orbital infiltration. A surgical excision

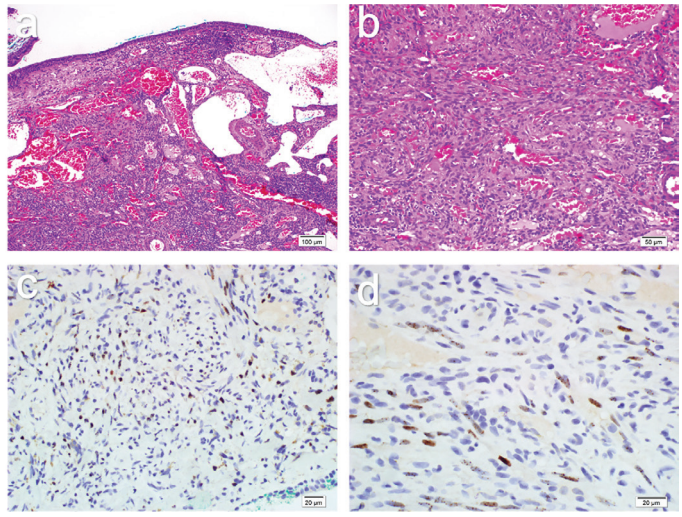

Figure 3. This is the pathology slide image of the patient with negative HIV serology. A nodular lesion composed of spindle cell fascicles observed with hematoxylin and eosin staining at x10 magnification (a). At x20 magnification with hematoxylin and eosin staining, spindle cells are intermingled with sieve-like, slit-shaped, blood-filled vascular structures (b). Patchy immunohistochemical staining of HHV-8 at x40 magnification (c). At x60 magnification, the characteristic paranuclear "dot-like" staining pattern of HHV-8 observed in Kaposi sarcoma (d).

HIV: Human immunodeficiency virus, HHV-8: Human herpes virus 8

of the conjunctival mass, followed by cryotherapy and amniotic membrane transplantation, was performed. Histopathology confirmed KS, showing positive staining for CD31, CD34, and HHV-8, with increased Ki67 activity (Figure 3). The patient was followed for one year, with no recurrence or new conjunctival lesions observed. HIV seroconversion was not detected, and systemic involvement was ruled out through orbital MRI and PET-CT scans. Figure 4 illustrates the clinical appearance of KS and the postoperative outcome.

DISCUSSION

KS manifests in four variants: Classic (Mediterranean), Endemic (African), Iatrogenic (Transplant-related), and AIDS-associated (Epidemic)[8]. This case report highlights the clinical presentation of ocular KS in both HIV-positive and HIV-negative patients. KS, caused by oncogenic HHV-8, is the most common neoplasm in AIDS patients, though ocular involvement is rare[9]. To date, only three cases of ocular KS as an initial manifestation of HIV have been documented, all involving the conjunctiva[10-12]. Ocular KS in HIV-negative individuals is exceedingly uncommon[13]. Ocular KS typically presents as a raised, reddish-brown mucocutaneous lesion, requiring differentiation from

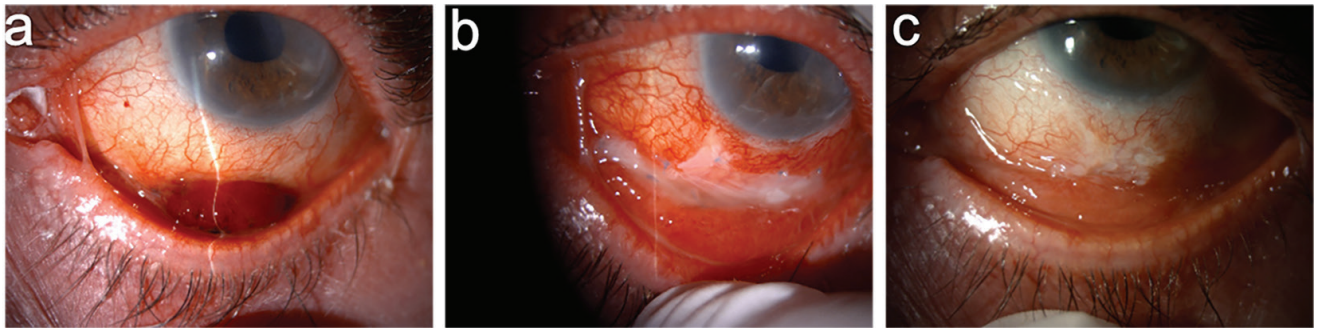

Figure 4. A painless, reddish mass consistent with Kaposi sarcoma was located on the left inferior fornix (a). Surgical excision of the lesion with adjuvant cryotherapy, and amniotic membrane transplantation was performed (b). No recurrence or new lesions were observed during the first-year postoperative follow-up (c).

conditions such as angiosarcoma, hemangioma, and pyogenic granuloma[7]. In the HIV-positive patient, KS developed during ongoing immunosuppression despite anti-retroviral therapy[2].

In contrast, KS in HIV-negative individuals often occurs following immunosuppression due to transplants, but may also arise due to localized immune dysregulation or genetic predispositions, with factors like chronic inflammation, trauma, or ultraviolet radiation triggering HHV-8 activation and promoting angiogenesis[14,15]. Furthermore, genetic variations in immune regulatory genes like vascular endothelial growth factor and IL-6 might also contribute to KS progression[16]. Ocular KS in HIV-negative individuals is rare but should be considered in the differential diagnosis of vascular lesions, particularly in elderly patients; as classic KS, which primarily affects Mediterranean and Eastern European populations, can occur in this group[9]. Despite differences in underlying mechanisms, the clinical manifestations are usually similar. Our HIV-negative patient exhibited no significant immunosuppressive factors, suggesting that advanced age or other underlying factors may play a role in KS development in immunocompetent individuals. The clinical course, disease progression, and treatment outcomes may vary in HIV-negative cases, where localized treatments could be more effective than systemic approaches typically used for HIV-related KS. This highlights the necessity of individualized diagnostic and therapeutic strategies for HIV-negative KS, considering the distinct pathogenic mechanisms.

According to the National Comprehensive Cancer Network guidelines, localized therapies are recommended for minor lesions, and systemic treatments are advised for refractory cases and in advanced disease[17]. Although originally developed for AIDS-related KS, these guidelines are applicable to non-HIV-related cases and emphasize the importance of tailoring treatment strategies to the individual patient's needs. Management typically involves surgical excision, with adjuvant therapy tailored to the severity of the disease and the patient's overall health. Ocular KS affecting the conjunctiva and eyelids generally has a non-aggressive course and can be treated with simple excision[3]. Adjunctive interventions may include radiotherapy, chemotherapy, cryotherapy, amniotic membrane transplantation, and intraoperative mitomycin-C application[2,8,18]. Recently, combined weekly docetaxel and anti-retroviral therapy have been explored as alternatives[19]. In our cases, surgical excision of the conjunctival tumors was followed by cryotherapy and amniotic membrane transplantation, with pathological examination revealing negative surgical margins, thus eliminating the need for further intervention. No systemic involvement was detected through orbital MRI and PET-CT scans, making systemic treatment unnecessary. The HIV-positive patient received only cryotherapy for the eyelid lesion, which demonstrated favorable regression without recurrence or new lesions during follow-up.

CONCLUSION

Ocular KS can occur in both HIV-positive and, rarely, HIV-negative patients. Our second case highlights the need to consider KS in the differential diagnosis of subconjunctival hemorrhage, even in immunocompetent individuals without a history of immunosuppression. Both patients responded well to surgical excision followed by cryotherapy and amniotic membrane transplantation, with no recurrence observed during the 1-year follow-up.

ETHICS

Informed Consent: Written informed consent was obtained from the patients for the preparation of this case report.

FOOTNOTES

Author Contributions

Surgical and Medical Practices: E.D., Concept: E.D., Design: E.E.E., U.A., Data Collection and/or Processing: E.E.E., F.Y., Analysis and/or Interpretation: E.E.E., F.Y., Literature Search: E.E.E., U.A., Writing: E.D., E.E.E.

Conflict of Interest: The authors have no conflict of interest to declare.

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