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CASE REPORT

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Recurrent Kaposi sarcoma of the ear in an HIV-negative patient: A case report with review of the literature. Is ear a predilection site for Kaposi sarcoma in HIV-negatives?

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Abstract

While Kaposi sarcoma (KS) of the head and neck is common in HIV-positives, it is a rare presentation in HIV-negatives. It is important to consider KS in the differential diagnosis of ear lesions in HIV-negative patients.

KEYWORD

dermatology

1 | INTRODUCTION

Kaposi sarcoma (KS) is an angioproliferative disorder. While the head and neck KS is common in HIV-positives, it is rare in HIV-negatives. Our case and the past 24 reported cases of ear KS reviewed here highlight the importance of considering KS in the differential diagnosis of ear lesions in HIV-negatives.

Kaposi sarcoma (KS) is a rare borderline angioproliferative disorder characterized by multiple vascular mucosal or cutaneous lesions.[1]

It has four major types: classic (predominantly in elderly men) (CKS), African endemic (AEKS), immunosuppression associated or transplant-associated (ITKS), and AIDS-associated.[2,3]

The classic form typically presents with cutaneous lesions on the lower extremities.[1] While the head and neck are the common sites for mucocutaneous lesions in HIV patients with KS, the presence of lesions on the head and neck in HIV-negative patients is a rare phenomenon.[4,5]

Among the reported cases of Kaposi sarcoma, auricular involvement is very rare. In a study of 11 KS cases presented on head and neck, though the majority of cases were HIV-positive, the two patients with KS lesions on their external ears were both HIV-negative. Therefore, they highlighted the importance of considering KS as a differential diagnosis for vascular lesions on the ears of HIV-negative patients.[6] This study aims to present a case of HIV-negative patient with multiple recurrent papules on his ear diagnosed as Kaposi sarcoma that developed KS lesions on his foot years later with a review of literature on KS presented on ears (Table 1).

2 | CASE PRESENTATION

A 43-year-old man was first presented to our dermatology clinic in 2014 with multiple erythematous dome-shaped papules on his right auricle. He has had these lesions from 6 months before his presentation to our clinic (Figure 1A). A biopsy was taken from his auricular papules at that

TABLE 1 Clinical features of external ear Kaposi sarcoma cases in this study and previous studies

Case	References	Year	Age/Sex	Race	HIV status	Initial tumor location	Treatment	Outcome/last follow-up	Comorbidities
1	Epstein et al.[8]	1941	37 F	Japanese	Unknown	Right ear	Excision	During the subsequent 3 years developed two adjacent tumor nodules	
2	Naunton and Stoller[9]	1960	68 M	North American	Unknown	Right Helix lip	Not mentioned	Not mentioned	
3	Rothman et al.[10]	1962	68/...	Greek	Unknown	Helix of ear	Excision	Recurred after 8 years	
4	Gibbs et al.[11]	1963	73 F	North American	Unknown	Multiple nodules On each ear Left foot	Not mentioned	Not mentioned	
5	Howland et al.[12]	1966	85/M	White	Unknown	Lesion on right ear, tongue, chin, and eyelid	Excision, radiation	Died without known disease after 3 years due to atherosclerotic renal disease	
6	Hardy et al.[13]	1976	48/M	Puerto Rican	Unknown	Lesions on the left ear, left wrist, and both feet	Excision, radiation, bleomycin, and vincristine	Alive and well at 3 years follow-up	
7	Mikkelsen et al.[14]	1977	59/M	Eskimo	Unknown	Lesions on the right earlobe, feet, legs, and right palm	Radiation therapy; some decrease in size	Died with the disease at 21 months (uremia)	
8	Stearns et al.[15]	1983	66 M	Indian	Unknown	Left external auditory meatus.	Excision	Not mentioned	
9	Gnepp et al.[5]	1984	55 M	Italian	Unknown	Both pinna and both feet Nasal vestibule	Biopsy and radiation therapy	Alive and well at 17 years with the disease	
10	Babuccu et al.[16]	2003	36 M	White	Negative	Left pinna	Excision	During a 2-year follow-up, no recurrences, no new lesions, or HIV seroconversion were detected	
11	Hussein et al.[17]	2008	3 M	Egyptian	Negative	Dorsum of the right ear. Cutaneous dissemination. Lymph node	Not mentioned	Not mentioned	Severe lymphocytopenia

(Continues)

TABLE 1 (Continued)

Case	References	Year	Age/Sex	Race	HIV status	Initial tumor location	Treatment	Outcome/last follow-up	Comorbidities
12	Altunay et al.[18]	2012	27 M	Turkish	Negative	Right helix, mental region, the right retroauricular region. Tip of the nose	Chemotherapy and radiotherapy	Not mentioned	
13	Colletti et al.[19]	2013	57 M	Italian	Negative	Right/left helix	Excision	During a 3-year follow-up no involvements of visceral organs, no changes in his health conditions	
14	Izquierdo Cuenca et al.[20]	2013	81 M	White	Negative	Right pinna	Not mentioned	Not mentioned	
15	Busi et al.[21]	2014	72 F	White	Negative	Right pinna and external auditory canal. Multiple lesions on the right arm and left leg	Local medication with gentamicin and betamethasone	After 18 months, no other localizations have appeared in the external ear	History of tuberculosis and non-Hodgkin lymphoma
16	Francés et al.[22]	2016	77 F	Spanish	Negative	Anterior helix Of the right pinna	Excision	During 2 years of follow-up, no recurrences, or new immunosuppressive diseases	
17	Rachadi et al.[23]	2016	64 F	Moroccan	Negative	Left pinna Visceral involvement (stomach, colon, liver, and spleen)	Bleomycin	Improvement	A case of bullous pemphigoid under treatment with corticosteroid
18	Chai et al.[24]	2018	47 M	Chinese	Positive	Right external auditory canal	Excision tenofovir, lamivudine efavirenz	After follow-up for 2 years, no local recurrence or metastasis	
19	Agaimy et al.[6]	2018	60 F	German	Negative	Skin ear (pinna)	Excision	Alive with no evidence of disease after 46 months follow-up	

(Continues)

TABLE 1 (Continued)

Case	References	Year	Age/Sex	Race	HIV status	Initial tumor location	Treatment	Outcome/last follow-up	Comorbidities
20	Agaimy et al.[6]	2018	78 M	German	Negative	External auditory canal, Disseminated KS on all Extremities 1 month after excision of ear lesion	Excision, 5 cycles liposomal Doxorubicin for disseminated disease	Alive, ongoing remission after 18 months of follow-up	
21	Baykal et al.[25]	2019	50 M	Turkish	Negative	Ears, Upper and lower extremity, penis. Urethra	Sirolimus, excision, radiotherapy, chemotherapy	Relapse and dissemination after transplantation. showing no response to therapy, remission following transplant rejection	A case of kidney transplantation receiving azathioprine, corticosteroid, Mycophenolate mofetil
22	Baykal et al.[25]	2019	16 F	Turkish	Negative	Ear, upper and lower extremity, face, bone	IFN-alpha, chemotherapy	No remission in a 10-year follow-up	A case of Congenital immunodeficiency
23	Rupp et al.[26]	2019	79 M	Swiss	Negative	Left ear's concha	Excision local external beam radiotherapy	Free of disease after 15 months of clinical and radiological follow-up.	
24	McNally et al.[27]	2020	72 M	American	Positive	Enlarged right pinna (verrucous, papulonodules lesions) left antitragus	Not mentioned	Not mentioned	
25	Etesami et al.	2020	43 M	Iranian	Negative	Right auricle Lower extremities	Total excision	Recurred after 4 and 6 years	

time. While our most probable clinical impression was Angiolymphoid hyperplasia with eosinophilia (ALHE) or pseudolymphoma, the microscopic evaluation was consistent with KS (Figure 2A–E). Histopathologic examination of a skin biopsy from the ear showed nodular proliferation of spindled endothelial cells arranged in intersecting fascicles with intervening slit and sieve-like vascular channels. There were some blood-filled vascular spaces between spindle cells with red blood cell extravasation and patchy infiltrate of lymphocytes and plasma cells (Figure 2A,B). Some mitotic figures and apoptotic bodies were also identified. Immunohistochemistry staining reveals positive immunoreaction of tumor cells for CD31 and CD34 as well as HHV8 which show nuclear immunoreactivity (Figure 2C–E).

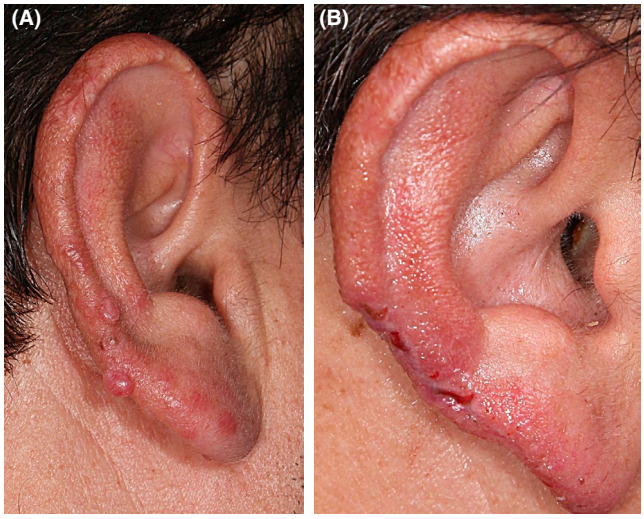

FIGURE 1 (A) Multiple erythematous dome-shaped papules on the right auricle, (B) after total excision

Because his lesions were limited to his ear, the lesions were totally excised (Figure 1B). In 2018, he was presented to our clinics with recurrence of one solitary papule on his right ear, the papule was totally excised, and the histopathology was consistent with KS again. The patient did not come back for further evaluation at that time. In April 2020, he was presented to our clinic with the recurrence of papules on his right ear and the development of an erythematous plaque on his right foot since a year ago. Two biopsies were taken from his ear and foot lesions that both were consistent with KS. Routine laboratory evaluations including complete blood

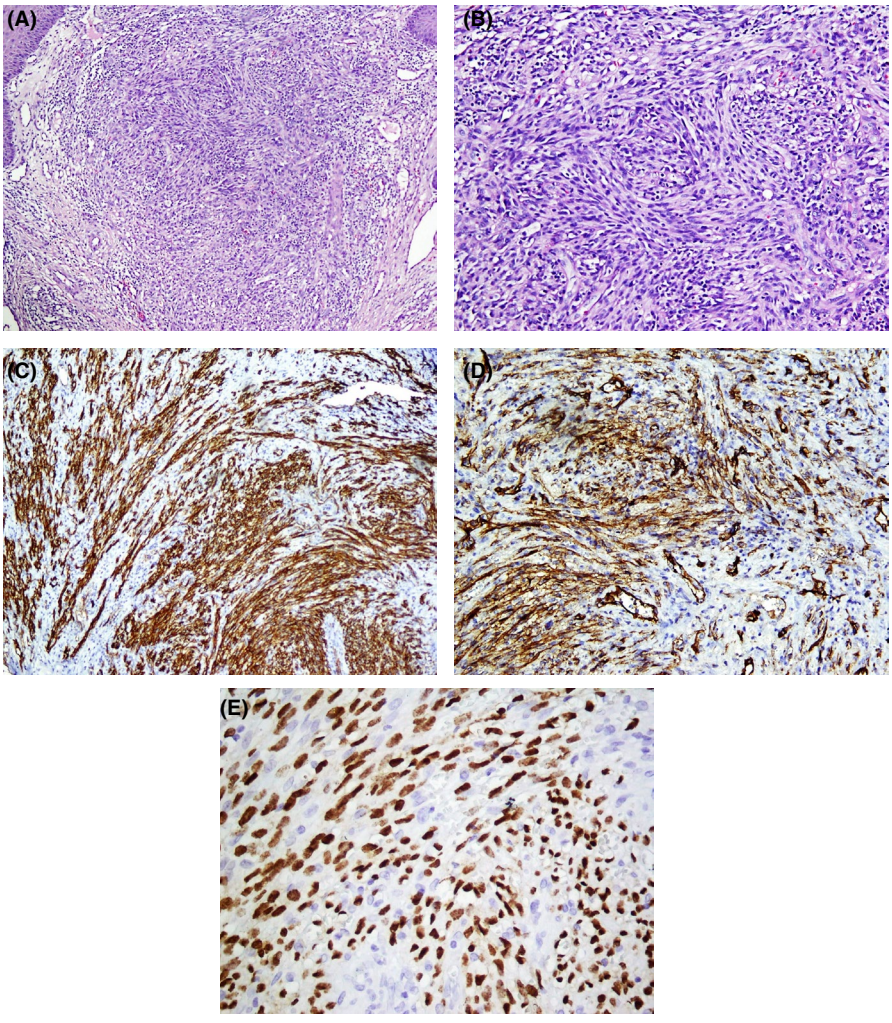

FIGURE 2 (A) Intersecting fascicles of spindled cells with intervening slit- and sieve-like vascular spaces surrounded by patchy lymphoplasmacytic infiltrate (H&E ×10), (B) high power of intersecting fascicles with blood-filled, sieve-like vascular channels (H&E ×20), positive immunoreaction for CD31 (C), CD34 (D), and HHV8 (E) which shows nuclear immunoreaction

count (CBC), liver, and renal function tests were normal, and HIV test was negative. The patient was otherwise healthy without any history of immunodeficiency. He was not taking any medication.

3 | DISCUSSION

While oral (59.1%) and craniofacial (43.9%) involvement is common in HIV-positives,[1] Kaposi sarcoma of the head and neck is rare (approximately <5% of the KS cases) in the HIV-negative individuals.[6] The most common presentation of KS in HIV-negatives is multiple bilateral lesions of the lower extremities.[7] Among the head and neck KS, the incidence of auricular involvement is much lower, so it should be considered a distinct manifestation. The presence of a recurrent, auricular KS with an atypical presentation in a young immunocompetent individual is a very rare finding.

In this article, we presented a case of recurrent KS on the ear with a literature review on ear KS cases (Table 1).[5,6,8–27] The literature review disclosed 24 cases since the year 1941 until 2020, highlighting the rarity of this presentation. Sixteen males and seven females aged 3–85 years (median, 62 years; mean, 57.4 years) were retrieved. Of these 24 cases of ear skin KS, two cases were HIV-positive,[24,27] 13 cases were HIV-negative,[6,16–23,25,26] and others were unknown. Among these, four cases had visceral involvement including lymph node, bone, urethra, stomach, colon, liver, and spleen, and the rest were limited to the skin including just limited to the auricle ($n = 11$), ear and mucosal sites ($n = 4$), ear and extremities ($n = 9$), and ear and other sites in the head and neck region (chin and eyelid) ($n = 3$). Among the 13 HIV-negatives, five cases had some degrees of immunosuppression (one case kidney transplantation,[25] one case congenital immunodeficiency,[25] one case receiving systemic corticosteroid,[23] one case non-Hodgkin lymphoma,[21] and the last a case of severe lymphocytopenia[17]). While excision was the most common treatment option, other modalities were antiretroviral medications for HIV-positives, radiotherapy and chemotherapy with liposomal doxorubicin, bleomycin, vincristine, and IFN-alpha for more widespread disease. Among 17 cases that their follow-up was available, ranging from 15 months to 17 years, the majority of them were free of disease after the initial treatment ($n = 12$), three cases had recurrent lesions, one case was alive with disease, and one died with disease because of uremia. While KS in HIV-negative patients has an indolent course, our case was highly recurrent, despite total excision with free margins, it has recurred twice in 5 years, and after that, a new lesion on the foot appeared. So the recurrence rate of the KS in the ear needs to be further studied.

While KS pathogenesis is multifactorial and both genetic and environment are responsible, human herpes virus 8 (HHV8) is the main causal factor in the development of KS in all variants irrespective of the clinicopathological setting of the disease.[4,28] HHV8 contributes to cell growth, signaling apoptosis, angiogenesis, and immunomodulation. It produces some proteins that inhibit host adaptive and innate immunity.[1,4] While the increased risk of KS in HIV-positives and iatrogenically immunosuppressed cases is well understood, the occurrence in immunologically competent individuals remains largely unelucidated.[7] Agaimy et al.[6] hypothesized that maybe impaired local immunosurveillance and pro-inflammatory cytokines release is the causative factor. Although the exact reason why the ear is a predilection site in HIV-negative patients who develop KS in head and neck region is not clear, Francés et al.[22] proposed that in addition to some factors such as trauma and infection in acral sites, insufficient vascularization makes it difficult for immune system to access.

Due to the rarity of head and neck, KS, especially in HIV-negative patients, unusual presentations of KS may be challenging if not considered in the differential diagnosis. The occurrence of KS in atypical sites like ear leads to unrecognition and misdiagnosis. The possibility of occult HIV infection should be considered beside. They may be misdiagnosed as other spindle cell tumors pathologically or other vascular lesions such as ALHE clinically. HHV8 immunohistochemistry was positive in 95% of KS lesions irrespective of HIV positivity,[4] so it is a good marker to detect KS.

In summary, we presented a case of recurrent ear KS in a young HIV-negative and otherwise healthy individual with a review of the literature on 24 cases of ear KS from 1941 to 2020 implicating ear as a predilection site for head and neck KS in HIV-negative patients; therefore, we highly suggest to consider KS as a differential diagnosis for lesions on ears.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

IE: has made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, drafting the manuscript, and revising it critically, given final approval of the version to be published. YK: has made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, drafting the manuscript, and revising it critically. AG: has made substantial contributions to conception and design, drafting the manuscript, and revising it critically. AR: has made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, drafting the manuscript, and revising it critically.

ETHICAL APPROVAL

The study was approved by ethical committee of Tehran University of Medical Sciences. Informed consent was obtained from the patient.

DATA AVAILABILITY STATEMENT

Author elects to not share data.

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