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CASE REPORT

Pyogenic granuloma-like Kaposi sarcoma: Case report and review of literature

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ABSTRACT

Pyogenic granuloma-like Kaposi sarcoma (PGLKS) is an uncommon variant of Kaposi sarcoma (KS), which mimics benign pyogenic granuloma both clinically and histologically. We report a case of PGLKS of the toe occurring in a HIV-positive individual. It presented as a 2cm skin swelling of 2 weeks' duration which was clinically felt to be a pyogenic granuloma. Histopathological examination revealed a polypoid atypical vascular lesion with overlying peripheral epidermal collarette. Spindle cell proliferation typically seen in KS was also identified, which was positive for human herpesvirus 8 (HHV8) by immunohistochemistry, confirming the diagnosis of PGLKS. Upon review of the literature, our case is the 29th case of PGLKS reported to date, and only the sixth in Asian population. Particular attention to histomorphology, and demonstration of HHV8 in lesional tissue will aid accurate diagnosis of this rare entity.

KEYWORDS: Kaposi sarcoma, pyogenic granuloma, human herpesvirus 8, human immunodeficiency virus, histopathology

INTRODUCTION

Pyogenic granuloma-like Kaposi sarcoma (PGLKS) is a recent addition to histological variants of Kaposi sarcoma (KS). As the name implies, the appearance closely simulates benign pyogenic granuloma, both clinically and histologically, thus carrying a risk of misdiagnosis. PGLKS has been reported in both human immunodeficiency virus (HIV)-positive and negative patients. We report a case of PGLKS in a HIV-positive patient seen in our institution and performed a literature search on SNOMED, PubMed Central and Google Scholar databases for other reported PGLKS cases thus far. To the best of our knowledge, this is the first PGLKS case to be reported in Malaysia.

CASE PRESENTATION

A 28-year-old Malaysian man of Indian descent presented to the Dermatology Clinic with a two-week history of a swelling on his right 4th toe, which bled on trauma. He was HIV-positive with CD4 count of 27 cells/mm^3 and was on highly active antiretroviral therapy (HAART) but had defaulted treatment. He was previously seen in the Dermatology Clinic for molluscum contagiosum on his face, but also defaulted follow-up.

Examination revealed a solitary lesion 2x2cm with firm, lobulated surface, clinically felt to be a pyogenic granuloma. The lesion was excised and sent for histopathological examination. Histopathological examination revealed a nodular, polypoid skin with surface hyperkeratosis and focal ulceration. The dermis was replaced by a cellular lesion composed of proliferated vascular channels, predominantly thin walled vessels, with slit-like anastomosing pattern and an epidermal collarette (Figure 1). These were admixed with small arteriole-like vessels and occasional ectatic vessels. The vessels were lined by endothelial cells showing mild to moderate atypia. In other areas, the proliferation was almost solid and was composed of spindle cells with no obvious lumina (Figure 2). Mitotic figures were easily identifiable (average of 6 in 10 high

power fields). Extravasated red blood cells and haemosiderin pigments were abundant. Scattered eosinophilic globules were also seen (Figure 3). The lesion appeared to extend to the deep excision margin. Immunohistochemistry showed positivity for CD34 and CD31 as well as for human herpesvirus 8 (HHV-8; Figure 4). The morphological features and immunohistochemical profile were consistent with pyogenic granuloma-like Kaposi sarcoma (PGLKS).

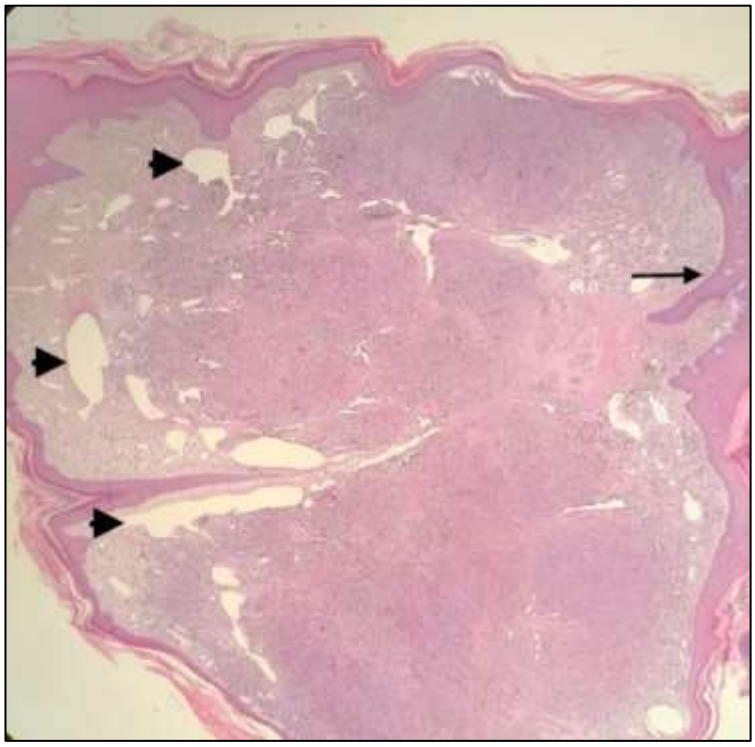

Figure 1 Scanning view of the lesion (H&E, 2x).

Low-power view illustrating a polypoidal dermal vascular lesion with an epidermal collarette (black arrow). The dermal vascular proliferation showed a mixture of slit-like vascular channels with spindle cell proliferation and small capillary-sized and arteriole-like vessels, as well as ectatic vascular channels (black arrowheads).

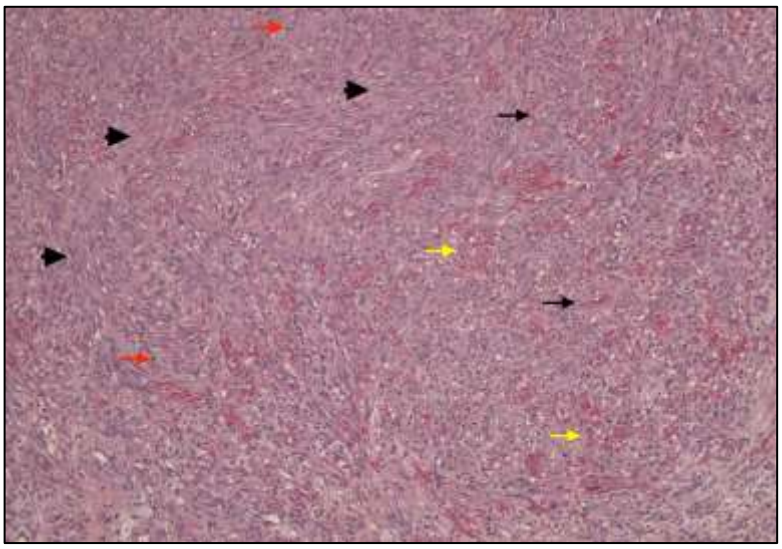

Figure 2 Medium-power view of the lesion (H&E, 10x).

There was variation in the size and shape of the vascular channels containing red blood cells (black arrows), with proliferation of spindle cells with no obvious vascular lumina (black arrowheads). Red cell extravasation was prominent (yellow arrows). Mitoses were also seen (red arrows).

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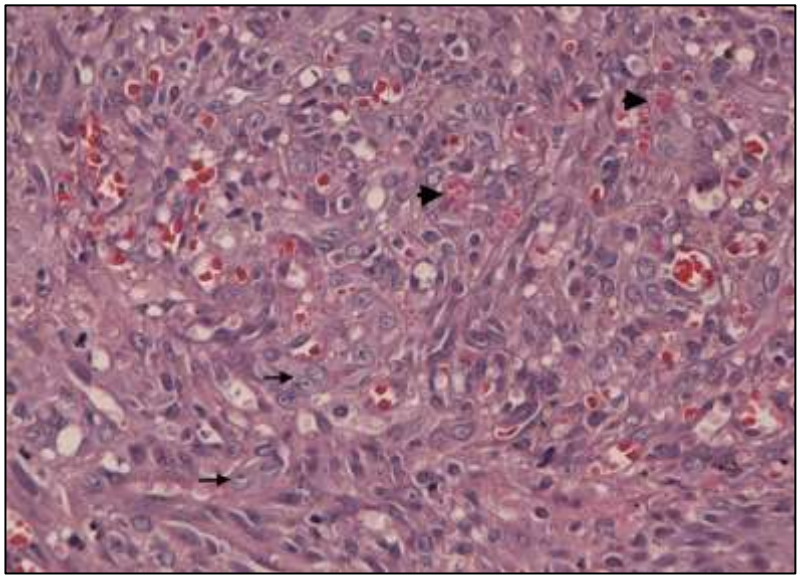

Figure 3 High-power view of the lesion (H&E, 40x).

There was mild to moderate nuclear atypia (black arrows), red blood cell extravasation and eosinophilic globules (black arrowheads), which are typical histopathological features of Kaposi sarcoma.

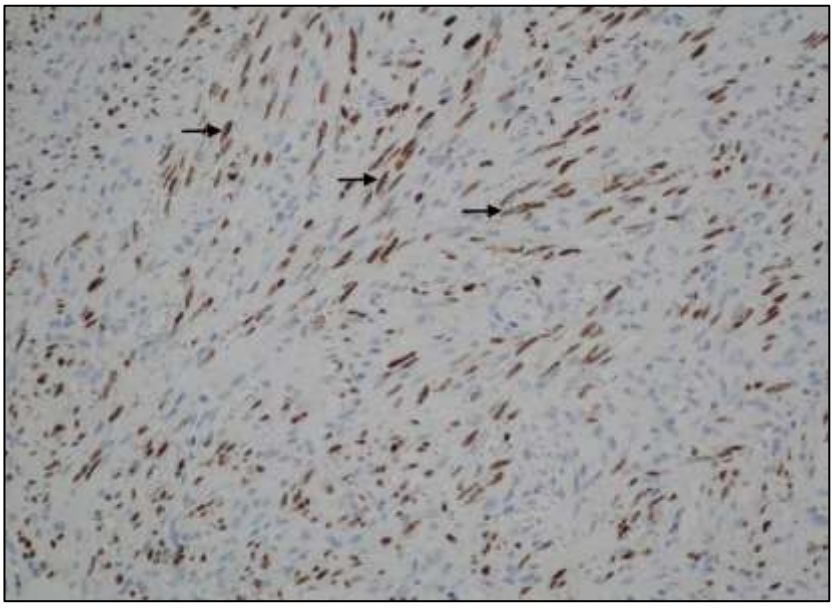

Figure 4 HHV-8 imunohistochemical stain of the lesion (HHV8, 20x).

The spindle cells showed nuclear positivity for HHV-8 immunohistochemistry (black arrows), confirming the diagnosis of Kaposi sarcoma.

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Table 1: PGLKS cases reported in the literature

Authors	Year	No of cases	Age	Sex	HIV status	CD4 Count (cells/µl)	Country / Region	Sites of lesion / Clinical description	Methods of diagnosis	Comments
Present case	2017	1	28	M	Positive Defaulted HAART	27	Malaysia / Asia	Toe	Histopathology IHC HHV8	-
Korekawa et al [1]	2018	1	74	F	Negative	NA	Japan / Asia	Toe	Histopathology IHC HHV8	-
Umar A et al [2]	2018	1	37	M	Positive (on HAART x 1 month)	54	Nigeria / Africa	Multiple – thighs, shin, foot, earlobe, size approx. 3x2cm	Histopathology	-
Darjani A et al [3]	2017	1	57	M	Negative	NA	Iran / Middle East	Left hand and left foot	Histopathology IHC HHV8 PCR for HHV8 DNA	
McClain CM et al [4]	2016	4	46 84 54 68	M M M M	Negative Unknown Positive Negative	NA	USA	Plantar foot - Verrucous keratotic plaque Plantar foot – ulcerated nodule Jawline/cheek – red/purple papule Plantar foot - blue papule	Histopathology IHC HHV8	-
Megaly M et al [5]	2015	1	30	M	Positive (off HAART x 2 years)	NA	USA	Lateral aspect of 2nd toe - 3cm red, firm mass	Histopathology IHC CD34, HHV8	-
Cabibi D et al [6]	2015	6	Mean >60	M = 5 F = 1	All negative	NA	Italy / Europe	3 hands 3 foot All solitary reddish nodules, size range 0.8-4cm	Histopathology IHC FVIII, SMA, CD31, CD34, HHV8. PCR for HHV8 DNA. All cases D240 negative	The three cases of the hands overlapped with those in 2009[11] Review of 50 PGs and 23 KS. 6/50 PG reclassified as PGLKS.

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Authors	Year	No of cases	Age	Sex	HIV status	CD4 Count (cells/µl)	Country / Region	Sites of lesion / Clinical description	Methods of diagnosis	Comments
Lee MK et al [7]	2015	1	81	M	Not specified	NA	Korea / Asia	Medial side left sole – 1.5cm red, exophytic nodule	Histopathology IHC CD31, CD34, D240, HHV8	Single nodule on the sole of foot
Lee DY et al [8]	2014	1	61	M	Not specified	NA	Korea / Asia	Below the toenail – red coloured nodule	Histopathology IHC HHV8	KS diagnosed at same site one year previously (multiple lesions on sole and toe)
Kim HJ et al [9]	2013	1	74	M	Negative	NA	Korea / Asia	Medial side of left heel (one-month history) -1.5cm bluish-red nodule	Histopathology PCR for HHV8 DNA	Close examination revealed multiple other nodules on lateral side of same heel (range 0.5-1cm)
Scott PL et al [10]	2012	1	61	M	Positive	92	USA	Left plantar foot – 2.5cm exophytic nodule	Histopathology IHC HHV8	-
Cabibi D et al [11]	2009	3	79	M	Negative	NA	Italy / Europe	Hands (on finger and palmar surface) – solitary red nodules ranging from 1.3-2.1cm	Histopathology IHC FVIII, SMA, CD31, CD34, HHV8 Nested PCR of tissue	No recurrence after two years follow-up
			76	M	Negative					
			65	M	Negative					
Urquhart et al [12]	2006	6	54	F	Negative	NA	USA	Right foot - friable pink exophytic papule	Histopathology IHC HHV8	Comparing 6 KS and 28 PGs
			43	M	Negative	NA		Groin - pedunculated lesion		
			73	M	Unknown	NA		Right ankle - several verrucous violaceous papules		
			59	M	Negative	NA		Left 2nd toe - eroded vascular nodule		
			85	M	Unknown	NA		Left 5th digit - blue translucent papule		
			74	M	Unknown	NA		Right calf - unknown		

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Authors	Year	No of cases	Age	Sex	HIV status	CD4 Count (cells/µl)	Country / Region	Sites of lesion / Clinical description	Methods of diagnosis	Comments
Ryan P et al [13]	2002	2	72 75	M M	Negative Unknown	NA NA	Ireland / Europe	Painful nodule on left ankle (KS) and developed several progressive lesions on left leg First web space of left foot, 0.6cm, and similar smaller lesions on fourth toe and left thigh	Histopathology PCR of tissue for HHV8	-
Fukunaga M [14]	2000	1	53	M	Negative	NA	Japan / Asia	Dorsal foot - painless nodule 21 x 12mm	Histopathology IHC FVIII	-
Wyatt ME et al [15]	1998	1	25	F	Positive	NA	Africa	Left nasal vestibule, - fleshy 0.75cm lesion	Histopathology	Presented during pregnancy. Excised in postpartum period but recurred two months later

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DISCUSSION

PGLKS is a recently described, rare variant of Kaposi sarcoma. A search on PubMed, SCOPUS and Google Scholar databases using the keywords "Kaposi Sarcoma" and "Pyogenic Granuloma" yielded 15 relevant publications relating to case reports and case series of PGLKS. All the cases are presented in Table 1. Including the present case, there were 29 cases of PGLKS reported to-date; only six of which were Asian cases [1,7-9,14] while most were from USA [4-5,10,12] and Europe [6,11,13] (12 and 8 cases respectively). Distal extremities were the most common site (23/29 cases), followed by lower limbs (4/29) and the head area (2/29 cases). Males were predominantly affected (25/29 cases), with male to female ratio of 7.25:1. In terms of HIV status, most PGLKS patients were HIV-negative (16/29); HIV-positive patients comprised 6 cases while the status of 7 cases were unspecified or unknown. The age range was wide, ranging from 25 – 81 years, with a mean of 60 years.

The majority of reported cases of PGLKS demonstrated the presence of HHV-8 within the lesional cells by either immunohistochemical or molecular methods. The role of Human Herpesvirus 8 (HHV-8) in the pathogenesis of KS is well-established [16,17]. While a definitive conclusion about the cellular origin of KS remains elusive, theories of cell origin include reprogramming of HHV-8-infected blood vascular endothelial cells to lymphatic endothelial cells and uncommitted endothelial progenitor cell [16]. This partly explains the immunophenotype of the neoplastic cells within KS, which show overlapping lymphatic and vascular endothelial cell differentiation, thus precluding definitive conclusion drawn on the cell of origin.

The identification of HHV-8 in KS serves as the best supportive finding in the diagnosis of KS and its variants to date, thus discriminating it from other entities. In general, the main non-KS histopathological differential diagnosis in this setting may include other vascular lesions such as PG, bacillary angiomatosis, spindle cell haemangioma and angiosarcoma; the latter two may show predominant spindled morphology. Specifically referring to the case presented, the constellation of nodular/polypoid architecture with epidermal collarette, surface ulceration, vascular proliferation and a spindled component without overt atypia raised the main differential diagnoses of PG and PGLKS. Bacillary angiomatosis was considered less likely, given the lack of bacterial colonies and associated inflammation despite its association with HIV positivity. Spindle cell haemangioma usually contains vacuolated and epithelioid endothelial cells, and angiosarcoma typically shows overt endothelial atypia; both were absent in this case. When faced with a diagnostic dilemma, nuclear positivity for HHV-8 by immunohistochemistry (IHC) provides the most reliable supportive evidence for a diagnosis of PGLKS. We have also demonstrated HHV-8 positivity by immunohistochemistry in the current case. Given the wide availability and accessibility of the IHC, it quickly becomes preferable to the more tedious HHV8 DNA polymerase chain reaction (PCR) analysis. In addition, there is also a higher rate of false positivity linked to the latter [12].

In addition to HHV8 IHC, other vascular markers (CD31, CD34 and D2-40) have also been used to aid diagnosis to some extent. D2-40 is typically positive in KS cases, providing evidence of lymphatic differentiation of the neoplastic cells. D2-40 negativity however, does not exclude the diagnosis of PGLKS as previously illustrated by Cabibi D et al [6]. They hypothesized that the D2-40 negativity of the vessels may be due to the fact that this lesion represents a very early stage of the infection; in this setting, while more mature endothelial markers are focally and progressively lost, the lymphatic differentiation of endothelial CD34-positive precursors has not occurred yet. Alternatively, D2-40-negative PGLKS may represent HHV-8 infection of a pre-existing pyogenic granuloma [6].

In a HIV-positive individual, KS is an acquired immune deficiency syndrome (AIDS)-defining illness. AIDS-associated KS (AIDS-KS) commonly arises in the setting of low CD4 count and typically manifests as a disseminated disease. It is interesting to note that more than half of the PGLKS cases reported thus far are HIV-negative and show a predilection in males. Whether there are additional risk factors that predispose to the development of PGLKS in this cohort remain to be identified. In HIV-negative individuals and HIV-positive individuals on HAART, the behaviour of KS

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may be more indolent [17]. However, being a relatively new entity, the true behaviour of a localized PGLKS is yet to be determined.

It is important to think of PGLKS when encountering a PG-like lesion to avoid missing the diagnosis. The fact that PGLKS can be seen in both HIV-positive and HIV-negative patients and the fact it closely mimics typical PG clinically and on histopathological examination makes the diagnosis even more challenging. Particular attention to histomorphology, as well as utilizing ancillary studies where necessary will allow accurate identification of this uncommon lesion.

CONCLUSION

PGLKS is a rare entity with shared histological features of pyogenic granuloma and Kaposi sarcoma. Diagnosis relies on histopathological examination as these are often unsuspected clinically. Ancillary studies, especially HHV8 immunohistochemistry are useful in supporting its diagnosis.

Conflicts of interest

None.

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None.

Authors' contribution

All authors designed, written and reviewed the manuscript prior to submission.

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