CASE REPORT

Collision of vascular malignancies: Kaposi sarcoma and spindle-cell angiosarcoma in a HIV-negative patient

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Introduction: It is very uncommon for Kaposi sarcoma (KS) and angiosarcoma (AS) to occur simultaneously at the same anatomical site, especially in immunocompetent, HIV-negative people. Due to variations in prognosis and treatment, it is crucial to identify dual vascular malignancies.

Case Presentation: A 66-year-old man presented with a large exophytic tumor of the left foot at the site of previously diagnosed KS. Amputation of the second, third, and fourth toes was necessary for surgical treatment. At histopathological examination, a malignant spindle-cell vascular with strong positivity for endothelial markers was observed, with negative human herpesvirus 8 (HHV-8) staining, confirming a new vascular neoplasm, AS, in a patient with an initial KS lesion.

Conclusions: This case demonstrates that both KS and a distinct high-grade AS can develop in the same area in patients who are HIV-negative. Since multiple primary vascular tumours may coexist and substantially impact diagnosis, prognosis, and treatment.

Keywords: angiosarcoma, immunohistochemistry, kaposi sarcoma, vascular tumours

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Introduction

Vascular neoplasms comprise a heterogeneous spectrum of endothelial-cell tumors, ranging from benign lesions to aggressive malignancies [1]. Notable malignant vascular tumors include Kaposi sarcoma (KS) and angiosarcoma (AS), each with distinct clinical and molecular profiles. Advances in clinicopathologic criteria and molecular genetics have refined this classification, acknowledging significant overlap in appearance but divergent pathogenetic mechanisms [1,2].

Kaposi sarcoma is a low-grade angioproliferative tumor of lymphatic and blood-vessel endothelium caused by human herpesvirus 8 (HHV-8/KSHV) [3]. KS cells carry latent KSHV genomes and express LANA-1, a key diagnostic marker [3,4]. Immunohistochemistry confirms HHV-8, with spindle cells positive for CD31/CD34 and diffuse nuclear LANA-1 staining, which is highly specific for KS [3]. KSHV, discovered in 1994, is the causative agent of all KS variants [4,5]. In immunocompetent patients, classic KS is often indolent but can progress to extensive cutaneous or visceral disease if untreated [3,6].

On the other hand, AS is an uncommon, high-grade endothelial cancer that makes up 1-2% of soft tissue sarcomas [3]. It typically affects elderly Caucasian patients on the head and neck, especially the scalp [7,8], and is linked to risk factors like chronic lymphoedema and previous radiation [8,9]. AS is consistently HHV-8 negative, in contrast to KS [9].

The concurrent occurrence of both KS and AS in the same patient is exceedingly rare, especially in an HIV-negative, immunocompetent individual. Only a few case reports and series have documented such coincidences [10,11]. This case illustrates the diagnostic challenges involved in distinguishing between the solid variant of Kaposi sarcoma and spindle-cell angiosarcoma, as well as the difficulties in interpretation when immunohistochemical and molecular investigations are limited. The concomitant occurrence of these two vascular neoplasms in an immunocompetent patient is exceptionally rare and further supports the detailed reporting of this case.

Case presentation

In 2025, a 66-year-old male HIV-negative patient was assessed for the first time for numerous vascular nodular cutaneous lesions on his lower limbs and trunk. He did not have a history of organ transplantation, chemotherapy, long-term corticosteroid use, immunodeficiency, or high-risk behaviours. HHV-8-positive biopsy of a cutaneous lesion confirmed the diagnosis of sporadic (classic) KS, which was supported by repeated HIV testing that came back negative. He was receiving systemic anthracycline therapy for refractory KS at follow-up in the Department of Plastic Surgery at the Mureş County Clinical Emergency Hospital because of his numerous violaceous nod-

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ules and plaques. The lesions were most prevalent on the thighs and lower extremities, and showed a poor response to treatment, which was consistent with disseminated cutaneous KS.

Over several months, the patient developed a rapidly enlarging, exophytic, ulcerated tumor on the left foot, which predominantly involved the second, third, and fourth toes and the metatarsal heads of the corresponding toes. The lesion was described clinically as a "monstrous" nodular mass that was prone to ulceration and bleeding, with progressive local destruction and impairment of function. Due to concerns regarding size, local invasion, and potential for complications, the patient underwent surgical treatment including amputation of the second, third, and fourth toes of the left foot, preserving only the first and fifth toes. Upon admission, the patient signed an informed consent form agreeing to the publication of his anonymized medical data.

Histopathological findings

The amputated specimen measured 65 × 80 × 30 mm and consisted of the forefoot with digits II-IV. On gross examination, multiple grey-brown nodular areas measuring up to 60 × 50 × 15 mm were noted at the level of the third toe, with proximal extension. The tumour was located at a minimum distance of 5 mm from the nearest surgical resection margins, while the distance from the other lateral margins measured 5 mm and 15 mm, respectively. All surgical margins were free of tumour.



Figure 1. A. Clinical image of Kaposi sarcoma lesions on the left thigh.
B. Gross image of the amputated foot specimen.

Microscopically, the newly developed lesion consisted of a malignant spindle-cell proliferation with a predominantly infiltrative architecture. Irregular, anastomosing vascular channels dissecting dermal and subcutaneous collagen bundles were observed, imparting a characteristic dissecting growth pattern. The tumour cells were spindle-shaped with scant cytoplasm, pleomorphic nuclei, prominent nucleoli, and marked nuclear atypia. A very high mitotic rate was identified (55 mitoses per 10 high-power fields), including atypical mitotic figures.

Importantly, no gradual morphological transition was identified between the Kaposi sarcoma component and the spindle-cell vascular proliferation. Instead, two distinct tumoural populations were observed in direct contact, without an intervening zone of morphological blending, findings consistent with a collision tumour.

Immunohistochemical stains revealed diffuse and strong positivity for the tumour cells for the vascular markers CD31 and CD34. Additional immunohistochemical markers, including S100, SOX10, and cytokeratin AE1/AE3, were negative in the tumour cells. The Ki-67 proliferative index was approximately 20%. These findings were consistent with a high-grade malignant vascular tumour, spindle cell AS. The surgical margins were free of tumor.

Differential diagnosis and diagnostic workup

Given the patient's known history of HHV-8-positive KS and the anatomical overlap between the previous KS lesions and the newly developed aggressive tumour, an initial diagnostic dilemma arose regarding the nature of the lesion. Unlike the patient's previous HHV-8-positive KS lesions, the amputated tumor's HHV-8 immunohistochemistry was negative, establishing the coexistence of two separate vascular malignancies: HIV-negative KS and secondary angiosarcoma. Under multidisciplinary follow-up, the patient continued to receive anthracycline-based therapy for KS; however, lesions continued without full remission. Finally, complete clinical follow-up data, including information regarding local recurrence, metastatic progression, and survival status, were not available.

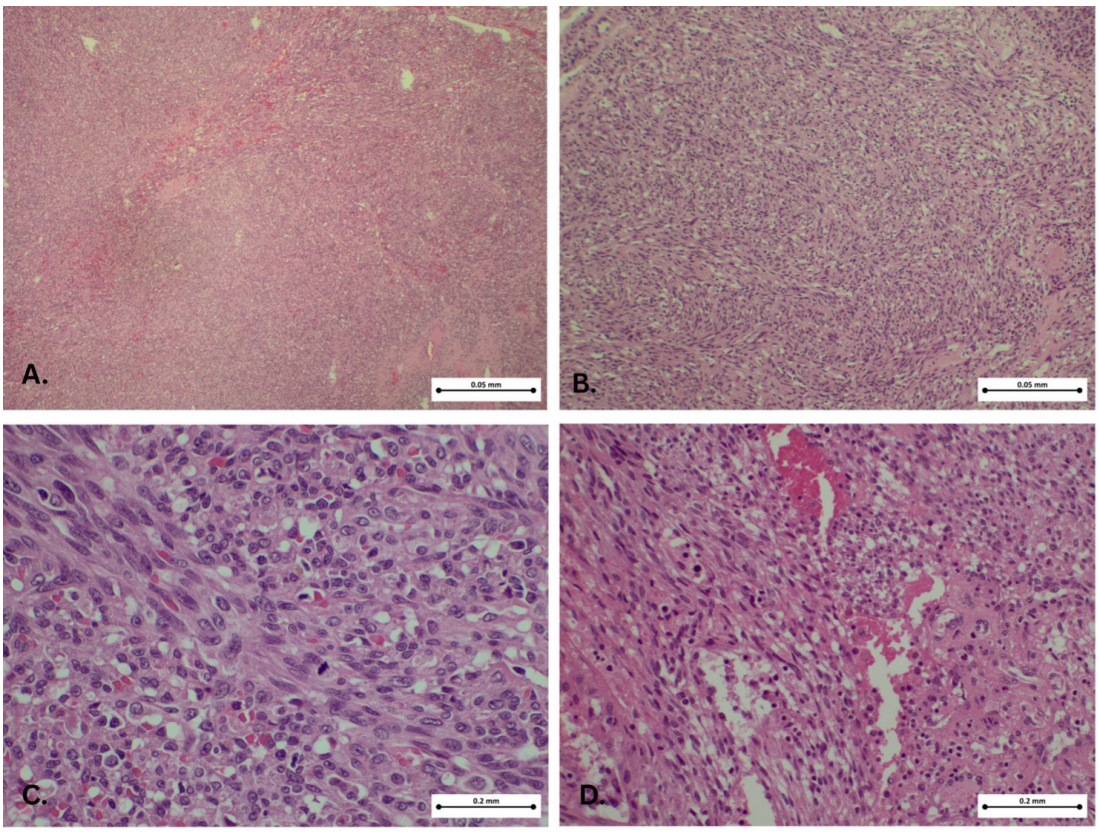


Figure 2 - H&E stain showing spindle-cell malignant vascular proliferation.

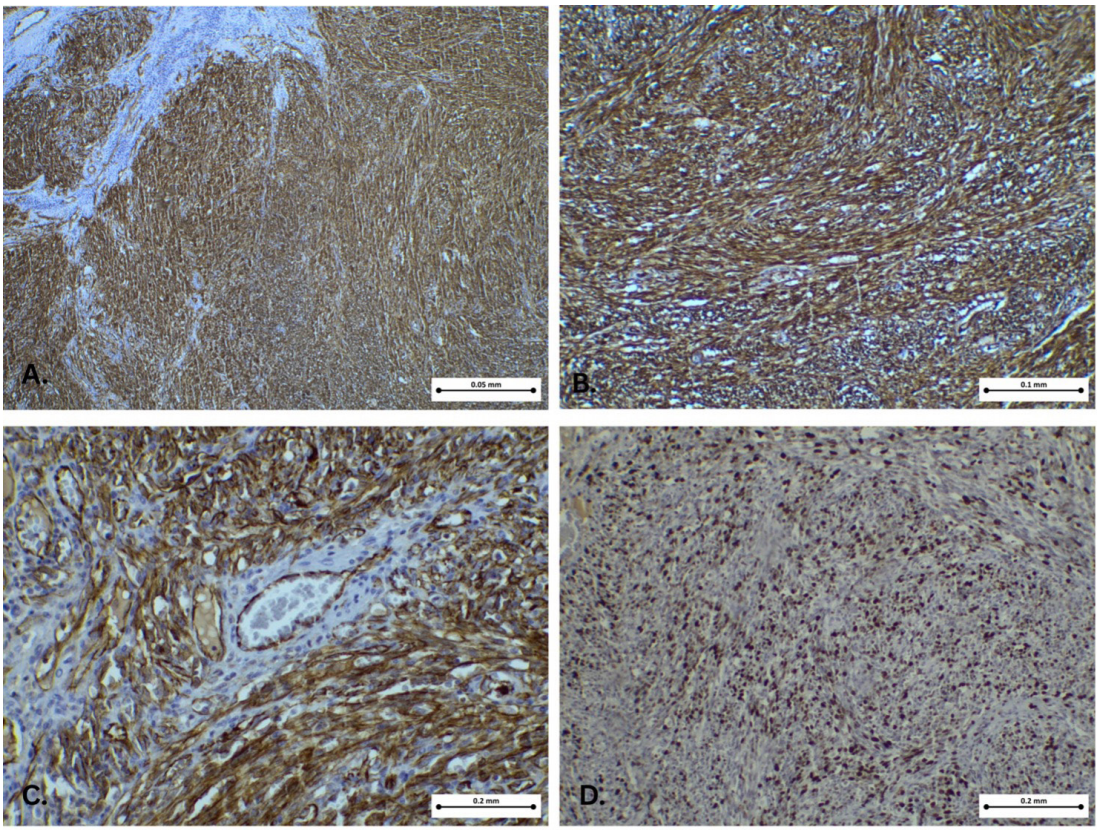


Figure 3 - A,B. CD34 immunohistochemical staining showing tumor spindle cells; C. CD31 highlighting vascular endothelium; D. Ki67 index.

Discussion

Kaposi sarcoma and AS have rarely been reported to coexist, which makes this case particularly unusual. Previous reports of co-occurring KS and AS have generally occurred in complex or immunosuppressed patients. For example, Gambassi et al. reported an elderly HIV-negative man with classical KS whose tumor later gave rise to a secondary, low-grade AS at a distant site. Similarly, Sezgin et al. reported a patient with chronic lymphocytic leukemia who developed KS followed by an independent cutaneous AS on the foot. They also reiterated the importance of focusing on the most aggressive malignancy and routine dermatologic follow-up for secondary tumors in patients with KS, as these patients are at high risk for developing additional tumors [12]. Clinically, the coexistence of these neoplasms has important implications: angiosarcomas are aggressive and need immediate treatment, and any abnormally fast-growing lesion, even in a pre-existing KS area, should be biopsied rather than presumed to be a sign of KS progression. Up to 25% of classical KS patients may develop a second primary tumor, underscoring the necessity of thorough evaluation, particularly in elderly HIV-negative individuals [11].

Why did this patient develop two independent vascular tumors with different characteristics? One is the possibility of a treatment-associated secondary angiosarcoma. MYC gene amplification has been reported frequently in secondary angiosarcomas, but unfortunately, testing for MYC amplification was not available in this case. Therefore, a causal association with prior treatment cannot be firmly established, and any discussion regarding the primary or secondary nature of the angiosarcoma must remain cautious and speculative. Another hypothesis is that this patient's vascular endothelium was simply predisposed (by HHV-8-driven KS and associated chronic inflammation) to undergo malignant transformation along a different vascular tumor lineage later.

Immunohistochemistry (CD31, CD34, ERG, von Willebrand factor) confirms vascular origin and helps rule out carcinoma or melanoma, while secondary AS, particularly post-radiation or in lymphoedema, often demonstrates MYC amplification. In the evaluation of poorly differentiated vascular tumours, ERG is currently considered one of the most sensitive and specific markers of endothelial differentiation and is particularly useful in confirming the diagnosis of angiosarcoma. In the present case, ERG immunostaining could not be performed, representing an additional diagnostic limitation and necessitating reliance on the correlation between morphology and the available immunohistochemical findings.

An essential aspect of this case is the distinction between spindle-cell angiosarcoma and the solid variant of Kaposi sarcoma, a recognized morphological subtype that may closely mimic angiosarcoma. Features favouring angiosarcoma in the present case included a dissecting growth pattern with irregular vascular channels tunnelling through collagen bundles, marked nuclear atypia, prominent nucleoli, and a very high mitotic index. The absence of HHV-8 expression in the newly developed lesion, in contrast to the pre-existing HHV-8-positive Kaposi sarcoma lesions, further supports the interpretation of a distinct vascular neoplasm.

The LANA-1 antibody, which could have provided further support for the differential diagnosis and tumour classification, was not available at the time of investigation, and this represents another important limitation of the present case report.

Careful clinicopathological evaluation was essential, as both tumours expressed endothelial markers (CD31, CD34), but only the KS lesions were HHV-8 positive [9,12]. The angiosarcoma was HHV-8 negative, with a high mitotic rate and elevated Ki-67, confirming a high-grade malignancy and supporting its distinction from KS. The Ki-67 proliferative index was approximately 20% and was assessed on a separate histological slide. It should be noted that the area selected for Ki-67 evaluation did not necessarily correspond to the mitotic hotspot. This may explain the discrepancy between the very high mitotic count and the relatively modest percentage of Ki-67-positive cells, suggesting a possible underestimation of the tumour's true proliferative activity.

In the present case, the absence of a clearly identifiable morphological transition zone between the two components favours the interpretation of a collision tumour. However, in the absence of additional molecular data, a transformation process cannot be completely excluded, although this concept remains controversial in the literature.

Conclusion

This case underscores the need for re-biopsy of any new lesion arising in the vicinity of a known Kaposi sarcoma, particularly when it demonstrates rapid growth or atypical morphological features. It also highlights the importance of careful integration of clinical and morphological findings when a complete immunohistochemical and molecular panel is not available to avoid misinterpretation and potential diagnostic delay in complex vascular lesions.

Authors' contributions

DS (Writing - original draft; Project administration; Investigation; Funding acquisition)
ARCS (Writing - review & editing; Validation; Formal analysis; Visualization; Data curation; Conceptualization; Project administration)
PMS (Resources; Software; Data curation; Formal analysis)
ACT (Conceptualization; Methodology; Writing - review & editing; Visualization)
OSC (Supervision; Visualization; Funding acquisition)

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