Submandibular nodal involvement as the initial presentation of HIV-negative Kaposi sarcoma: a case report

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Submandibular nodal involvement as the initial presentation of HIV-negative Kaposi sarcoma: a case report

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Abstract

Background Kaposi sarcoma (KS) is an angioproliferative malignancy driven by human herpesvirus 8 (HHV-8) that most often manifests as cutaneous lesions. Nodal involvement in HIV-negative, immunocompetent individuals, especially as an initial presentation, is exceedingly rare. Head and neck KS accounts for less than 5% of non-AIDS-associated cases, with cervical lymphadenopathy representing only 4.4% of lesion distributions in this population.

Case presentation A 71-year-old HIV-negative Italian man presented with a painless, progressively enlarging submandibular lymphadenopathy. Surgical excision followed by histopathology and immunohistochemistry confirmed nodal KS. Subsequent full-body skin examination identified a previously unrecognized violaceous lesion on the hallux, which was histopathologically confirmed as KS.

Conclusions This case highlights the diagnostic challenges posed by atypical KS presentations and emphasizes the need to include KS in the differential diagnosis of unexplained cervical lymphadenopathy, even in immunocompetent patients without clinically evident cutaneous lesions. Comprehensive dermatologic screening and long-term multidisciplinary surveillance are advised to detect and manage potential disease progression.

Keywords Kaposi sarcoma, Classic Kaposi sarcoma, Human herpesvirus 8, Cervical lymphadenopathy, Submandibular lymphadenopathy, HIV seronegativity

Introduction

Kaposi sarcoma (KS) is a multifaceted, angioproliferative disorder that is universally associated with infection by human herpesvirus 8 (HHV-8). First described by Moritz Kaposi in 1872, KS is now recognized to encompass four distinct clinical variants: classic indolent, endemic African, AIDS-associated, and iatrogenic. While AIDS-related KS is the most common and aggressive form, particularly in immunocompromised patients, classic KS typically presents as an indolent cutaneous disease affecting older males of Mediterranean or Eastern European descent. Characteristically, classic KS manifests as violaceous to reddish–blue macules, plaques, or nodules predominantly on the lower extremities [1].

Despite its well-known cutaneous predilection, KS may occasionally involve extracutaneous sites. In the head and neck region, oral lesions are more common, particularly in immunosuppressed patients; however, lymph node involvement in HIV-negative individuals is exceedingly uncommon [2]. This observation is underscored by the

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limited number of reports documenting nodal KS in the absence of HIV infection, and even fewer cases describe involvement of a cervical lymph node.

In this case report, we describe an unusual manifestation of KS in an HIV-negative, immunocompetent man, in whom submandibular lymph node involvement was the presenting feature. This atypical finding served as the initial clue prompting further diagnostic investigation, highlighting a clinical scenario that challenges conventional diagnostic algorithms.

Case presentation

A 71-year-old man of Mediterranean descent presented to our otolaryngology clinic in September 2024 with a six-week history of painless, progressively enlarging swelling in the left submandibular region. He had no history of malignancy or immunodeficiency, denied tobacco and intravenous drug use, and reported only occasional alcohol consumption. Physical examination revealed a firm, mobile, 3-cm mass inferior to the left mandible; no cutaneous or mucosal lesions were detected elsewhere in the head and neck region.

An initial ultrasound-guided fine-needle aspiration was inconclusive. Contrast-enhanced computed tomography (CECT) of the neck demonstrated a 27 × 17 mm well-circumscribed enhancing nodular lesion adjacent to the left submandibular gland (Fig. 1). Routine preoperative laboratory studies were unremarkable.

The patient underwent excision of the dominant left level IB lymph node together with a smaller pigmented periglandular lymph node located lateral to the left submandibular gland. Intraoperative frozen section showed no evidence of malignancy in the dominant node, whereas the smaller node displayed a spindle-cell proliferation. The submandibular gland was preserved because it appeared macroscopically uninvolved.

On permanent sections, the 8-mm node exhibited near-complete architectural effacement by intersecting fascicles of bland spindle cells, slit-like vascular spaces, and extravasated erythrocytes, with focal cytologic atypia, mitotic activity, and no tumour necrosis. Immunohistochemistry confirmed KS (positive for CD31, CD34, and HHV-8/LANA-1; negative for S100, actin, CD56, and CD117) (Figs. 2 and 3). The 25-mm node showed only reactive sinus histiocytosis.

Postoperative HIV serologic testing was negative. Whole-body PET–CT showed no evidence of hypermetabolic disease. Subsequent full-body dermatological examination identified a clinically occult, violaceous papule on the plantar surface of the right hallux. An excisional punch biopsy of this cutaneous lesion confirmed KS.

The patient was referred to a haematologist–oncologist for further staging and management.

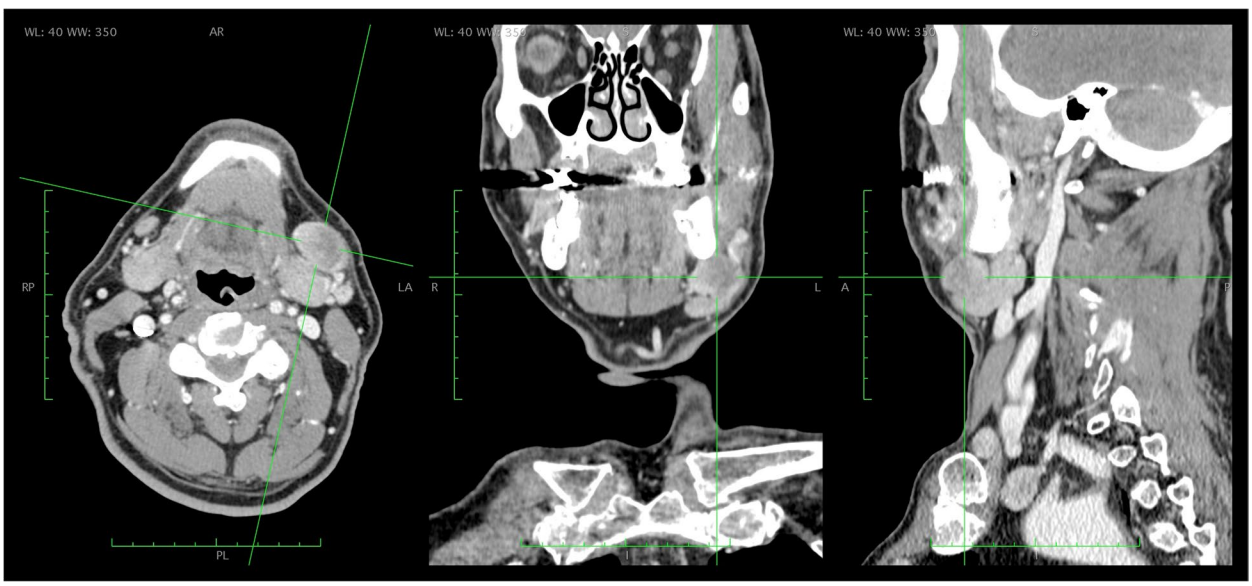

Fig. 1 CECT of the neck showing the left submandibular mass in three orthogonal planes. Axial (left), coronal (centre), and sagittal (right) reconstructions depict a well-circumscribed, homogeneously enhancing mass measuring 27 × 17 mm in the left submandibular (level IB) region (green cross-hairs). The lesion is located anterior to the submandibular gland and appears closely abutting the residual glandular parenchyma by a 12 mm bridge of soft tissue

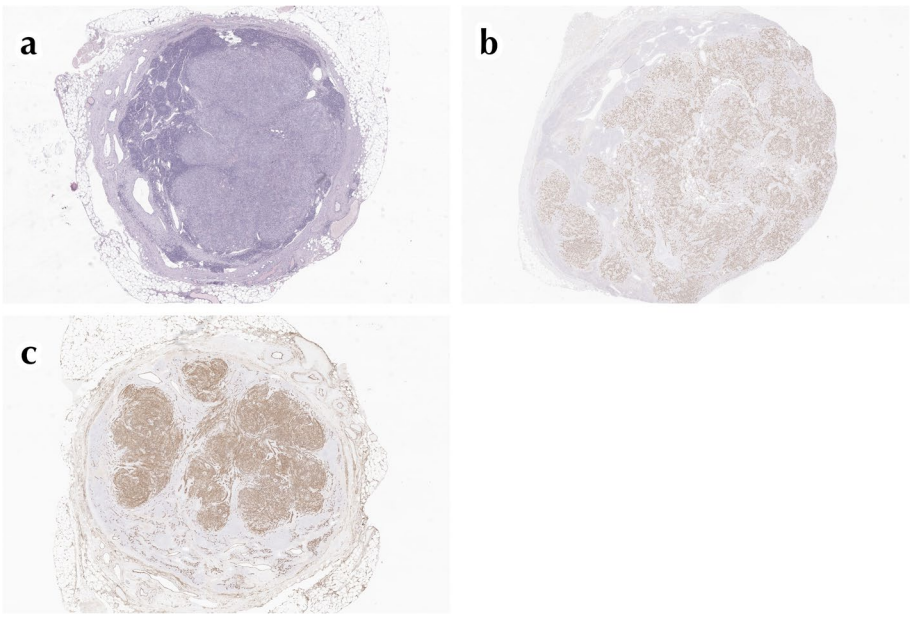

Fig. 2 Low-power overview of nodal KS (original magnification × 2). **A** Hematoxylin and eosin (H&E)–stained section shows near-total effacement of the nodal architecture by multiple, well-circumscribed lobules of spindle-cell neoplasm. **B** Immunolabelling for human herpesvirus 8 latent nuclear antigen-1 (HHV-8/LANA-1) is positive in the nuclei of KS spindle cells, confirming viral aetiology. **C** CD34 immunostaining is diffusely positive in the membranes of the spindle cells

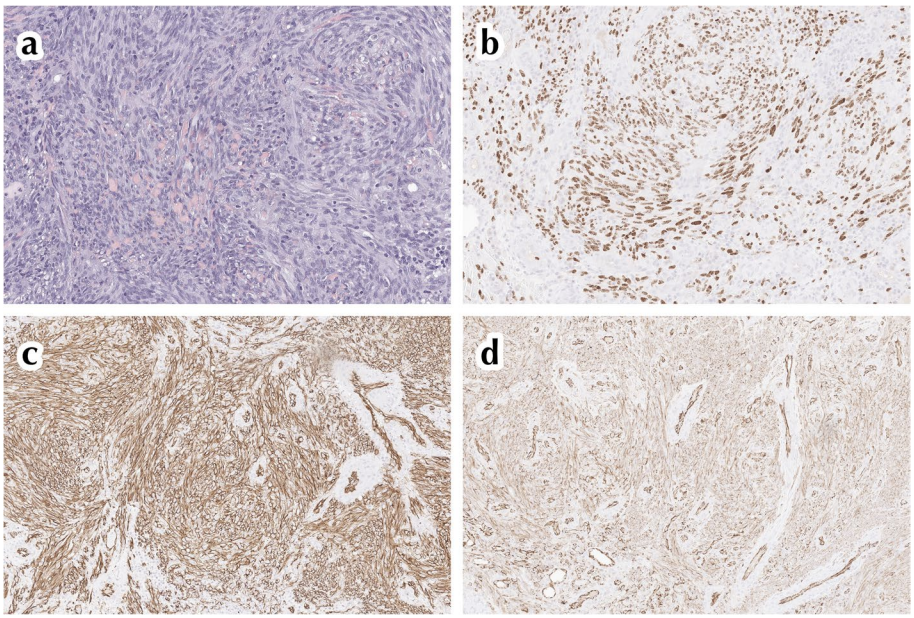

Fig. 3 High-power histologic and immunohistochemical details of the lesion (original magnification × 20). **A** KS nodules are composed of intersecting fascicles of bland spindle cells, with slit-like vascular spaces and scattered extravasated erythrocytes (H&E stain). **B** HHV-8/LANA-1 immunostaining shows intense nuclear labelling of spindle cells. **C** CD34 positivity in the spindle cells is a marker of vascular origin of the neoplastic cells. **D** CD31 immunostaining, another vascular marker, outlines the anastomosing endothelial channels

Discussion and conclusions

Head and neck involvement by KS in HIV-negative individuals is, in itself, uncommon. While oral mucosal lesions are the most frequently reported head and neck manifestations in this patient group, nodal involvement by KS is exceptionally rare [2–4].

Literature reviews indicate that head and neck KS accounts for less than 5% of non-AIDS-associated KS cases [5]. Patrikidou et al., in an extensive review of 251 non-AIDS head and neck KS cases, found cervical lymphadenopathy accounted for only 4.4% of lesion distributions [2]. Abramson and Simons also noted the low incidence of cervical lymph node involvement in adults with classic KS [6]. Agaimy et al. reported lymph node involvement in three of their 11 head and neck KS cases [5]. Among their three HIV-negative patients with nodal disease, only one presented with an intraparotid lymph node as the initial site of involvement rather than a cervical node.

A particularly noteworthy aspect of this case is the diagnostic sequence. Although surgery was prompted by the radiologically dominant submandibular mass, the diagnosis of KS was established in a separate small pigmented lymph node adjacent to the left submandibular gland, whereas the larger node showed only reactive changes. The nodal finding therefore provided the initial clinical clue to the diagnosis, after which targeted dermatological examination disclosed an otherwise unrecognized hallux lesion. This contrasts with the more common scenario in which cutaneous lesions are the first manifestation, or oral lesions precede other KS sites in approximately 20% of patients [5]. Accordingly, cervical lymphadenopathy as the presenting feature of KS in an HIV-negative individual poses a considerable diagnostic challenge and supports including KS in the differential diagnosis of unexplained spindle-cell proliferations involving head and neck lymph nodes, even in the absence of clinically evident cutaneous lesions [4, 5]. Given the broad histopathological spectrum of such lesions, the differential diagnosis includes lobular capillary haemangioma, characterized by a circumscribed lobular architecture; Kaposiform haemangioendothelioma, which may morphologically resemble KS; angiosarcoma, which exhibits marked cytologic atypia and dissecting vascular channels; and spindle cell carcinoma, which is positive for epithelial markers, but negative for endothelial markers). Crucially, unlike KS, all of these entities are HHV-8 negative [7].

This case underscores the necessity for a thorough, full-body dermatological examination in all patients diagnosed with KS, regardless of the initial site of presentation or HIV status. Abramson and Simons, as well as Patrikidou et al., reported that a significant majority (approximately 84%) of head and neck KS cases in HIV-negative individuals were associated with concurrent skin lesions in other regions [2, 6]. This suggests that the apparent incidence of 'primary' or 'isolated' nodal KS may depend, at least in part, on the thoroughness of the initial skin examination. It is plausible that in some previously reported cases of apparently isolated head and neck KS, subtle or asymptomatic distant cutaneous lesions may have been overlooked if a comprehensive dermatological survey was not performed. The delayed discovery of the hallux lesion in our patient, found only after the nodal KS diagnosis, reinforces this point. A limitation of this report is the short follow-up, which precludes conclusions regarding long-term disease behaviour, risk of progression, and the potential need for systemic therapy.

Local excision provided definitive histological diagnosis and initial local management, consistent with current recommendations for limited classic KS. Nevertheless, given the inherently multifocal nature of classic KS, long-term clinical behaviour may be unpredictable, and a minority of patients may experience progression or visceral involvement even decades after initial presentation. We therefore advocate (1) meticulous full-body skin and mucosal examination and (2) long-term surveillance coordinated among dermatology, oncology, and primary care.

Informed consent

Written informed consent for publication of the case details and all accompanying materials was obtained from the patient. All potentially identifying information has been removed or anonymized to safeguard patient confidentiality.

Authors' contributions

M.C.: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. B.E.F.: Project administration, Supervision, Writing – review & editing. P.C.: Methodology, Resources, Writing – review & editing. C.P.: Resources, Writing – review & editing. V.F.: Methodology, Supervision, Resources, Writing – review & editing. A.L.: Conceptualization, Methodology, Supervision, Resources, Writing – original draft, Writing – review & editing.

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Data availability

Data sharing is not applicable to this article because no datasets were generated or analysed in the course of this study.

Declarations

Ethics approval and consent to participate

In accordance with institutional and national policies, ethics committee approval was not required for this case report.

Consent for publication

Written informed consent for publication of the case details and all accompanying materials was obtained from the patient. All potentially identifying information has been removed or anonymized to safeguard patient confidentiality.

Competing interests

The authors declare no competing interests.

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