Head and Neck Pathology (2019) 13:664–667
https://doi.org/10.1007/s12105-018-0954-y

SINE QUA NON CLINICOPATHOLOGIC CORRELATION

Primary Nasopharyngeal Kaposi Sarcoma as Index Diagnosis of AIDS in a Previously Healthy Man

Gwyneth S. T. Soon[1] · Fredrik Petersson[1] · Mark K. T. Thong[2] · Char Loo Tan[1,3]

Received: 12 July 2018 / Accepted: 18 July 2018 / Published online: 23 July 2018

Abstract

A 38-year-old, previously healthy man presented with blood-stained saliva and epistaxis. A 3 mm nasopharyngeal lesion was found. A biopsy was performed and microscopic examination revealed a Kaposi sarcoma. The patient was subsequently found to be positive for human immunodeficiency virus (HIV). The diagnosis of Kaposi sarcoma in the presence of HIV infection advanced his disease to Acquired Immunodeficiency Syndrome (AIDS). Primary manifestation of Kaposi sarcoma in the nasopharynx is extremely rare. The histologic differential diagnosis of Kaposi sarcoma in this unusual site, especially without the clinical history of immunosuppression, is broad. Awareness that nasopharynx can be a primary involvement site of Kaposi sarcoma and serves as index diagnosis of AIDS is important given its serious clinical implication.

Keywords Kaposi sarcoma · Nasopharynx · Nasal cavity · AIDS · HIV · HHV8

History

A 38-year-old Asian male with no significant medical history presented with episodes of blood-stained saliva and epistaxis, associated with bilateral cervical swelling of 1–2 months' duration. Further questioning revealed weight loss of 12 kg over the past year and loss of appetite. He denied any fever or night sweats. On physical examination, there was bilateral cervical lymphadenopathy; the two largest lymph nodes were mobile and firm, each measuring 1.5 cm in maximum diameter at the right and left level V. A flexible naso-endoscopy was performed, revealing a 3 mm reddish granular mass at the inferior aspect of the posterior wall of the left postnasal space (Fig. 1). No contact bleeding was seen, and biopsy of the mass was performed. The patient also underwent fine needle aspiration (FNA) of the enlarged left cervical lymph node.

✉ Char Loo Tan
char_loo_tan@nuhs.edu.sg

[1] Department of Pathology, National University Health System, Singapore, Singapore

[2] Department of Otolaryngology, National University Health System, Singapore, Singapore

[3] Department of Pathology, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074, Singapore

Diagnosis

Histology of the left postnasal space mass biopsy showed pieces of upper respiratory tract-type mucosa with a cellular tumor in the subepithelial stroma, composed of fascicles of spindle cells displaying mild nuclear atypia surrounding slit-like and angulated vessels (Fig. 2a). Extravasated red blood cells and scattered intra- and extra-cellular hyaline globules were seen (Fig. 2b). There were several mitotic figures. A mild lymphoplasmacytic infiltrate was also present. On immunohistochemistry, the spindle cells showed diffuse nuclear positivity for ERG and human herpesvirus 8 (HHV-8) (Fig. 2c, d). CD34 expression was also seen, as well as very focal weak staining with smooth muscle actin and androgen receptor. The tumor cells were negative for cytokeratins (AE1/3), S100-protein and STAT6. The final diagnosis was that of a Kaposi sarcoma (KS). FNA of the left cervical lymph node showed hemodiluted smears with a mixed lymphoid population, favoring a reactive lymph node. No atypical spindle cell population was seen.

Upon diagnosis, the patient underwent further investigations, and was found to be retroviral screen positive and a HHV-8 serum level was 6.5×10^4 copies of viral DNA/mL. The diagnosis of KS in the presence of HIV infection hence advanced his disease to Acquired Immunodeficiency Syndrome (AIDS). Staging computed tomographic scans showed an unremarkable nasopharynx, oropharynx and

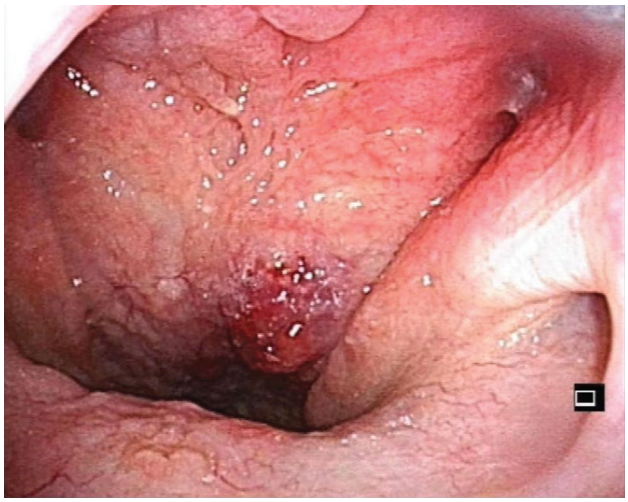

Fig. 1 Nasendoscopic findings show a small reddish granular mass in the left postnasal space

hypopharynx. Mildly enlarged level V nodes (up to 1.1 cm in the short axis) were seen, while the rest of the lymph nodes were not enlarged by size criteria. No significant abnormality was detected in the thorax, abdomen and pelvis. Esophagogastroduodenoscopy and colonoscopy showed no gastrointestinal mucosal involvement. No cutaneous lesions were identified. The patient was started on antiretroviral therapy, with conservative management of his tumor due to the lack of visceral organ involvement, small size of the nasopharyngeal mass and absence of local complications. He is on close follow-up and remains well 8 months after the initial diagnosis.

Discussion

KS is a vasoformative spindle cell tumor with distinctive clinicopathologic, epidemiological and immunophenotypic features [1]. Regardless of the different clinical settings, HHV-8 infection is identified in nearly all cases, strongly

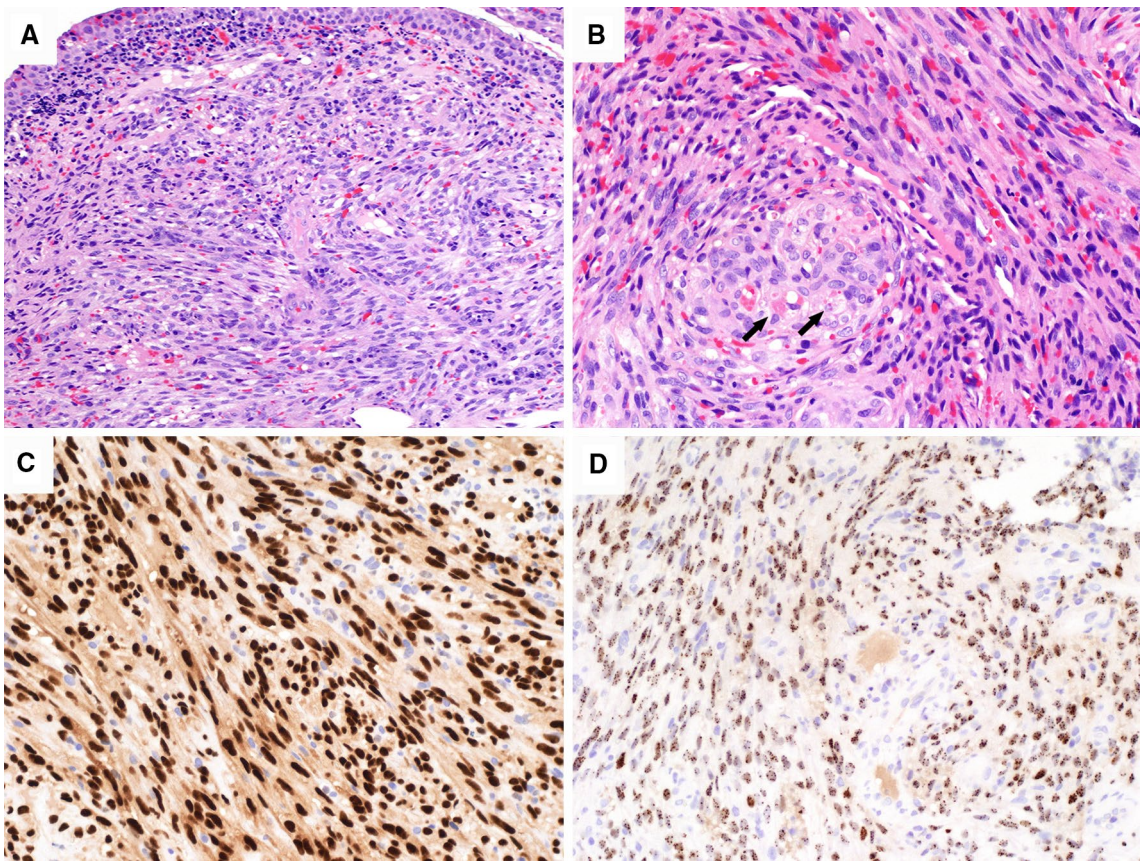

Fig. 2 Histologic and immunohistochemical findings of the postnasal space biopsy. **a** A cellular spindle cell proliferation is seen in the subepithelial stroma of the mucosa (hematoxylin and eosin, original magnification ×100). **b** The spindle cells show mild nuclear atypia associated with red blood cell extravasation and hyaline globules (arrows) (hematoxylin and eosin, original magnification ×200). **c** Immunohistochemical findings show positive nuclear staining with ERG, and **d** HHV-8, clinching the diagnosis of a Kaposi sarcoma (original magnification ×200)

suggesting that HHV-8 is involved in the pathogenesis of KS [2]. KS lesions commonly present at mucocutaneous sites as patch, plaque or nodules, but may involve all visceral organs and anatomic locations, such as lymph nodes, bones, skeletal muscle and brain [3]. Involvement of the head and neck region is more prevalent in the AIDS-related form, with the oral cavity being the most commonly affected mucosal site [4, 5]. Primary involvement of the nasal cavity, particularly the nasopharynx, is distinctively rarer with only few reports in the literature [5–14]. The clinical characteristics of these patients are summarized in Table 1. In the presence of HIV infection, KS serves as a defining disease for AIDS. Indeed, to our knowledge, our patient is only the second reported case in the English literature to have nasopharyngeal KS as the index diagnosis of AIDS [11]. Interestingly, six patients with primary KS of the nasal cavity were not associated with HIV infection [7–9, 12, 13]. Nevertheless, given the important clinical implications of the diagnosis of KS, it is prudent to perform a comprehensive workup to exclude an underlying retroviral infection in all patients with a newly diagnosed KS, as in our case.

The histologic diagnosis of KS can be challenging, given that its morphologic features vary with the stage of disease and there is a variety of different histological variants [15, 16]. The diagnostic difficulty is further compounded when KS occurs in an unusual site, such as the nasopharynx, and without the knowledge of the clinical settings. In the early stages of the disease, the irregularly shaped, slit-like vascular spaces can be subtle. It may be obscured by the heavy reactive lymphoid infiltrate native to the nasopharyngeal region, which may be especially florid in HIV patients [17], or mistaken as reactive or benign vascular proliferations such as bacillary angiomatosis or pyogenic granuloma [10]. In the later stages whereby the spindle cell proliferation is evident, a spectrum of vascular-forming, spindle cell neoplasms of the nasopharynx need to be considered, such as nasopharyngeal angiofibroma, sinonasal glomangiopericytoma, solitary fibrous tumor and kaposiform hemangioendothelioma [18]. In the clinical setting of immunosuppression, the differentials of KS, EBV-associated smooth muscle tumor [19] and mycobacterial spindle cell pseudotumor [20], are to be included. While most of the KS show low grade nuclear features, anaplastic KS has been described [21, 22], and this may be mistaken for aggressive tumors, such as angiosarcoma or even nasopharyngeal carcinoma. The latter can have a predominantly spindled appearance and is a particularly pertinent consideration in the Southeast Asian region and when associated with cervical lymph node swelling.

The key diagnostic features of KS include the presence of slit-like vessels, extravasated red blood cells and hyaline globules. The co-expression of vascular markers such as CD31, CD34 and ERG with HHV-8 is crucial in clinching the diagnosis of KS, as demonstrated in our case. HHV-8 expression should not be present in the aforementioned differential diagnoses. The diagnosis of KS by FNA is fraught with difficulties; these samples are often hemorrhagic due to the vascular nature of the lesion and the lesional spindle cells are often fragile and frequently exhibit nuclear streaking [23]. There is thus a need for a high degree of clinical awareness and close clinical

Table 1 Clinical characteristics of nasal cavity and nasopharyngeal Kaposi sarcoma in English literature

Case	No. of cases	Age, sex	Size	Other KS involvements	HIV	KS as AIDS index diagnosis	Treatment	Outcome/follow up duration
Stafford et al. [5]	1	NA	NA	NA	+	NA	NA	NA
Celenk et al. [6]	1	37M	3 cm	No	+	No	Radiation	Well/1 year
Chen et al. [7]	1	31F	NA	No	−	NA	Excision, radiation	Well/4 years
Mouden et al. [8]	1	56F	7.7 cm	No	−	NA	Chemo	Well/1 year
Venizelos et al. [9]	1	59F	0.8 cm	No	−	No	Excision	Well/4 years
Wyatt et al. [10]	1	25F	0.75 cm	No	+	No	Excision	Recurred in 2 months
Yang et al. [11]	1	28M	NA	Cutaneous lesions developed subsequently	+	Yes	Radiation, HAART	Well/3 years
Stavrakas et al. [12]	2	37F	NA	NA	−	NA	Chemo	Well/2.5 years
		37M	NA	NA	−	NA	Radiation	Well/5 months
Gnepp et al. [13]	1	53M	NA	NA	−	NA	Excision	Recurred at 9 months/alive at 16 months
Singh et al. [14]	3	NA	NA	NA	+	NA	NA	NA
Current case	1	38M	0.3 cm	No	+	Yes	HAART	Well/8 months

F female, *M* male, *NA* not available, *HAART* highly active antiretroviral therapy

correlation due to the potential of false-negative results when obtaining hemodiluted smears containing only a limited cellular yield displaying the artifactual changes mentioned above.

In conclusion, KS can rarely involve the nasopharynx, and may be the first presentation in an undiagnosed AIDS patient. It is hence prudent to perform a comprehensive clinical workup to exclude a retroviral infection in all patients with newly diagnosed KS, so as to avoid any unnecessary delay in the initiation of appropriate therapy. The histologic differential diagnosis of KS in this unusual site is wide and can pose several diagnostic challenges. HHV-8 is the most specific immunohistochemical marker available to help in distinguishing KS from its mimics.

Compliance with Ethical Standards

Conflict of interest The authors have no disclosures or conflict of interest to declare.

References

1. Thompson LDRRJ, Wenig BM. Kaposi sarcoma. In: El-Naggar A, Chan J, Takata T, Grandis J, Blootweg P, editors. WHO classification of tumours. Pathology and genetics of head and neck tumours. 4th ed. Lyon: IARC Press; 2017. pp. 124–5.
2. Gessain A, Duprez R. Spindle cells and their role in Kaposi's sarcoma. Int J Biochem Cell Biol. 2005;37(12):2457–65. https://doi.org/10.1016/j.biocel.2005.01.018.
3. Pantanowitz L, Dezube BJ. Kaposi sarcoma in unusual locations. BMC Cancer. 2008;8:190. https://doi.org/10.1186/1471-2407-8-190.
4. Agaimy A, Mueller SK, Harrer T, Bauer S, Thompson LDR. Head and neck Kaposi sarcoma: clinicopathological analysis of 11 cases. Head Neck Pathol. 2018. https://doi.org/10.1007/s12105-018-0902-x.
5. Stafford ND, Herdman RC, Forster S, Munro AJ. Kaposi's sarcoma of the head and neck in patients with AIDS. J Laryngol Otol. 1989;103(4):379–82.
6. Celenk F, Yilmaz M, Asal K, Ekinci O, Tokgoz N. AIDS-related primary Kaposi sarcoma of the nasopharynx. Ear Nose Throat J. 2011;90(6):E1–4.
7. Chen KH, Chen TD, Chen CW, Lee LY. Iatrogenic Kaposi's sarcoma in nasal cavity: a case report. World J Surg Oncol. 2014;12:172. https://doi.org/10.1186/1477-7819-12-172.
8. Mouden K, Khmou M, Loughmari S, Semmar A, El Kacemi H, El Khannoussi B, et al. Primary Kaposi's sarcoma of the nasal cavity: a case report and review of the literature. Clin Sarcoma Res. 2016;6:4. https://doi.org/10.1186/s13569-016-0044-4.
9. Venizelos I, Andreadis C, Tatsiou Z. Primary Kaposi's sarcoma of the nasal cavity not associated with AIDS. Eur Arch Otorhinolaryngol. 2008;265(6):717–20. https://doi.org/10.1007/s00405-007-0505-8.
10. Wyatt ME, Finlayson CJ, Moore-Gillon V. Kaposi's sarcoma masquerading as pyogenic granuloma of the nasal mucosa. J Laryngol Otol. 1998;112(3):280–2.
11. Yang M-C, Hsu Y-H, Liu D-W, Chou Y-F. AIDS-related Kaposi's sarcoma of the nasopharynx. Tzu Chi Med J. 2009;21(4):342–4. https://doi.org/10.1016/S1016-3190(09)60068-9.
12. Stavrakas M, Nixon I, Andi K, Oakley R, Jeannon JP, Lyons A, et al. Head and neck sarcomas: clinical and histopathological presentation, treatment modalities, and outcomes. J Laryngol Otol. 2016;130(9):850–9. https://doi.org/10.1017/S0022215116008604.
13. Gnepp DR, Chandler W, Hyams V. Primary Kaposi's sarcoma of the head and neck. Ann Intern Med. 1984;100(1):107–14.
14. Singh B, Har-el G, Lucente FE. Kaposi's sarcoma of the head and neck in patients with acquired immunodeficiency syndrome. Otolaryngol Head Neck Surg. 1994;111(5):618–24. https://doi.org/10.1177/019459989411100513.
15. Radu O, Pantanowitz L. Kaposi sarcoma. Arch Pathol Lab Med. 2013;137(2):289–94. https://doi.org/10.5858/arpa.2012-0101-RS.
16. Grayson W, Pantanowitz L. Histological variants of cutaneous Kaposi sarcoma. Diagn Pathol. 2008;3:31. https://doi.org/10.1186/1746-1596-3-31.
17. Drake-Lee A, Stevenson M, Donaldson I. Mass in the post nasal space and acquired immune deficiency syndrome. J Laryngol Otol. 1996;110(8):787–8.
18. Wong BL, Dwivedi RC, Masterson L, Riffat F, Marker A, Jani P. Kaposiform hemangioendothelioma of paranasal sinus. Laryngoscope. 2014;124(9):2103–6. https://doi.org/10.1002/lary.24669.
19. Thong JF, Chuah KL. EBV-associated smooth muscle tumour presenting as a parapharyngeal mass—a rare presentation. Auris Nasus Larynx. 2009;36(1):120–2. https://doi.org/10.1016/j.anl.2008.02.006.
20. Gunia S, Behrens MH, Stosiek P. Mycobacterial spindle cell pseudotumor (MSP) of the nasal septum clinically mimicking Kaposi's sarcoma: case report. Rhinology. 2005;43(1):70–1.
21. Cox FH, Helwig EB. Kaposi's sarcoma. Cancer. 1959;12(2):289–98.
22. Templeton AC. Kaposi's sarcoma. Pathol Annu. 1981;16(Pt 2):315–36.
23. Hales M, Bottles K, Miller T, Donegan E, Ljung BM. Diagnosis of Kaposi's sarcoma by fine-needle aspiration biopsy. Am J Clin Pathol. 1987;88(1):20–5.