



Cutaneous Kaposi Sarcoma of a Non-HIV Infected Patient in Korea

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Authors' contributions

This work was carried out in collaboration between all authors. Author SL was the major contributor in acquiring all the information needed and writing the manuscript. Authors MSK and SGP analyzed and interpreted the patient's clinical data. Author SCL revised the manuscript critically for important intellectual content and gave final approval of the version to be published. Author IC gathered information from the patient and performed the follow up. All authors read and approved the final manuscript.

Case Study

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ABSTRACT

Aims: We present this case to report clinical knowledge about unusual feature of classic Kaposi sarcoma in Korea.

Presentation of Case: We report on a case involving an unusual clinical feature of a 76-year-old HIV-seronegative, HHV-8 infected Korean male, which was histologically confirmed as cutaneous Kaposi sarcoma (KS) on the ankle and foot dorsum.

Discussion: KS is an intermediate-grade angioproliferative neoplasm derived from lymphatic endothelium in association with AIDS and human herpes virus 8 (HHV-8) infections. The tumor does not commonly affect non-HIV infected persons. Development of the disease occurs through the complicated interplay of HHV-8 with genetic, immunologic, and environmental factors. We discuss several risk factors presenting in most patients but were not observed in this patient, who did not fit easily into any of the well-known subtypes.

Conclusion: Diagnosis of KS is often not possible solely on the basis of morphological characteristics. Based on our review of the literature, this is a sporadic case of classic KS according to its unusual clinical features.

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1. INTRODUCTION

Kaposi sarcoma (KS) represents approximately 1% of all diagnosed malignant tumors worldwide [1]. Until the late 1960s, KS was described as a rare, indolent, multifocal tumor arising mainly in lower extremity of elderly males of Mediterranean and Eastern European descent, a clinical pattern now known as the 'classic' form of the disease [2]. The current interest in this entity comes from recognition that KS is based on a primary clue of acquired immune deficiency syndrome (AIDS) [2]. However, human herpes virus 8 (HHV-8), also known as KS herpes virus (KSHV), can play an essential role in the pathogenesis of KS [3]. When these predisposing serologic conditions are incompatible with patients' symptoms, we are faced with diagnostic hesitation, depending solely on histopathologic features. Knowledge of unusual presentations of KS on the lower extremity is informative for a practical pathologic field in order to properly identify biopsy and diagnose this condition. Only its appropriate recognition will allow for administration of suitable and timely treatment.

2. PRESENTATION OF CASE

A 76-year-old Korean male presented with seven violaceous papules and nodules with tenderness on the left foot and ankle. The masses were present for a period of 2-3 years and increased in size over time. On physical examination, the patient presented with pitting edema. Dermatologic examination showed coarseness and hyperpigmentation of the integument around the lesion. The largest nodule had a regular border and measured 1 cm in diameter, with a dark purple color and was surrounded by extensive hyperkeratotic hemorrhagic crust but not soft. The smaller lesions were similar in size but without evidence of hemorrhagic features (Fig.1a &1b).

Excisional biopsy was performed under the impression of lymphangioma circumscriptum or livedo reticularis. Microscopically, low-power view showed a well-defined lobulated mass in dermis composed of spindle cells with intersecting fascicles (Fig.1c). High-power view showed proliferation of spindle cells with scattered slit-like vascular spaces containing red blood cells (Fig.1d). Numerous extravasated erythrocytes were present within the lesion. Cytologically, the spindle cells in the nodules were plump, elongated with abundant eosinophilic cytoplasm. Oval to flattened nuclei with coarse chromatin and mild atypia were evident. Mitotic figures were infrequent. Immunohistochemical analysis demonstrated CD34 (Fig. 1e) and CD31 (Fig. 1f) immunoreactivity in spindle cells and vascular endothelial cells, respectively. However, spindle cells showed no smooth muscle actin or S-100 protein immunostaining. This constellation of histopathologic and immunophenotypic features was compatible with classic Kaposi sarcoma (classic KS), nodular stage.

Therefore, close history taking and systemic workup was performed for confirmation with etiology of KS. The patient denied any recent trauma, including incidental trauma from shoes or occupation. Past medical history was nonspecific with the exception of undergoing unilateral hip replacement seven years ago. He also denied travel abroad or atypical sexual intercourse as well as organ transplantation or blood transfusion.

Radiologic finding with a whole body positron emission tomography-computerized tomography (PET-CT) scan showed diffuse hypermetabolism in the edematous left lower leg, which was suspicious for tumoral uptake, however, no metastatic disease was

observed. Enhancing computerized-tomographic venography showed no evidence of deep vein thrombosis in bilateral lower extremity in delayed phase; however, extensive subcutaneous edema was recognized.

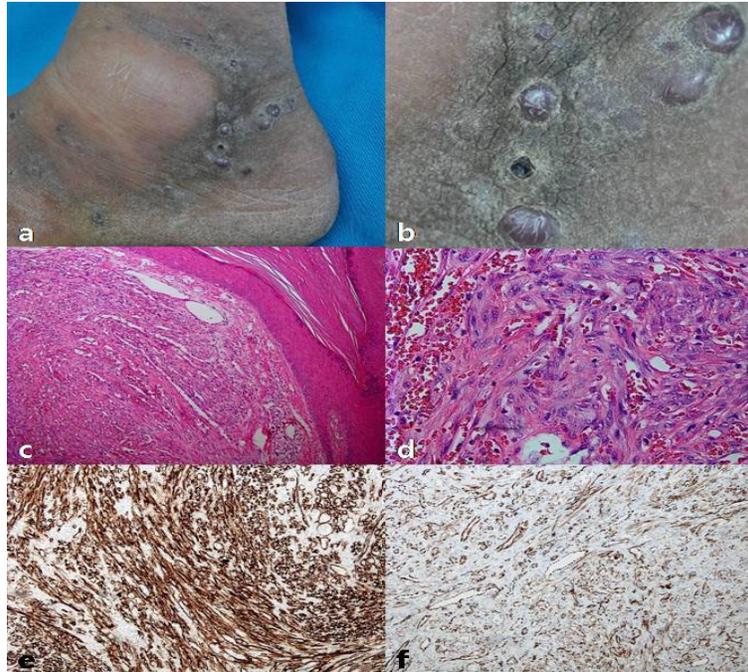


Fig. 1. Gross and microscopic findings. (a) Multiple violaceous papules with hyperkeratotic crust on the ankle and lateral area of the left foot. (b) High power view of (a). (c) Microscopically, a nodular lesion in dermis showed proliferation of spindle cells with intersecting fascicles and slit-like spaces. (d) High-power view showed atypical spindle cells with scattered slit-like vascular spaces containing red blood cells. Immunohistochemical staining for CD34 (e) and CD31 (f) showed strong positive reaction in spindle cells and vascular lining cells, respectively

Serologic and laboratory workup was performed, including complete blood count with absolute and percentage lymphocyte count, percentage CD4 and CD8 T-cell count, blood chemistry profile and coagulation study; none of the results showed any abnormality. HIV serology was negative, whereas polymerase chain reaction (PCR) with HHV-8 DNA from a skin biopsy paraffin block section was positive (Fig. 2).

In consideration of multifocality of the tumor, radiation therapy was started. However, one month later, before completion of initial treatment, other lesions appeared on his right leg with subcutaneous edematous change. Treatment with daily radiation therapy of 3,000 centi-Gray on both legs was restarted for palliative purposes over a period of three weeks with monitoring by a watchful attendant in the oncologic department ward. Complete remission was achieved after nine additional applications of radiation therapy two months later and the postradiative course was uneventful over a period of eight months.

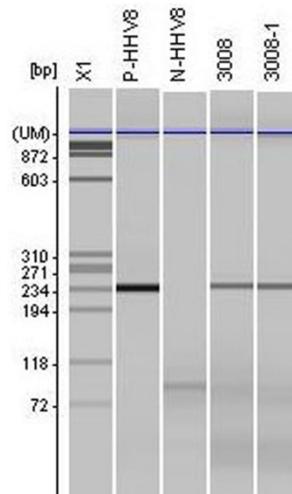


Fig. 2. Polymerase chain reaction for HHV-8 ORF26 in a tissue sample. X1: molecular weight marker; P-HHV8: positive control for HHV-8; N-HHV8: negative control for HHV-8; 3008: present case, showed a 234 bp band; 3008-1: present case, repeated, showed a 234 bp band

3. DISCUSSION

In 1872, Moritz Kaposi, a Hungarian dermatologist, first described classic KS, which was an uncommon, aggressive cutaneous tumor that he described as "idiopathic multiple pigmented sarcoma of the skin" [4]. The infectious agent of KS was recognized by Chang et al. and was named KSHV or HHV-8 [5]. The viral pathogen is detected in KS cells of all epidemiological-clinical types of the tumor regardless of geographic location or patient demographics [6] and is found in peripheral blood mononuclear cells before development of KS [7]. The course of KS ranges from indolent, only affecting skin, to fulminant with extensive visceral involvement. Histologically, KS is divided into three stages, early patch, plaque and nodular stages. In the early patch stage, widely dilated, anastomosing, thin-walled vascular spaces are noted in the upper half of the dermis. Next, in plaque stage, there is proliferation of spindle shaped cells with extravasated erythrocytes and aggregates of blood vessels lined by prominent endothelial cells. Last, the nodular stage, showed extensive proliferation of spindle shaped, somewhat pleomorphic cells having dark prominent nuclei, proliferation of small vessels with solid aggregates of endothelial cells and extravasation of erythrocytes [8].

KS is classified according to four subtypes, which are primarily differentiated by clinical presentation: classic and three different at-risk populations: endemic, iatrogenic and epidemic (AIDS related) [9]. These four categories of KS are as follows:

- i) Classic Kaposi sarcoma (elderly men of Mediterranean and Eastern European decent).
- ii) Endemic Kaposi sarcoma (middle-aged adults and children in Equatorial Africa without HIV).
- iii) Immunosuppression-associated Kaposi sarcoma (after iatrogenic immunosuppression).
- iv) Epidemic Kaposi sarcoma (AIDS-associated).

Classic KS onset usually occurs in the fifth to eighth decade with a male predominance of almost 2.4:1. The disease usually progresses slowly and is particularly frequent in lower extremities. The tumor may be a sign of underlying malignancy in association with hematopoietic malignancies - multiple myeloma and non-Hodgkin's lymphoma [10]. Endemic KS presents with a high frequency of extracutaneous manifestations and follows a rapidly progressive course with a particularly variant form affecting African children [11]. Iatrogenic KS is relatively frequent. It develops within a few months to several years after transplantation of solid organs or immunosuppressive treatment for a variety of conditions. The incidence of KS in recipients of solid organs is approximately 500 times that found in the general population [12] and the clinical presentation of KS in the iatrogenic KS is often limited to skin involvement [12]. AIDS-related epidemic type KS is more aggressive, as it is predominantly multifocal and disseminated and is associated with a patient's demise. It is the most common tumor found in the HIV infected group.

The case presented here is of particular interest because this patient failed to neatly fit into any of the predisposing factors related to classification. Several cases of KS have been reported in Korea. Among the cases, cases that were excluded serologically, epidemiologically and immunologically were confirmed as classic KS. After review of the literature, we have concluded that the incidence of classic KS in non-HIV elderly males is extremely rare in Korea [8,13,14]. Our patient, a 76-year-old male who presented with multiple cutaneous lesions in lower extremity with a long standing, indolent course is not in a high risk group. In these cases, including our patient, detection of HHV-8 using a molecular method in a tumorous lesion is a diagnostic gold standard for the classic KS. PCR was used for detection of the virus and we identified HHV-8 DNA in the tissue sample.

4. CONCLUSION

The authors report on a sporadic case of classic KS according to its unusual clinical features. Diagnosis of classic KS is often not possible solely on the basis of morphological characteristics. Conduct of further studies is needed in order to attain a better understanding of the precise molecular pathogenesis of HHV-8. To the best of our knowledge and based on our review of the literature, clinical and histological recognition of classic KS is important to confirming the diagnosis, which may have variable morphological variants and diverse stages.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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