Spontaneous Remission of Classic Kaposi Sarcoma in an Elderly Filipino Female

Ma. Bernadette T. Sedano, MD[1], Mark Gerald R. Serrano, MD, DPDS[2], Jolene Kristine Dumlao, MD, FPDS[3]

ABSTRACT

Background: Kaposi sarcoma (KS) is a lymphoangioproliferative condition linked to human herpesvirus-8. KS presents in four clinical variants: classic, iatrogenic, endemic, and AIDS-related. The classic type has a chronic course and primarily affects people of Eastern European Jewish or Mediterranean heritage, with a higher incidence in males.[1] Approximately 70% of patients respond partially or satisfactorily to treatment, 20% experience recurrence, and 10% show progression despite treatment.[2] Furthermore, there have been documented cases of self-regression in the classic type of KS.[3]

Observation: We report a case of a 74-year-old, filipino, female, who has no known comorbities, presented with a one-year history of multiple, non-pruritic, non-tender, violaceous, firm, nodules, widely disseminated ranging from 0.5 cm to 1 cm in its widest diameter which showed spontaneous regression. The histopathological analysis revealed spindle cells within collagen bundles and an associated vascular proliferation, which is indicative of Kaposi Sarcoma. Immunostaining with CD31 highlighted the presence of vascular channels within these collagen bundles. HIV test showed negative result. She was referred to an oncology clinic for further treatment but did not comply. Ten months after, patient followed up with clear lesions showing spontaneous resolution of KS.

Key message: This case presents a classic Kaposi Sarcoma in aelderly, filipino, female who spontaneously regressed without any therapy.

INTRODUCTION

Kaposi sarcoma (KS) is a lymphoangioproliferative condition linked to human herpesvirus-8. KS presents in four clinical variants: classic, iatrogenic, endemic, and AIDS-related.[1] These variants share common histological characteristics, including the presence of proliferating malignant spindle cells and ill-defined vascular channels or slits. Classic KS, initially documented by Moritz Kaposi in 1872, predominantly affects older men from Eastern European and Mediterranean regions.[4] These tumors follow an indolent course and usually start on the skin as unilateral or bilateral bluish-red macules resembling hematomas on the lower extremities. They progress slowly both horizontally and vertically, evolving into firm plaques and eventually nodules.[5] Treatment options are mainly determined by the type and location of the lesions which include radiation therapy, chemotherapy, and surgical excision.[6] Spontaneous regression of Kaposi's sarcoma is a rare occurrence, except in the iatrogenic immunosuppressive type. Nevertheless, there have been reported instances of classic Kaposi sarcoma exhibiting spontaneous regression.[3]

Disclosures: The author has formally acknowledged and signed a disclosure affirming the absence of any financial or other relationships (including personal connections), intellectual biases, political or religious affiliations, and institutional ties that could potentially result in a conflict of interest.

[1] Resident, Southern Isabela Medical Center Department of Dermatology and Venereology
[2] Consultant, Southern Isabela Medical Center Department of Dermatology and Venereology
[3] Consultant, Dermatopathologist Southern Isabela Medical Center Department of Dermatology and Venereology

CASE REPORT

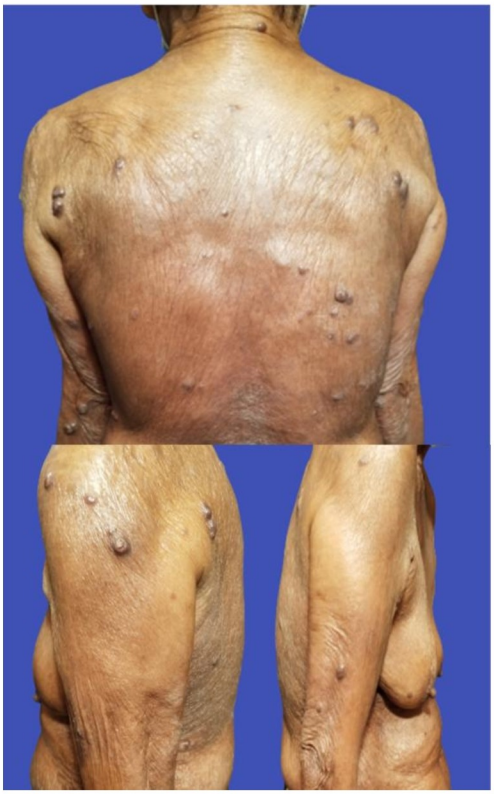
A 74-year-old Filipino female presented with a one-year history of multiple non-pruritic erythematous macules that initially appeared on her lower extremities and gradually progressed into violaceous firm nodules not associated withweight loss, poor appetite, cough, colds, abdominal discomfort, or changes in bowel habits. Her past medical history did not include any blood-related conditions, diabetes, cancer, recent blood transfusions, or organ transplants.Additionally, her sexual history revealed monogamy and no documented cases of sexually transmitted diseases.

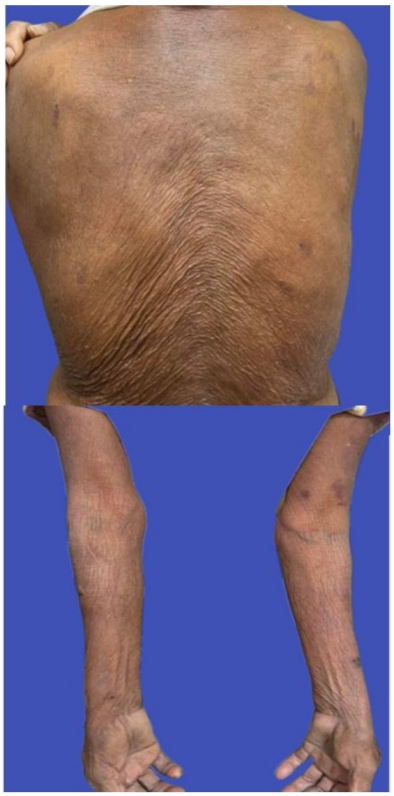
Physical examination revealed patient in a clinically stable condition, with no signs of mucosal lesions or enlarged lymph nodes. Dermatologic examination revealed multiple erythematous to violaceous firm, non-tender nodules on the face, trunk, upper, and lower extremities (Figure 1A).

Laboratory tests results, complete blood count, creatinine, blood urea nitrogen, SGPT, SGOT, TPAG, fasting blood sugar, lipid profile, urinalysis, stool analysis, RPR/VDRL, and HIV tests, were all within normal limits. Computed tomography scans of the neck, chest, and entire abdomen were unremarkable.

Histopathological analysis revealed the spindle cells in nodular aggregates, with some dissecting within collagen bundles. In certain areas, there was evidence of vascular proliferation, with small blood vessels protruding into a vascular space (Figure 3). Immunostaining with CD31 further emphasized the presence of vascular channels within the collagen bundles, a finding consistent with the diagnosis of Kaposi Sarcoma.

The patient was referred to oncology service for further treatment but was non-compliant. She followed up ten months later which showed resolution of previously noted KS lesions. Upon investigation, patient denied any treatment done for her condition signifying spontaneous resolution of KS (Figure 1B).





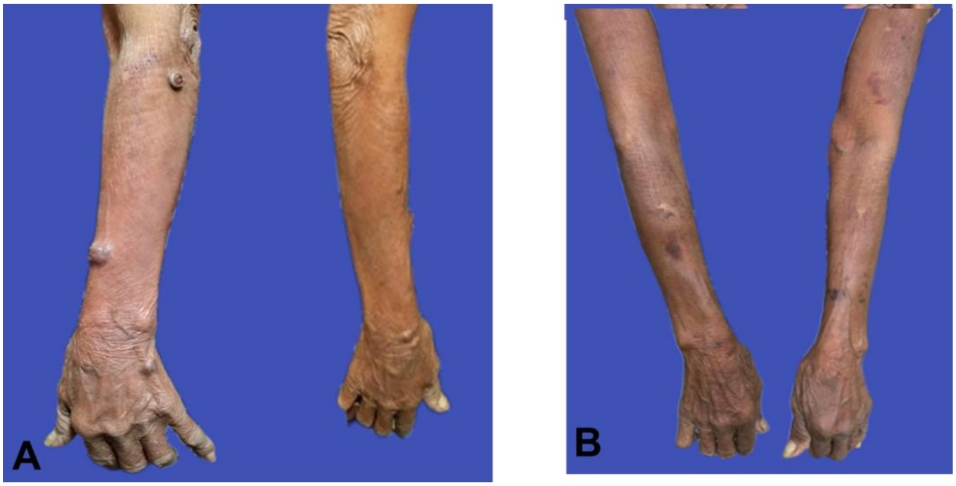


FIGURE 1. A. *Skin lesions showing violaceous firm nodules on the back, and upper extremities, measuring between 0.5cm and 1 cm in their widest diameter.* ***B.*** *Patient skin showing spontaneous resolution of KS lesions.*

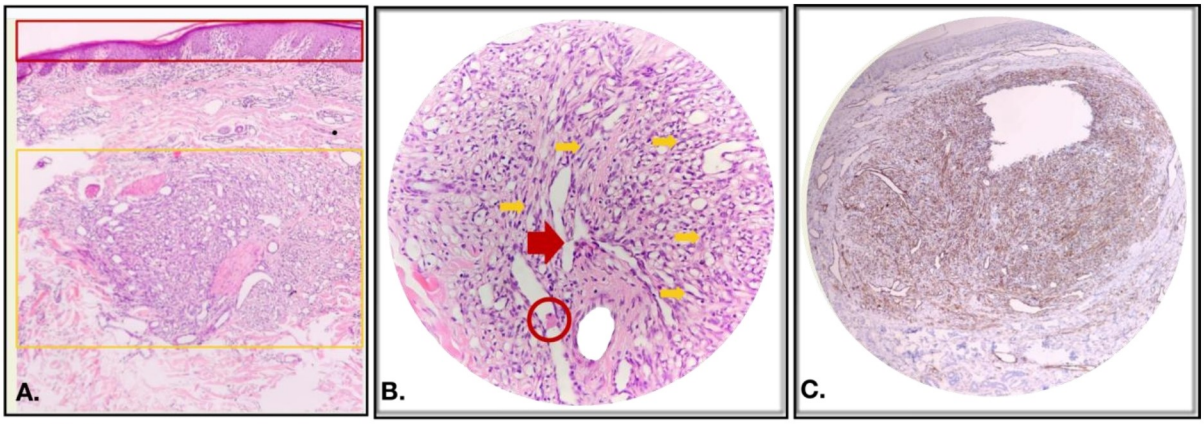


FIGURE 2.

A. H&E 10x magnification: *Basketweave orthokeratosis (red box). Moderate superficial perivascular infiltrates composed of lymphocytes and few extravasated erythrocytes (yellow box).*

B. H&E 40x magnification: S*pindle cells in nodular aggregates, some dissecting within collagen bundles. (yellow arrow). Vascular proliferation with small-vessel protrusion into a vascular space, promontory sign (red arrow) containing few extravasated erythrocytes (red circle).*

C. Immunohistochemical staining: *CD31 highlighted vascular channels between collagen bundles.*

DISCUSSION

Kaposi's sarcoma (KS) is a rare and malignant vascular condition that arises from lymphatic endothelial cells. It primarily affects the skin and mucous membranes but can also involve the lymphatic system and internal organs like the gastrointestinal tract, lungs, or liver. This condition was initially documented in 1872 by Moritz Kaposi.[7] Prevalence of KS remains unknown and still considered rare in the Philippines despite recognition as one the common malignancies associated with HIV infection. However, it is expected to increase due to the rising number of Filipinos being diagnosed with HIV infection each day.[8]

There are four primary types, classic (occurring sporadically), African (endemic), transplant or immunosuppression-related (iatrogenic), and acquired immune deficiency syndrome (AIDS)-related (epidemic) KS.[1] Classic KS predominantly affects men, with a male-to-female ratio ranging from 2:1 to 17:1, and is commonly observed in people of Eastern European and Mediterranean descent. This subtype typically appears after the age of 60. The primary risk factors linked to the development of classic KS are prior HHV-8 infection and increasing age. Endemic KS, which is not associated with HIV infection, is also prevalent in equatorial Africa, particularly among children and adolescent males. It accounts for 9% of all cancers in Central Africa, particularly in sub-Saharan Africa. Iatrogenic KS may develop in individuals who are subjected to extended periods of immunosuppressive therapy. The chances of developing KS are notably increased, ranging from 50 to 500 times higher, in organ transplant recipients when compared to the general population. Epidemic HIV-associated KS is the most common AIDS-defining neoplasm, and since the start of the HIV pandemic, has become the most common form of KS. The advancement of this condition can exhibit considerable variation, extending from isolated, stable lesions that persist for years to fast and fatal courses. Approximately 95% of all KS are attributed to human herpes virus 8 (HHV-8).[7]

HHV8 is a herpesvirus that has an affinity for lymphatic and blood vessel cells. Its genetic makeup contains numerous proteins responsible for promoting cell growth, preventing cell death, and inducing inflammation. In KS, many of the spindle cells primarily express dormant HHV8 genes, but some also express lytic genes. These lytic genes might play a role in the formation of new blood vessels and in signaling between cells, contributing to the development of KS. While various laboratory and animal models have been created to study this virus, a comprehensive system that accurately represents the full process of KS development is still lacking.[9]

The primary mode of HHV8 transmission is through horizontal means, primarily via saliva. However, it necessitates prolonged and frequent contact for transmission to occur, as seen in cases such as mother-to-child transmission or sexual interactions.[10] Although KSHV transmission through blood transfusions is rare, isolated instances of transmission through organ transplants have been reported. Conversely, vertical transmission routes seem to have a minimal role in the virus's spread.[9]

Diagnosing KS begins with a thorough history and physical examination, but the key step is histopathological testing, that including H&E and immunohistochemical staining.[7,11] These examinations often show the presence of spindle cell growth within intricate blood vessels in the dermis, along with the "promontory sign" denoting branching vessels around larger ectatic pre-existing vessels and skin adnexa. Findings may also include extravasated red blood cells, macrophages filled with hemosiderin, occasional hyaline globules, and the presence of lymphocytes and plasma cells. As KS progresses, these features become more prominent, and the slit-like openings in the vessels become more noticeable. Immunohistochemistry is crucial for identifying endothelial cells in KS and aiding diagnosis. CD34 and CD31 staining indicates differences from normal endothelial cells. Spindle cells in KS lesions test positive for CD31 and CD34.[11] Additionally, while qualitative or quantitative assessments of HHV-8 PCR and HHV-8 antibody tests can be conducted due to HHV8's association with KS, these tests are not routinely necessary in clinical practice. HIV serology should be also carried out to exclude AIDS-related KS.[7]

Goals of treatment of KS is to induce regression of the lesions, control the disease's progression, and alleviate symptoms. Currently, there is no a universally accepted "standard therapy regimen" for KS treatment. The choice of treatment should depend on prognostic factors, the patient's overall health, and their preferences. Local treatment options include surgery, local immunotherapy, cryotherapy, local chemotherapy, and electrochemotherapy. These approaches have been investigated in clinical trials, especially for classic KS. For treating deeper or mucosal lesions radiotherapy can be effective. However, if with lymph node involvement, or with internal organ complications, it is important to promptly consider systemic treatment, regardless of the specific type of KS.[7] Spontaneous regression of KS is rare, except in the case of iatrogenic immunosuppressive type, but there have been reported instances of classic Kaposi sarcoma demonstrating spontaneous regression.[3]

CONCLUSION

We present a rare case of spontaneously resolved, immuno and histopathologically confirmed case of Classic Kaposi Sarcoma in an elderly Filipino female.

REFERENCES:

1. Kang S, Amagai M, Bruckner A, et al. (2019) Fitzpatrick's Dermatology. 9th ed. McGraw-Hill.
2. Cabrera, P., et.al. (2019). Spontaneous Remission of a Widely Disseminated Classic Kaposi's Sarcoma. *Proceedings of the 24th World Congress of Dermatology*, Milan.
3. Jang, Y. H., Choi, Y. H., et.al. (2011). Classic Type of Kaposi's Sarcoma Showing Spontaneous Regression. *Korean Journal of Dermatology*, *49*(7), 625-628.
4. Qian, Y.-T., & Ma, D.-L. (2019). Atypical Presentation of Classic Kaposi's Sarcoma. *The Lancet*, June 22, 2019. https://doi.org/10.1016/S0140-6736(19)31148-1
5. Goldsmith L, Katz S, Gilchrest. B, et al. (2012) Fitzpatrick's Dermatology. 8th ed. McGraw-Hill.
6. PDQ® Adult Treatment Editorial Board. (2022). PDQ Kaposi Sarcoma Treatment. Bethesda, MD: National Cancer Institute. Available at: https://www.cancer.gov/types/soft-tissue-sarcoma/hp/kaposi-treatment-pdq
7. Esser, S., Schöfer, H., & Hoffmann, C. et.al. (2022). Guidelines for the Kaposi Sarcoma. *Journal der Deutschen Dermatologischen Gesellschaft*. doi:10.1111/ddg.14788
8. Catedral, L. I. G., Caro-Chang, L. A., & Tan, H. N. et.al. (2020). AIDS-Related Kaposi Sarcoma in a Tertiary University Hospital in Manila, Philippines: A Report of Six Cases. *Spring Hope Cancer Foundation & Young Oncologist Group of Asia*. doi:10.1055/s-0040-1713317
9. Bubman, D., & Cesarman, E. (2003). Pathogenesis of Kaposi's Sarcoma. *Hematology/Oncology Clinics of North America*. doi:10.1016/s0889-8588(03)00044-3
10. Schneider, J. W., & Dittmer, D. P. (2018). Diagnosis and Treatment of Kaposi Sarcoma. *National Library of Medicine*. doi:10.1007/s40257-017-0270-4
11. Bishop, B. N., & Lynch, D. T. (2023, June 5). Kaposi Sarcoma. National Library of Medicine. StatPearls Publishing LLC. Copyright © 2023.