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Review Article

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Update on Kaposi Sarcoma Not Related to HIV

Melisa Hunis MD and Adrian Hunis MD*

School of Medicine, Universidad de Buenos Aires, Argentina

***Corresponding author**
Adrian Hunis MD, School of Medicine, Universidad de Buenos Aires, Argentina

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Definition

Kaposi Sarcoma (KS) is a vascular neoplasm characterized by the proliferation of spindle-shaped cells forming vascular channels, typically associated with human herpesvirus 8 (HHV-8) infection. Non-HIV-related Kaposi Sarcoma refers to cases not associated with HIV infection, encompassing classic, endemic (African), and iatrogenic (immunosuppression-related) types, as opposed to the epidemic (AIDS-related) form [1].

Epidemiology

Non-HIV-related KS is less common than the epidemic form. Classic KS predominantly affects elderly men of Mediterranean or Eastern European descent. Endemic KS occurs in sub-Saharan Africa, while iatrogenic KS is seen in organ transplant recipients and other immunosuppressed patients. The incidence of classic KS is estimated at 0.2–0.8 per 100,000 in endemic regions [2].

Table 1: Epidemiological Features of Non-HIV-Related Kaposi Sarcoma

Type	Geographic Distribution	Age Group	Risk Factors
Classic	Mediterranean, Eastern Europe	Elderly (>60 yrs)	Male sex, HHV-8 infection
Endemic	Sub-Saharan Africa	All ages	HHV-8, genetic susceptibility
Iatrogenic	Worldwide	All ages	Immunosuppression, HHV-8

Race, Sex, and Frequency

Classic KS is most frequent among men of Mediterranean or Ashkenazi Jewish descent, with a male-to-female ratio of 10–15:1. Endemic KS affects both sexes but is more common in men. Iatrogenic KS can affect any race or sex, depending on the underlying cause of immunosuppression [3].

Male 90%

Female 10%

Pathology, Genetic and Molecular Data

Anatomical Pathology

KS lesions progress through patch, plaque, and nodular stages. Histologically, they show spindle-cell proliferation, slit-like vascular spaces, extravasated erythrocytes, and hemosiderin-laden macrophages. Mitotic figures and inflammatory infiltrates are common [4].

Genetic and Molecular Data

- HHV-8 (KSHV): All forms of KS are associated with HHV-8 infection.
- Genetic Susceptibility: Polymorphisms in cytokine genes (e.g., IL-6, IL-10) may influence susceptibility.
- Molecular Pathogenesis: HHV-8 encodes proteins that promote angiogenesis, inhibit apoptosis, and modulate immune responses (e.g., vGPCR, vIL-6) [5].

Table 2: Molecular Markers in Kaposi Sarcoma

Marker	Role	Diagnostic Utility
HHV-8 LANA-1	Viral latency protein	Immunohistochemistry
CD34, CD31	Endothelial markers	Immunophenotyping
D2-40	Lymphatic marker	Immunophenotyping

Diagnosis and Biopsy

Diagnosis is based on clinical suspicion, confirmed by histopathological examination. Biopsy reveals characteristic spindle cells, vascular channels, and HHV-8 positivity by immunohistochemistry (LANA-1). Differential diagnosis includes other vascular tumors and inflammatory conditions [6].

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Complementary Studies and Imaging

- Laboratory: CBC, renal and liver function, HHV-8 serology.
- Imaging:
  - CT/MRI: To assess visceral involvement.
  - Endoscopy: For gastrointestinal lesions.
  - Ultrasound: For lymph node and soft tissue involvement [7].

Clinical Features

Classic KS presents as slow-growing, violaceous macules, plaques, or nodules, often on the lower extremities. (Photo 1)

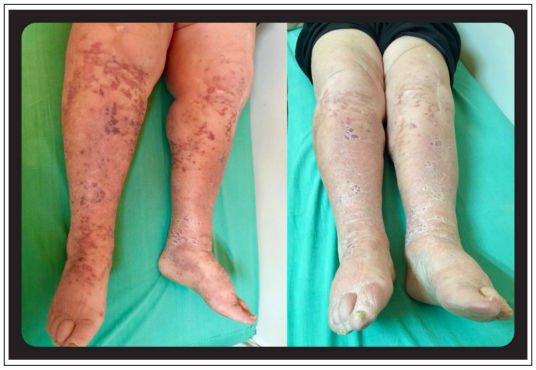

Photo 1: Skin lesions by Kaposi's Sarcoma, before and after treatment with Liposomal Doxorubicin. Courtesy of Dr. Adrián Hunis

Lesions may ulcerate or become painful. Endemic KS can be more aggressive, especially in children. Iatrogenic KS may regress with reduction of immunosuppression [8].

Table 3: Clinical Features of Non-HIV-Related KS

Feature	Classic KS	Endemic KS	Iatrogenic KS
Lesion location	Lower limbs	Lower limbs, face	Any site
Course	Indolent	Variable	Variable
Systemic signs	Rare	May be present	May be present

Treatments

Treatment depends on the type, extent, and symptoms:

- Local Therapy: Surgery, cryotherapy, radiotherapy for localized lesions.
- Systemic Therapy:
- Chemotherapy: Liposomal doxorubicin, paclitaxel (Photo 2)
- Immunomodulators: Interferon-alpha.
- Immunosuppression reduction: In iatrogenic KS, reducing immunosuppression may induce remission.
- Targeted Therapy: Trials with mTOR inhibitors, anti-angiogenic agents [9].

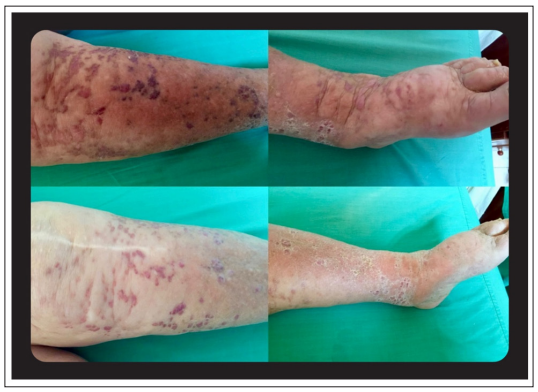

Photo 2: Female patient, treated with Liposomal Doxorubicin Courtesy Dr. Adrian Hunis

Evolution

Classic KS is typically indolent, with slow progression over years. Endemic KS may be more aggressive, especially in children. Iatrogenic KS can regress with modification of immunosuppression. Visceral involvement worsens prognosis. Overall survival is good for localized disease but worse for disseminated or visceral cases [10].

Conclusions

Non-HIV-related Kaposi Sarcoma remains a rare but important vascular tumor with distinct epidemiological and clinical features. HHV-8 infection is central to its pathogenesis. Diagnosis relies on histopathology and immunohistochemistry. Treatment is tailored to disease extent and patient comorbidities, with generally favorable outcomes for localized disease. Ongoing research into molecular pathways may yield novel therapies.

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