

# Three varieties of Kaposi's sarcoma with gastrointestinal involvement

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## Abstract

This article presents the cases of four adult patients with three varieties of Kaposi's sarcoma: epidemic, associated with human immunodeficiency virus infections; iatrogenic, associated with chronic immune suppression (and in this case in a man with alcoholic cirrhosis); and classic, occurring in elderly patient without previously known immunosuppression. All four cases had gastrointestinal involvement. A brief review of the disease is included.

## Keywords

Kaposi's sarcoma, sarcoma, gastrointestinal compromise.

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## INTRODUCTION

Kaposi's sarcoma (KS) is a complex malignant tumor of mesenchymal origin which is associated with human herpes virus 8 (KSHV). It normally coincides with an immune disorder that promotes an environment that is ideal for its development (1, 2). There are four types of KS: classical, endemic, African and iatrogenic. The endemic and African types have specific racial and geographic distributions, are more benign, and are associated with HIV/AIDS. To date, iatrogenic KS has been described in close association with immunosuppression used with transplantation and has the worst prognosis. The most common location of KS is in the skin. The second most common is in lymph nodes, and in third place is the gastrointestinal tract. Endoscopic indications vary from ulcers to purple nodular submucosal lesions. The most important histological indications are vascular proliferation characterized by the presence of vascular slits, extravasation of erythrocytes with hemosiderin deposits, and immunohistochemistry that is positive for herpes virus-8 (1-5).

## CASE PRESENTATIONS

We present the cases of four patients with histologically confirmed Kaposi's sarcoma who were treated in the gastroenterology unit of the Hospital Universitario de la Samaritana in Bogotá, Colombia in 2012 and 2013. For educational purposes, Table 1 summarizes the most important characteristics of the patients and macroscopic and microscopic findings from these cases.

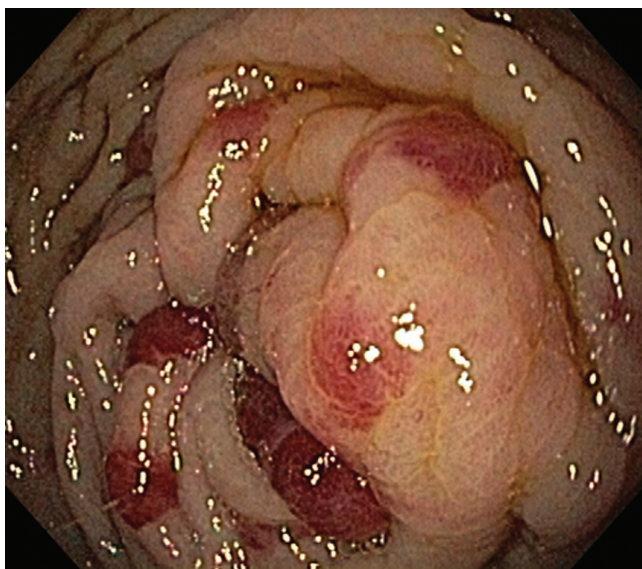
## DISCUSSION

In 1872, the Hungarian dermatologist Moritz Kaposi described five patients who had "sarcoma idiopaticum multiplexhemorrhagicum" with compromised blood and lymph vessels. This was the first time the disease was described so it was later named him as Kaposi's sarcoma (KS) (6). There are several types of KS. The classic type is usually diagnosed in elderly patients in Mediterranean populations or descendants of Jews from Eastern Europe. It grows slowly and consists mainly of skin lesions affecting the lower limbs.

**Table 1.** Main characteristics of patients with Kaposi's sarcoma

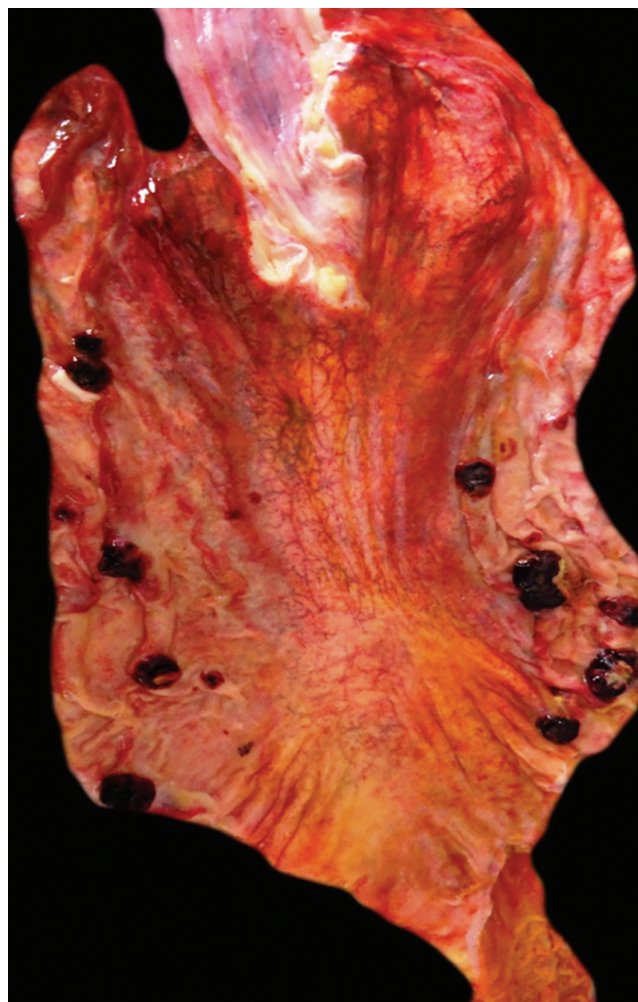
Patient	Sex	Age	Reasons for consulting physician	Risk Factor	Treatment	Location
1	Male	42	Perianal ulcers	HIV/AIDS	TMP-sulfa, Abacavir (ABC), lamivudine, efavirenz	Stomach, Colon (Figure 1)
2	Male	60	Hemoptysis, Dyspnea Anasarca	Chronic immunosuppression for microscopic polyangiitis, compromised lungs and kidneys	Cyclophosphamide, Azathioprine, Systemic prednisolone	Mouth, lungs, stomach, duodenum (Figures 2-4)
3	Male	66	Hematemesis, bloody stools	Alcoholic cirrhosis, Portal hypertension syndrome	Propranolol, spironolactone, lactulose	Stomach (Figure 5)
4	Female	89	Purple skin lesions and edema of the legs, inguinal lymphadenopathy	Advanced age, none demonstrated	None	Skin, stomach (Figure 6)

TMP-SMX: trimetoprim-sulfametoxazol; VIH: virus de inmunodeficiencia humana.



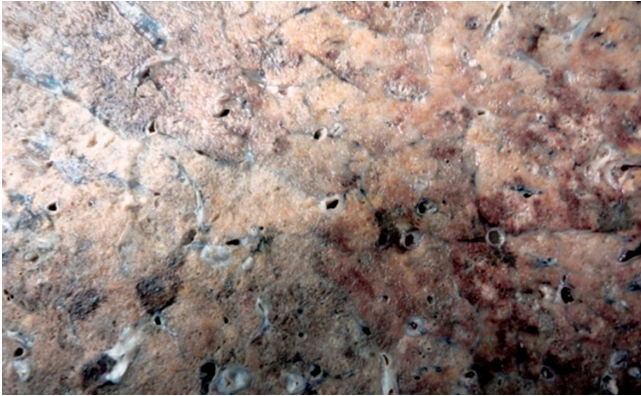
**Figure 1.** Endoscopic view of nummular lesions, violet KS in stomach.

The endemic type of KS has been described in black preadolescents and youth in sub-Saharan Africa. The epidemic type is associated with HIV/AIDS and has a gender ratio of compromise of 10 men to each woman affected. The risk of developing this type of KS is highest among homosexual men and those with low CD4 counts and high viral loads. The iatrogenic type of KS is secondary to immunosuppressant drugs, especially their use in treating diseases and in transplantation with most reports related to kidney transplants. Although the histology of the different types of KS is identical, the outcomes are different. KS associated with

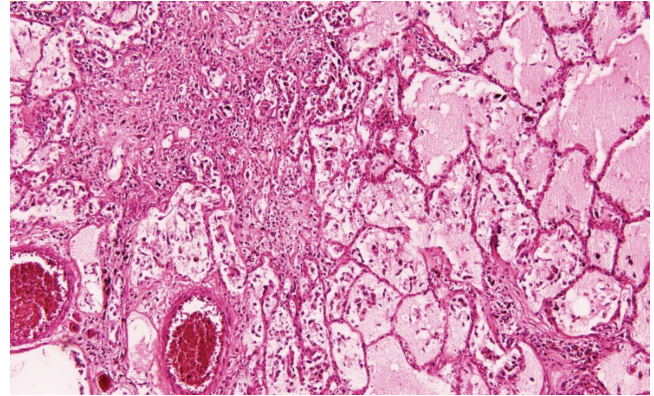


**Figure 2.** Autopsy sample showing multiple violet KS plaques in gastric mucosa.

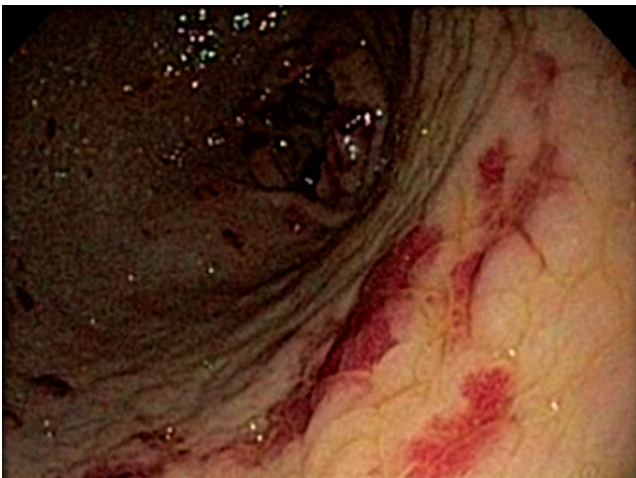




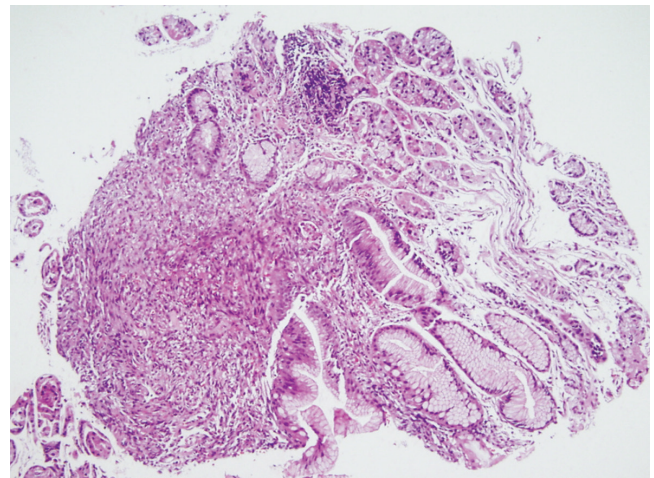
**Figure 3.** Autopsy sample showing multiple pulmonary KS nodules.



**Figure 4.** Histopathology of pulmonary KS.



**Figure 5.** Endoscopic view showing violet KS plaques in stomach.



**Figure 6.** Histopathology of gastric KS.

HIV/AIDS has the worst prognosis due to its rapid development and usually fatal outcome (1, 2, 6).

KS has been associated with infection by human herpes virus 8 (HV-8). The virus was described in 1994 and later found to be associated with KS leading to the use of the initials KSHV. In 2010 it was declared to be a Group I carcinogen by the International Agency for Research on Cancer (IARC) (7).

The prevalence of KSHV infection varies from place to place throughout the world. Areas in which it is endemic are associated with HIV/AIDS, but after the association of KS and HV was discovered its diagnosis increased dramatically. Rates of diagnosis subsequently stabilized after introduction of effective antiretroviral therapy (8). Although the overall seroprevalence of herpes virus-8 is not well known yet because of the great regional variability, it is estimated that the incidence of KS among HIV/AIDS patients is 20,000 times higher than in the general population and 300 times higher than among people with other

causes of immunosuppression (9). KS accounts for 60% of the tumors diagnosed in patients with HIV/AIDS (2, 8, 9).

For the year 2012, the Colombian National Public Health Monitoring System (Sistema Nacional de Vigilancia en Salud Pública – SIVIGILA) estimated that 122,197 people had HIV/AIDS in this country, but no specifics are known for KS. Saldarriaga and colleagues published a study which assessed patients with KS and HIV/AIDS in Cali between 1962 and 2007. The study was based on the population register of cancer patients and data from SIVIGILA. The time period with the highest rate of diagnosis for men, four per 100,000, was between the years 1996 and 2002. After 2002, diagnoses of extracutaneous KS increased from a previous level of was only 10% (10). We have no statistical data regarding the diagnosis of iatrogenic KS in Colombia. There are data in the literature indicating that classic KS accounted for 1% of neoplasms in patients with a mean age of 65 years for the year 1985 (11). In Medellin, Orozco and colleagues published a study that used the immunofluores-

cence technique to test the relationship between KS and HHV-8. The study found that 83.3% of a group of patients with KS and HIV/AIDS were positive for antibodies to HHV-8 (12).

The literature has frequently documented cases of Kaposi's sarcoma associated with HIV/AIDS. These are predominantly cases of skin lesions or lesions in visible mucous oral or pharyngeal membranes suspected of being KS and subsequently confirmed histopathologically (13). There are currently no international recommendations for active pursuit of the systemic disease. When there is gastrointestinal compromise, it is usually diagnosed incidentally and not as the result of direct suspicion of its existence. Although indications for performance of endoscopic studies on immunosuppressed patient are not different from those for their performance on immunocompetent patients, more than 50% of HIV/AIDS patients have gastrointestinal symptoms and the causative etiology is likely to be associated with an opportunistic infection (2, 13). KS with gastrointestinal involvement may be asymptomatic, but abdominal pain, gastrointestinal bleeding and even intestinal obstruction may present, and these symptoms are indications for endoscopic study. Endoscopic findings vary from purple or red submucosal nodules and plaques to polypoid formations (3, 14).

The first case reported here raises the question as to whether or not a patient who has been diagnosed with an advanced stage of HIV/AIDS but who does not have gastrointestinal symptoms should be subjected to gastrointestinal tract endoscopy as a screening test. This is especially relevant since it has been documented that up to 15% of patients with visceral KS do not occur have gastrointestinal compromise, so there is a likelihood of gastrointestinal KS despite the absence of skin lesions (15).

Very few cases of iatrogenic Kaposi's sarcoma have been reported in publications. Most are related to drug immunosuppression for rheumatologic diseases. In general, there are multiple reports of iatrogenic KS associated with transplants. In the English language literature, there are a few cases of patients who have been chronically immunocompromised pharmacologically with steroids and azathioprine and who have been diagnosed with ulcerative colitis, systemic lupus erythematosus and vasculitis (16,17).

In the Latin American literature in LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde) online medical and health science bibliographic database, some cases of iatrogenic KS in patients who have been chronically immunosuppressed with steroids for kidney transplants have been reported (18, 19). The second case that we report is rare. The immense magnitude of the compromise that triggered the death of the patient suggests that patients with immunosuppression from causes other than

HIV/AIDS, especially those with drug-induced immunosuppression associated with autoimmune diseases, are more susceptible to infection with HHV-8 and its manifestation as KS. This implies that the comorbidity worsens their prognosis. It also implies that prevalence may be increasing due to the progressively increasing diagnosis of rheumatic diseases and the early use of immunosuppressive therapies and to the increasing number of transplants of various organs and the higher survival rates achieved by these patients in our country.

The third case reported is a clarion call to consider that systemic diseases such as cirrhosis and alcoholism, which are frequent in our environment, lead to impaired immune function, to increased susceptibility to viral infections, and to development of gastrointestinal malignancies such as KS. This is in addition to the high frequency of squamous tumors of the mouth and esophagus and to gastric and pancreatic adenocarcinomas associated with these systemic diseases. Biopsies need to be taken from these patients from focal gastric lesions that are endoscopically similar to other vascular lesions such as portal hypertension gastropathy and gastric antral vascular ectasia (GAVE) syndrome (water melon stomach) (3, 5, 13, 14).

The last case presented demonstrates presence of classic KS in elderly patients with gastrointestinal compromise, lower limb edema and compromised inguinal lymph nodes. As reported in the literature, lower limb edema accompanies these lesions in 48% of cases, and compromised inguinal lymph nodes are found in 23% of these cases (20). This leads us to consider endoscopic diagnosis of possible gastrointestinal KS in elderly patients with cutaneous findings. This could be beneficial in terms of timely treatment with positive results for these patients.

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