

Primary Lymph Node Kaposi's Sarcoma in Two HIV Positive Patients Presenting with Generalized Lymphadenopathy and Pancytopenia in a Third Level Hospital in Guatemala

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Abstract

We present two unique cases in which two HIV positive patients with generalized lymphadenopathy and pancytopenia without any skin lesions were diagnosed with primary lymph node Kaposi's Sarcoma after excisional biopsy of an inguinal lymph node. Two men who have sex with men (MSM) patients between 20-23 years old, were admitted to Roosevelt Hospital in Guatemala because of generalized lymphadenopathy and pancytopenia. Excisional biopsy of inguinal lymph nodes was performed on both patients. Histologic evaluation of the surgical specimen revealed spindle-shaped cells with extravasated erythrocytes typical of Kaposi's sarcoma. After explaining the patients and discussing the cases with the oncology unit, both were treated with Paclitaxel showing reduced lymph nodes and hematological recovery by day 4.

Introduction

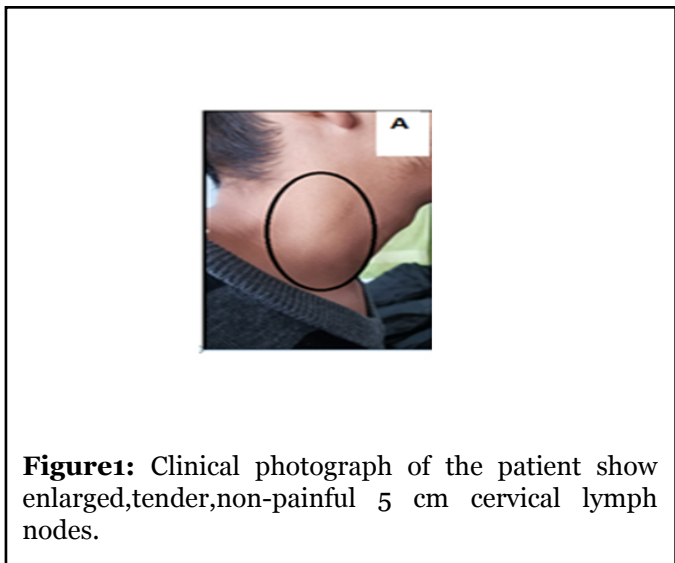
Kaposi's Sarcoma (KS) is a malignant systemic disease that originates from vascular endothelium with a variable clinical course. Once considered a rare disease, with the advent of the HIV epidemic, it has become one of the most common malignancies associated with the infection. It has different presentations: the classic Kaposi's sarcoma presenting with proliferative cutaneous lesions in lower extremities of elderly men of Mediterranean and Jewish origin. The endemic African Kaposi's sarcoma, affecting both children and adults, more aggressive and with frequent dissemination to bone, skin and lymph nodes, the epidemic, HIV-associated Kaposi's sarcoma 20,000 times more common in persons with AIDS than in the general population, and 300 times more common in AIDS than in other immunosuppressed host. Finally the organ transplanted associated KS caused by the immunosuppression therapy [1]. The Human Herpes Virus-8 infection (HHV8) characterizes all forms and

probably represents the same pathogenic process as the AIDS-associated Kaposi's sarcoma. Lesions of epidemic KS may arise on the skin and the mouth and may affect the lymph nodes and other organs, usually the gastrointestinal tract, lung, liver, and spleen. In contrast, classic KS usually involves only one or a few areas of skin, most often the lower legs. At the time of diagnosis of KS some people experience no symptoms, especially if their only lesions are on the skin. However, many of those with epidemic KS, even those without skin lesions, will have enlarged lymph nodes, fever or weight loss. Eventually, in almost all cases, epidemic KS spreads throughout the body. Extensive KS lung involvement can be fatal. Primary KS of lymph nodes is a rare presentation of the disease. We present two consecutive HIV patients without skin lesions and with generalized lymphadenopathy and pancytopenia diagnosed with Kaposi's sarcoma of lymph nodes with excisional biopsy.

Case 1

First case is a 23 year old patient, MSM, from an urban area of Guatemala who was admitted to Roosevelt Hospital because of epistaxis and generalized lymphadenopathy. His only medical history record was a HIV positive status since 2016 without adherence to ARV therapy. His current plasma HIV-1 RNA viral load was 35,400 copies per milliliter, and the blood CD4⁺ T-cell count was 29 per cubic millimeter (reference range, 348 to 1456). Patient had been well until 2 weeks earlier when he noted swelling of his bilateral cervical lymph nodes (Figure 1). Three days before admission, patients started with epistaxis. He also reported that he had had no fevers, night sweats, or weight loss.

On examination, the temperature was 37.6°C, the pulse 66 beats per minute, the blood pressure 112/82 mm Hg, the respiratory rate 16 breaths per minute, and the oxygen saturation 97% while the patient was breathing ambient air. The weight was 47.8 kg; the last recorded weight, which had been obtained 4 months earlier, was 55 kg. The patient did not appear to be ill, but he was pale, with active epistaxis. There were lymph nodes palpable on the entire cervical region bilaterally (Figure 1), both axilas and in the inguinal region. He also had epitrochlear lymph nodes. Examination of the heart and lungs was normal. Bowel sounds were present, and the abdomen was soft, without tenderness on palpation and there was no hepatosplenomegaly. The complete examination of the skin was normal.



Blood levels of electrolytes, glucose, and lactate dehydrogenase were normal, as were results of renal-function and liver-function tests; other laboratory test results are shown in Table 1. Tests for antibodies to hepatitis B virus (HBV) surface antigen and antibodies to HBV core antigen, hepatitis C virus antibodies, and *Treponema pallidum* antibodies, GeneXpert for TB, urine LAM, *Cryptococcus* blood latex and *Histoplasma* urine antigen were negative. We also performed a bone marrow aspiration, and *Mycobacterium* and Fungi culture were negative.

Variable	Reference Range, Adults *	On admission	
		Case 1	Case 2
Hematocrit (%)	41-53	5.6	8.9
Hemoglobin (g/dl)	13.5-17.5	16	21
White-cell count (per mm ³)	4,500-11,000	2,300	3,110
White-cell count (per mm ³)	4,500-11,000	2,300	3,110
Neutrophils	40-70	38	43
Lymphocytes	22-44	11	9
Monocytes	4-11	0	0
Eosinophils	0-8	0	0
Basophils	0-3	0	0
Platelet count (per mm ³)	150,000-400,000	23,000	38,000

*Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Roosevelt Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

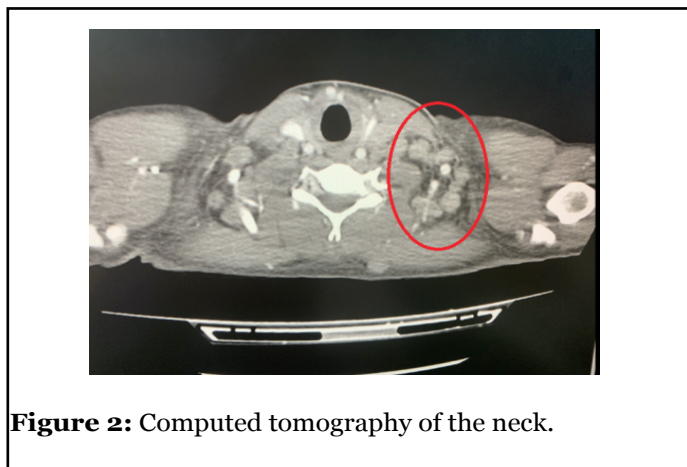


Figure 2: Computed tomography of the neck.

Computed tomography (CT) of the neck (Figure 2), performed after the administration of intravenous contrast material, revealed multiple bilateral lymph nodes in level I, II, III, and V, (≤ 5 cm in maximal short-axis diameter, red circle on Figure 2). The nodes did not show any enhancement/necrosis. CT of the chest, revealed multiple prominent cardio-phrenic lymph nodes (≤ 1 cm in maximal short-axis diameter) predominantly on the right side. There were also multiple enlarged axillary lymph nodes (≤ 3.4 cm in maximal short-axis diameter) on both sides. Complete abdomen CT revealed multiple paraaortic and inguinal lymph nodes (≤ 5 cm in maximal short-axis diameter).

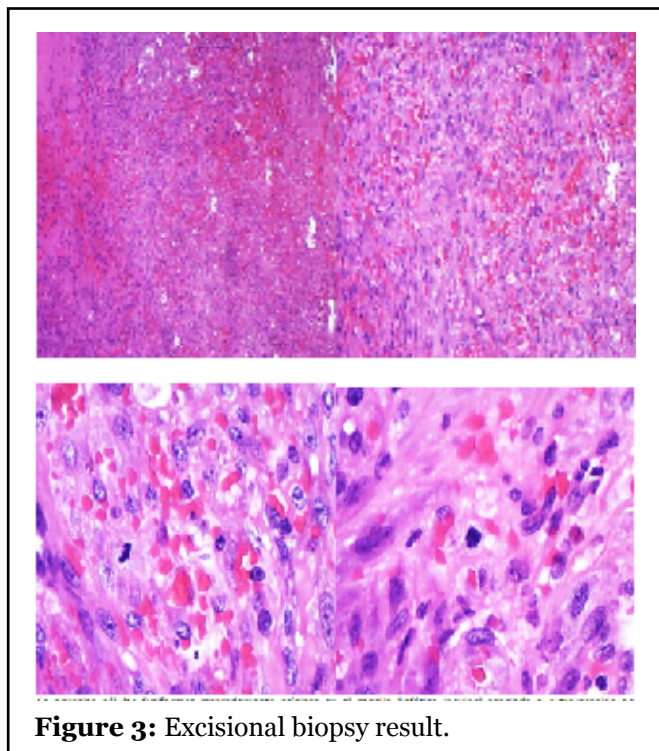


Figure 3: Excisional biopsy result.

We performed an excisional biopsy (Figure 3) of the palpable inguinal nodes. Gram stain of the biopsy was unremarkable, GeneXpert of TB, and fungi and *Mycobacterium* cultures were negative. The specimens showed cohesive clusters of spindle-shaped cells overlaid with relatively large intact fragments of tissue and small, overlapping spindle-shaped cells with ill-defined cytoplasmic borders and nuclear fragility. The most relevant cytological feature was the presence of fragments of spindle cell tissue. The nuclear distortion or streaking within these cell clusters appears to be a characteristic feature useful in diagnosis. Relatively small, loosely cohesive clusters of spindle cells were present with a radial arrangement of the overlapping, elongated nuclei within the fragments of tissue was seen relatively small, loosely cohesive clusters of spindle cells were present. Many tumor cells had one or more chromocenters, but most lacked visible nucleoli. This finding was consistent with Kaposi's sarcoma of lymph nodes (Figure 3).

The case was presented to the oncology unit and it was decided to start paclitaxel (only drug available in the hospital at this point) because the response rate with this drug has been quite high and the treatment is generally well tolerated. Paclitaxel was initiated at a dose of 135 mg/m² over 3 hours. On day 3 of treatment, lymph nodes were reduced in size by approximately 50-60%, epitrochlear nodes were absent at this point, and the hematology response is shown in table 2.

On day 5 of treatment, the patient was discharged with scheduled follow up in three weeks in the Chronic Infectious Diseases Integral Care Unit 'Dr. Carlos Mejía' (CIDICU) and oncology unit, however patient never attended the medical appointment. CIDICU has called the patient by phone, and he has reported he doesn't want to come to chemotherapy again and that his lymph nodes have enlarged again.

Case 2

The second case is a 25-year-old patient, MSM, from a rural area of Quiché, Guatemala, admitted to the same hospital because of generalized painful lymphadenopathy, weight loss and constitutional symptoms. His past medical record was unremarkable. A rapid screening test for HIV antibodies was positive, as was a fourth-generation combination assay for HIV-1. The plasma HIV-1 RNA viral load was 163,300 copies per milliliter, and the blood CD4⁺ T-cell count was 9 per cubic millimeter (reference range, 348 to 1456).

Patient had been well until 1 month earlier when he

started with fever and noted swelling of cervical and inguinal lymph nodes bilaterally that were painful. Two weeks earlier he noted he had lost weight because his clothes were loose.

On examination, the temperature was 38.7°C, the pulse 91 beats per minute, the blood pressure 122/78 mm Hg, the respiratory rate 19 breaths per minute, and the oxygen saturation 98% while the patient was breathing ambient air, his weight was 52 kg. The patient was pale without active bleeding. There were painful lymph nodes palpable bilaterally on the preauricular and suboccipital area, all the cervical region bilaterally, both axilla and in the inguinal region this last area being painful to palpation. He also had epitrochlear lymph nodes (Figure 2). Examination of the heart and lungs was normal. Bowel sounds were present, and the abdomen was soft, without tenderness on palpation and there was no enlarged liver or spleen. The complete examination of the skin was normal

Blood levels of electrolytes, glucose, and lactate dehydrogenase were normal, as were results of renal-function and liver-function tests; other laboratory test results are shown in Table 1. The infectious disease panel was negative in this patient as well.

CT of the neck (Figure 4) also reported multiple bilateral lymph nodes in level I, II, III, and V, (≤ 4.5 cm in maximal short-axis diameter), not showing any enhancement/necrosis. CT of the chest revealed thoracic lymph nodes (red stars) and multiple enlarged axillary lymph nodes (≤ 4 cm in maximal short-axis diameter, red arrows on Figure 4A) bilaterally. Complete abdomen CT (Red stars on Figure 4B) revealed para-aortic, precaval, laterocaval and inguinal lymph nodes (≤ 7 cm in maximal short-axis diameter).

An excisional inguinal lymph node biopsy (Figure 5) was also performed on this patient, Gram stain was unremarkable and the GeneXpert of TB and fungi and *Mycobacterium* cultures were also negative. The pathology report of the biopsy informed same finding as in case 1, diagnosing Kaposi's sarcoma of lymph nodes.

Patient was started on Paclitaxel at a dose of 135 mg/m² over 3 hours. On day 4 of treatment, lymph nodes were reduced in size, epitrochlear nodes were absent at this point, and the hematology response is shown in table 3.

On day 7 of Paclitaxel, patient was discharged from Hospital with scheduled follow up in 2 weeks in the CIDICU and oncology unit. The patient didn't attend to his follow up and was contacted by phone. He reported that he had presented fever and enlarged lymph nodes again but he couldn't come to his follow up. Forty five days after discharged, we received a phone call from a medical team in Quiché's National Hospital, informing us that the patient was admitted to that center with gingivorrhagia, petechia in lower limbs and generalized lymphadenopathy. We informed the team the need of a second round of chemotherapy and all the arrangements were performed to transfer the patient to our Hospital, however patient refused to be transferred and requested his discharge. Seven days after that, family members called CIDICU to inform us that patient had died at home.

Discussion

Kaposi sarcoma (KS) is an angioproliferative disorder that requires infection with human herpes virus 8 (HHV-8). There are four types based upon the clinical circumstances in which they develop: classic (the type originally described by Kaposi, which typically presents in middle or old age), endemic (several forms described in Sub-Saharan indigenous Africans prior to the acquired

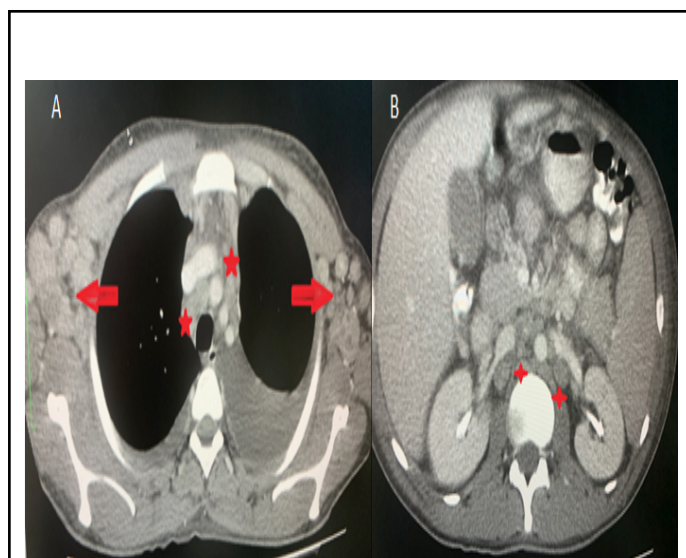


Figure 4: Thoracic and abdominal computed tomography.

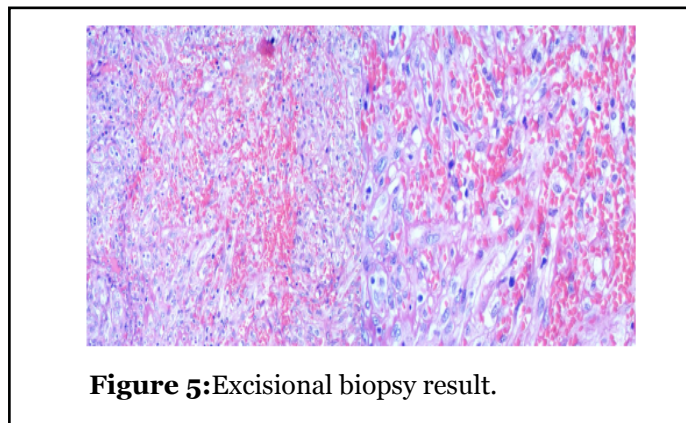


Figure 5: Excisional biopsy result.

immunodeficiency syndrome [AIDS] epidemic), iatrogenic (a type associated with immunosuppressive drug therapy, typically seen in renal allograft recipients), and AIDS-associated (epidemic KS) [2,3].

AIDS-related or epidemic KS is the most common tumor arising in HIV-infected persons. KS is considered an AIDS-defining illness in the United States Centers for Disease Control and Prevention (CDC) guidelines. In the United States, KS was over 20,000 times more common in persons with AIDS than in the general population prior to the widespread use of potent Antiretroviral Therapy (ART), although its incidence has declined substantially since that time. This type can present as cutaneous and visceral KS [4].

We present two cases of HIV positive patients with primary lymph node KS and pancytopenia, without any skin lesions during the hospital stay or during follow up. On physical examination, both patients had enlarged cervical, inguinal and epitrochlear lymph nodes. Nodal involvement of KS relatively uncommon and is rarely bulky. Nodal involvement was reported in 15% of 66 Greek patients with KS [5]. Diagnosis was achieved with the result of the inguinal excisional biopsy showing thin-walled vascular spaces in the upper dermis with a sparse mononuclear cell infiltrate of lymphocytes, plasma cells, and macrophages and spindle cell bundles accumulating around the areas of angioproliferation and extravasated erythrocytes and macrophages present between spindle cells. With the diagnosis confirmed, both patients were treated with Paclitaxel (only drug available at our hospital) at a dose of 135 mg/m² over 3 hours. Patient 1 had reduction of lymph nodes and hematological recovery by day 3. At this point, patient's epitrochlear nodes were absent. Patient's 2 response was similar by day 4. Systemic chemotherapy is generally used for patients with more advanced KS or when there is evidence of rapid disease progression. When chemotherapy is indicated, treatment with pegylated liposomal doxorubicin or liposomal daunorubicin is generally recommended as the first-line treatment for KS [6,7].

Other agents that have been used include paclitaxel, bleomycin, vinblastine, vincristine, and etoposide. Treatment with pegylated liposomal doxorubicin or liposomal daunorubicin is generally recommended as the first-line treatment for AIDS-related KS when systemic chemotherapy is indicated. Although paclitaxel is potentially more toxic than the liposomal anthracyclines, it has striking efficacy as a second-line treatment for KS and may be an alternative for initial therapy of patients with advanced, symptomatic KS [8]. The efficacy of paclitaxel was originally demonstrated in a phase II study in 28

evaluable patients, in which 20 (71 percent) had major responses to a regimen of 135 mg/m² every three weeks. Responses were noted in all five patients with pulmonary KS and all four who had previously received anthracycline therapy. Toxicity included grade 4 thrombocytopenia in six patients, and grade 4 neutropenia in 22 patients treated without hematopoietic growth factors [9].

Paclitaxel (100 mg/m² every two weeks) was compared with pegylated liposomal doxorubicin (20 mg/m² every three weeks) in a randomized trial conducted after the introduction of routine treatment with ART. In that trial, 73 evaluable patients were enrolled between 1998 and 2002; the trial was terminated prematurely because of poor accrual [10]. There were no statistically significant differences in response rate, progression-free survival, or overall survival. Treatment on both arms was associated with meaningful improvements in pain and swelling secondary to the tumor.

Conclusion

1. Primary lymph node Kaposi's Sarcoma is a vascular neoplasm characterized with generalized lymphadenopathy and without involvement of the skin.
2. Patients with lymph node Kaposi's sarcoma can present with pancytopenia.
3. Biopsy of selected lymph node in patients with primary lymph node Kaposi's sarcoma has the same pathological result as in any other KS.
4. Treatment with Paclitaxel in these patients produced hematological recovery.

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