Case Report

Kaposi Sarcoma Involving Axillary Lymph Nodes

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Introduction

Kaposi sarcoma (KS) used to be a rare vascular sarcoma occurring in the dermis of the sole. However with emergence of Acquired Immunodeficiency Syndrome (AIDS) not only its incidence has markedly climbed but also other tissues are frequently involved. These include oral cavity, nose, gastrointestinal tract, lymph nodes, lungs and liver. KS causes red or purple patches on the skin and/ or mucous membranes. Although most patients present with skin disease, KS involvement of lymph nodes or the gastrointestinal tract may occasionally precede the appearance of the cutaneous lesions.1

We report here a case of Kaposi sarcoma involving axillary lymph nodes without any cutaneous lesions and with an unknown HIV status. Although there was a high index of clinical suspicion, lymph node biopsy of the patient was the first to confirm the diagnosis of Kaposi sarcoma. Subsequently, serology revealed that the patient was indeed HIV positive and had markedly low levels of CD4 + helper T- cells. This case also emphasizes upon the use of oil immersion lens as a routine on histopathology sections as is this case the diagnosis was made on 1000 magnification that clearly revealed the nuclear atypia in the endothelial cells.

Case Report

A 40 years old male, resident of Azad Kashmir, presented with the complaints of low-grade fever, generalizedaches and pains and progressive weight loss for the past 4 months. He was also complaining of night sweats, generalized weakness and easy fatigue ability. He had been married for the past 2 yrs and had no children. He gave history of having traveled abroad to Iran 20 years back and stayed there for 4 years. He denied history of sexual contact, blood transfusion or intravenous drug abuse. However he did receive intravenous medication for some illness 20 years ago. There was no record available for the mentioned illness. There was no other significant medical, family or drug history. On examination he was a young man of lean built, lying in bed, pale, conscious and oriented. He seemed to be in agony due to aches and pains. His vital signs were stable. His left submandibular, bilateral axillary, and inguinal lymph nodes were enlarged. Systemic examination did not reveal any significant finding. On laboratory investigations ALT was 46 u/l, HbsAg was negative and anti HCV antibodies were negative. His Blood hemoglobin was 10.9 g/dl, haematocrit was 31.6%, TLC was 5000/ul and platelets were 151,000/ul. The differential leukocyte count showed 31% lymphocytes, 53% neutrophils and 16% mixed cells. ESR was 74. Chest x-ray was normal. Urine R/E revealed proteins ++ and 13-14 pus cells. Mantoux test and VDRL were both negative. Ultrasound abdomen showed normal study. His axillary lymph node biopsy was sent for histopathology that revealed Kaposi sarcoma. During his hospital stay he developed loose watery diarrhea with high grade fever. Modified ZN stain for cryptosporidium in stools was negative. His HIV screening was done and he was found to be HIV positive by both enzyme immunoassay and particle agglutination test. He had markedly low percentage (i.e. 3%. Normal= 29-57%) and absolute count (i.e. 57. Normal= 430-1010) of CD4+ T helper cells with reversal of CD4/CD8 ratio. He was given three cycles of chemotherapy for Kaposi sarcoma that included Inj. Doxorubicin, Inj Bleomycin and Inj Vincristine. The patient was discharged in a stable condition.

Materials and Methods

The specimen was fixed in 10% buffered formalin, routinely processed and embedded in
paraffin. Three-micrometer thick sections were cut and stained with hematoxylin and eosin.

**Figure 1:** Complete effacement of lymph node architecture. H & E (X 40)

**Figure 2:** Proliferation of atypical slit-like blood vessels. H & E (X 100)

**Figure 3:** Newly formed small blood containing erythrocytes. H & E (X 200)

**Figure 4:** Small blood vessels lined by atypical endothelial cells. H & E (X 400)

**Figure 5:** Highly atypical endothelial cells, lining slit like vascular spaces and having pleomorphic, hyperchromatic nuclei with some having prominent nucleoli. H & E (X 1000)

**Figure 6:** Another view showing atypia of endothelial cells lining blood vessels. H & E (X 1000).

Pathologic Findings

Grossly the specimen consisted of two yellowish brown irregular soft tissue fragments measuring 2.5x2x0.8 cm and 2x1.8x0.3 cm respectively. On cut sections 4 lymph nodes were identified, the largest being 1x0.8x0.2 cm in size. All lymph nodes had a homogenous grayish brown color on cut section.

Microscopically, sections from all 4 lymph nodes revealed complete effacement of architecture (Figure 1). There was marked proliferation of atypical blood vessels containing erythrocytes in their lumen (Figure 2). At 40 X only effacement of lymphoid architecture was seen. At 400 X magnification, numerous small vessels proliferation in the lymph node was noted but cellular morphology did not suggest malignancy (Figure 3 & 4), however under oil immersion lens with 1000 magnification, numerous slit-like blood vessels were quite evident (Figure 5), which were lined by atypical endothelial cells having pleomorphic, hyperchromatic nuclei.
with prominent nucleoli (Figure 6). The examination of the sections under oil immersion lens thus helped in confirming the diagnosis of Kaposi sarcoma beyond any doubt. On the basis of histologic findings a diagnosis suggestive of Kaposi Sarcoma was given.

Comments

Kaposi sarcoma (KS) was one of the first conditions recognized as an opportunistic sequel of HIV infection, and remains the most common AIDS-associated neoplasm. AIDS-associated KS occurs with increased frequency in all HIV transmission groups compared to the general population, but at a particularly high rate in homosexual men. All forms of KS are more common among men than women. The epidemiology of AIDS-associated KS has long suggested that an environmental or infectious, sexually transmitted cofactor might contribute to the development of KS. The search for such a cofactor led, in 1994, to the discovery of a novel herpes virus, human herpesvirus-8 (HHV-8), also known as the Kaposi sarcoma-associated herpes virus (KSHV). HHV-8/KSHV is found in all forms of KS, and infection with the virus appears to be necessary but not sufficient for KS to develop. Other factors believed to be involved in the development of AIDS-associated KS include altered expression and response to growth factors and cytokines, and modulation of KS growth by an HIV gene product, the Tat protein. AIDS-associated KS varies in its presentation from an indolent process with minimal clinical consequences to a disseminated, aggressive disease. All forms of KS are histologically similar, and include a spindle cell component, slit-like vascular spaces containing erythrocytes, focal hemosiderin deposits and a variable inflammatory cell infiltrate.

Classic KS usually occurs in males with a ratio of approximately 10 to 15 males to one female. The usual age is between 50 and 70. Classic KS tumors usually present with one or more asymptomatic red, purple, or brown patch, plaque, or nodular skin lesions. Most commonly runs a relatively benign, indolent course for 10 to 15 years or more with slow enlargement of the original tumors and the gradual development of additional lesions. Venous stasis and lymphedema of the involved lower extremity are frequent complications. In long-standing cases, systemic lesions can develop along the gastrointestinal tract, in lymph nodes, and in other organs. These visceral lesions are generally asymptomatic and are most often discovered only at autopsy, although clinically, GI bleeding can occur. Up to one-third of the patients with classic KS develop a second primary malignancy, most often non-Hodgkin's lymphoma.

African Kaposi's sarcoma was recognized in 1950 as a relatively common neoplasm endemic in native populations in equatorial Africa comprising approximately 9% of all cancers seen in Ugandan males. African KS is seen as either an indolent neoplasm or as an aggressive disease with fungating and exophytic tumors that may invade the subcutaneous and surrounding tissue including the underlying bone. In Africa, both the indolent and locally more aggressive forms of KS occur with a male:female ratio comparable to that observed with the classic KS tumor seen in North America and Europe. However, patients in Africa are significantly younger than their European counterparts. A lymphadenopathic form of KS is also seen in Africa, primarily in prepubescent children (male : female ratio 3:1). In these cases, the generalized lymphadenopathy is frequently associated with visceral organ involvement. The prognosis is very poor, with a 100% fatality rate within 3 years.

Immunosuppressive treatment-related Kaposi's sarcoma. In 1969, the first case of KS in association with immunosuppression in a renal transplant patient was described. Since that time a number of renal and other organ allograft recipients receiving prednisone and azathioprine have developed KS shortly after the onset of immunosuppressive therapy. The average time to develop KS after transplantation is about 16 months. Although the tumor in these iatrogenically immunosuppressed patients, often remains localized to the skin, widespread dissemination with mucocutaneous or visceral organ involvement is common. In some cases, the KS tumors have regressed as a result of reduction or changes in immunosuppressive therapy.

Epidemic Kaposi's Sarcoma. In 1981, a fulminant and disseminated form of KS in young homosexual or bisexual men was first reported as part of an epidemic now known as AIDS. The etiology of this disease appears to be a family of T-cell lymphotropic retroviruses, known as HIV. The underlying immunologic deficiency that characterizes HIV disease is an acquired disorder of cell-mediated immune functions. This immunologic deficiency predisposes the host to a variety of opportunistic infections and unusual neoplasms, especially KS. HIV
itself may play an indirect role in the development of KS. Epidemic KS is usually characterized by multifocal, widespread lesions at the onset of illness. These lesions may involve the skin; oral mucosa; lymph nodes; and visceral organs, such as the gastrointestinal tract, lung, liver and spleen. In an early report on the clinical manifestations of the disease, 49 patients were described. Eight percent had no skin involvement, 27% had localized or fewer than five skin lesions, and 63% had innumerable skin lesions widely distributed over the skin surface area. Sixty-one percent of the patients had generalized lymphadenopathy at the time of the first examination. Four of these patients who had generalized lymphadenopathy in the absence of skin lesions or detectable visceral organ involvement at the time of presentation were found to have biopsy-proven KS localized to the lymph nodes. In 45% of the patients studied, KS lesions were found in one or more sites along the gastrointestinal tract. Twenty-nine percent of the patients had either unexplained fever or weight loss when first seen. Thus, while most patients present with skin disease, KS involvement of lymph nodes or the gastrointestinal tract may occasionally precede the appearance of the cutaneous lesions.

Patients with AIDS-associated KS often have modestly enlarged lymph nodes. Routine lymph node biopsy often reveals focal KS involvement, although as with asymptomatic gastrointestinal KS, this finding appears to have little clinical consequence. Thus, routine biopsy of small lymph nodes is not recommended for the purpose of diagnosing nodal KS. Occasionally, however, massive nodal enlargement may occur, and KS may replace lymph nodes. This presentation may occur in the absence of KS elsewhere, and may be associated with edema. Because the causes of massive or asymmetric nodal enlargement include lymphoma or various HIV-associated infections, diagnostic biopsy is warranted in such cases. In a study carried by O’Connell et al biopsy of lymph nodes containing Kaposi’s sarcoma from 16 patients showed that the tumor is identical in appearance with that of Kaposi’s sarcoma of the skin, regardless of the age of the patient or the mode of presentation. Spread of tumor along sinusoids throughout the lymph node was seen only in the cases of two children with generalized lymphadenopathy, but discrete deposits were present both in lymph nodes regional to skin lesions and in lymph nodes from patients who had presented with primary lymphadenopathy. The reaction of the remainder of incompletely involved nodes was variable. Eventually, almost all patients with epidemic KS develop disseminated disease. Progression often proceeds in an orderly fashion from a few localized or widespread mucocutaneous lesions to more numerous and generalized skin disease with lymph node, gastrointestinal tract disease, and other organ involvement. Pleuropulmonary KS is an ominous sign usually occurring late in the course of the disease; especially in those patients whose death is directly attributed to KS. Most patients with epidemic KS die of one or more complicating opportunistic infections.

Non-Epidemic Gay-Related Kaposi’s sarcoma. There have been several reports documenting KS in homosexual men who persistently have no evidence of HIV infection. These patients have an indolent and cutaneous form of the disease, with new lesions appearing every few years. Lesions occur most commonly on the extremities and genitalia but can occur anywhere on the skin. Recently, human papillomavirus (HPV)-16 DNA sequences have been identified in approximately 25% of KS biopsy specimens from patients with the classic, epidemic and non-epidemic gay-related forms of the disease. This finding suggests that HPV is associated with, or has a role in, the pathogenesis of KS.

Various clinical and laboratory features of HIV-associated KS are associated with survival and have been used to develop KS staging systems. A particular difficulty in evaluating prognosis is that KS in HIV-infected individuals is a "disease within a disease." With advances in the therapy of HIV infection and its non-neoplastic complications, the natural history of HIV infection is modified and overall survival is prolonged. Although these advances have clearly been associated with a decreased incidence of KS and a better prognosis for patients with this tumor, ART may enable some patients with KS to live long enough to develop late KS complications, whereas others without KS may survive long enough to develop KS later in the course of their HIV infection.

Laboratory tests reported to be positive or negative predictors of survival in HIV-infected patients with KS include the CD4 T-lymphocyte count, CD4 to CD8 cell ratios, haematocrit, cutaneous anergy, lymphocyte proliferative responses, and serum levels of HIV p24 antigen, endogenous interferon-alfa, beta-2 microglobulin, and neopterin. Clinical features of patients with AIDS-associated KS, including the extent and distribution of KS lesions, the anatomic site of
initial KS presentation, the presence of lymphoma-like "B" symptoms (i.e., unexplained fever, weight loss, or night sweats), body-mass index, and a history of HIV-defining opportunistic infections (OIs), have all been associated with survival in univariate analyses. Many of these analyses of prognostic factors were conducted before the routine use of OI prophylaxis and ART, so their relevance to prognosis in the setting of these treatments is not known.

Several staging systems for KS have been proposed. A four-stage classification proposed by Krigel et al was based entirely on tumor extent and was designed to include AIDS-associated KS as well as the "non-HIV epidemic" forms of the disease. A subsequent classification by Mitsuyasu, Groopman, and colleagues designed specifically for AIDS-associated KS categorized patients by extent of tumor and the presence or absence of systemic "B" symptoms and OI history. Chachoua et al later proposed a classification that included the presence or absence of "B" symptoms and OIs and the CD4 count, but KS extent was not included as a staging variable.

### Table 1: AIDS Clinical Trials Group Staging Classification

<table>
<thead>
<tr>
<th>Good Risk (0) (All of the following)</th>
<th>Poor Risk (1) (Any of the following)</th>
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<tbody>
<tr>
<td>Tumor (T)</td>
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<tr>
<td>Confined to skin and/or lymph nodes and/or minimal oral disease*</td>
<td>Tumor-associated edema or ulceration</td>
</tr>
<tr>
<td>KS in other non-nodal visaera</td>
<td>Extensive or Gastrointestinal KS</td>
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<tr>
<td>Immune system (I)</td>
<td></td>
</tr>
<tr>
<td>CD4 cells &gt;/= 200/µL</td>
<td>CD4 cells &lt;200/mm3</td>
</tr>
<tr>
<td>No history of OI or Thrush</td>
<td>History of OI and/or thrush</td>
</tr>
<tr>
<td>Systemic illness (S)</td>
<td></td>
</tr>
<tr>
<td>No &quot;B&quot; symptoms**</td>
<td>&quot;B&quot; symptoms present</td>
</tr>
<tr>
<td>Performance status &gt;/= 70 (Karnofsky)</td>
<td>Performance status&lt;70</td>
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<tr>
<td>Other HIV-related illness (e.g., neurological disease, lymphoma)</td>
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* minimal oral disease is non-nodular KS confined to the palate
** "B" symptoms are unexplained fever, night sweats, greater than 10% involuntary weight loss, or diarrhea persisting more than 2 weeks.

Currently, the most widely used staging system is that proposed in 1988 by the Oncology Committee of the AIDS Clinical Trials Group (ACTG). This system takes tumor distribution, CD4 count, HIV-associated symptoms, and opportunistic complications into account, and separates patients into good- and poor-risk groups for each of these three variables (Table 1).

Treatment options for each patient are based on the type of KS present, the location and size of lesions, stage of KS, and the presence and severity of other serious medical conditions such as AIDS. The four treatments used to treat KS are surgery, chemotherapy, radiation therapy and biological therapy. In some cases 2 or more of these treatments are used together.

We present here a case of Kaposi sarcoma involving the axillary lymph nodes without any cutaneous lesions. He was diagnosed to be HIV positive subsequently. We recommend the routine examination of sections especially the doubtful ones under oil immersion lens as it greatly aids in diagnosis by making the cellular morphology more evident.

References


