CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 29-2013: A 32-Year-Old HIV-Positive African Man with Dyspnea and Skin Lesions

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PRESENTATION OF CASE

Dr. Emily K. Wong (Medicine, Massachusetts General Hospital): A 32-year-old man with human immunodeficiency virus (HIV) infection was admitted to a hospital in Durban, South Africa, because of dyspnea and cough. The hospital is associated with Massachusetts General Hospital.

Five months before admission, the patient was seen in an outpatient clinic in South Africa for evaluation of a lesion on his left upper eyelid. On examination, violaceous, raised lesions were present on the left eyelid and right side of the chest (Fig. 1A).

Dr. Pratistadevi K. Ramdial: Pathological examination of an excisional biopsy specimen of the chest lesion showed a malignant vasoformative tumor of the dermis. The tumor was composed of a nodular spindle-cell infiltrate arranged in short, interlacing bundles, with intervening slitlike vasculature and angiomatous foci. Intratumoral hemosiderin pigment, erythrocyte extravasation, hyaline globules, and a lymphoplasmacytic infiltrate were conspicuous findings (Fig. 1B). Immunohistochemical staining for human herpesvirus 8 (HHV-8) confirmed nuclear immunoreactivity in the spindle cells (Fig. 1C). These findings were consistent with a diagnosis of Kaposi's sarcoma.

Dr. Wong: An antibody test was positive for HIV type 1 (HIV-1), and the CD4 T-lymphocyte count was 330 per cubic millimeter (reference range, 500 to 2010). In preparation for the initiation of antiretroviral therapy (ART), the patient completed pretreatment classes. During the next 3 months, new skin lesions appeared on the thighs.

Sixteen weeks before admission, a productive cough developed. Two weeks later, a specimen of sputum was negative for *Mycobacterium tuberculosis* by polymerase-chain-reaction (PCR) testing and acid-fast bacilli staining and culture. The CD4 T-lymphocyte count was 268 per cubic millimeter.

Dr. Pumersha Naidoo: A chest radiograph obtained 14 weeks before admission showed nodular opacities, 5 to 7 mm in diameter, in both lungs, most prominently in the middle and lower zones; there was loss of definition of the right hilum, with irregular peribronchovascular thickening and air bronchograms.

No pleural effusions, hilar lymphadenopathy, or paraspinal masses were seen (Fig. 2A).

Dr. Wong: Eleven weeks before admission, therapy with tenofovir, lamivudine, and efavirenz was begun. A chest radiograph at the time of the initiation of ART revealed no changes. One week later, the patient was seen in the infectious diseases clinic at the hospital for evaluation of worsening productive cough, daily fevers of 2 weeks' duration, weight loss of 2 kg, and night sweats. He reported full adherence with the ART regimen and noted no change in his skin lesions during the week he was receiving therapy.

On examination, the temperature was normal. Small, violaceous lesions were noted on the left upper eyelid and thighs, with a healed surgical scar on the right side of the chest. The lungs and the remainder of the examination were normal. Additional sputum specimens were obtained; PCR testing and acid-fast bacilli staining and cultures for *M. tuberculosis* were negative. The patient returned home. Symptoms persisted, and a presumptive diagnosis of pulmonary tuberculosis was made. Seven weeks before admission, the administration of rifampin, pyrazinamide, ethambutol, and isoniazid was begun.

Worsening dyspnea, cough, malaise, anorexia, and an additional weight loss of 8 kg developed during the next 7 weeks, and the patient was admitted to the hospital. He reported increased numbers of skin lesions since his last visit, 10 weeks earlier. He had had a painless mass in the left inguinal region for the past 5 years, which he thought was a hernia caused by lifting weights. Approximately 3 weeks after the initiation of ART, the mass "erupted" and drained purulent material. Medications on admission included antiretroviral and antituberculous medications. The patient was born and lived in South Africa. He reported being heterosexual and monogamous with his wife. He had drunk alcohol socially until the onset of this illness; he did not smoke or use illicit drugs. His parents reportedly died of old age; his five siblings were healthy. He had no known exposure to tuberculosis.

On examination, the patient appeared cachectic, with temporal wasting. The oxygen saturation ranged between 93% and 96% while he was breathing ambient air, and dyspnea developed with minimal exertion. The blood pressure was 95/63 mm Hg, and the pulse 120 beats per minute. There were crepitations over the left middle and lower lung fields; the liver edge was palpable

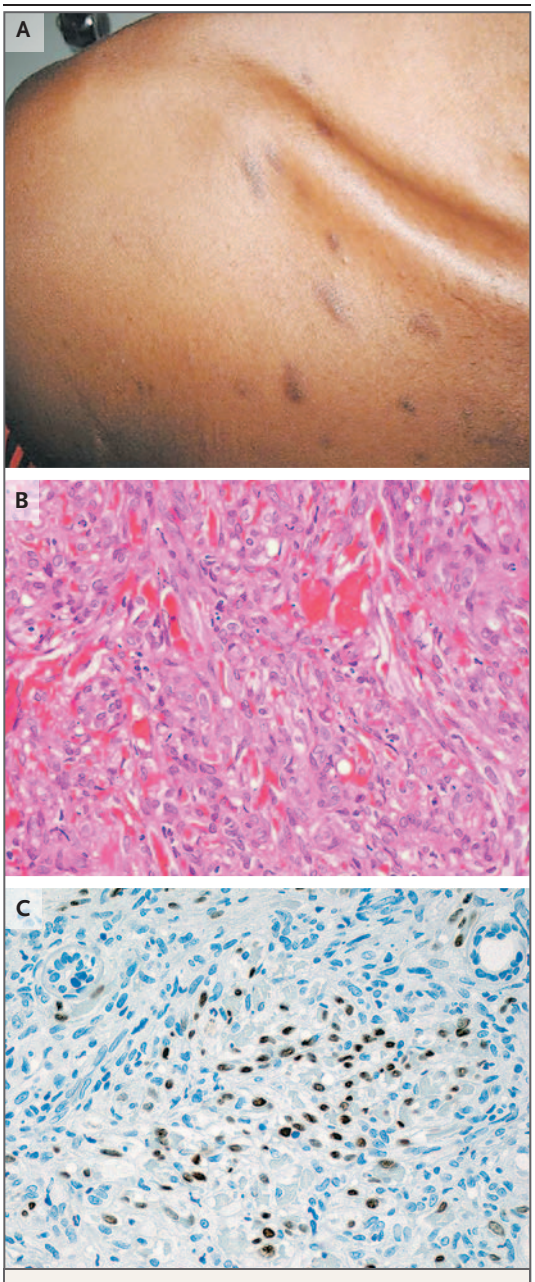

Figure 1. Physical Appearance and Pathological Examination of the Chest Lesion.

A photograph of the patient's skin shows violaceous, raised lesions that are representative of the lesion excised from the right side of the chest (Panel A). Pathological examination of a specimen of the patient's skin shows a malignant vasoformative tumor that is composed of a nodular spindle-cell infiltrate arranged in short, interlacing bundles, with intervening slitlike vasculature and angiomatous foci (Panel B, hematoxylin and eosin), features suggestive of Kaposi's sarcoma. Immunohistochemical staining for human herpesvirus 8 shows nuclear immunoreactivity in the spindle cells and confirms the diagnosis of Kaposi's sarcoma (Panel C).

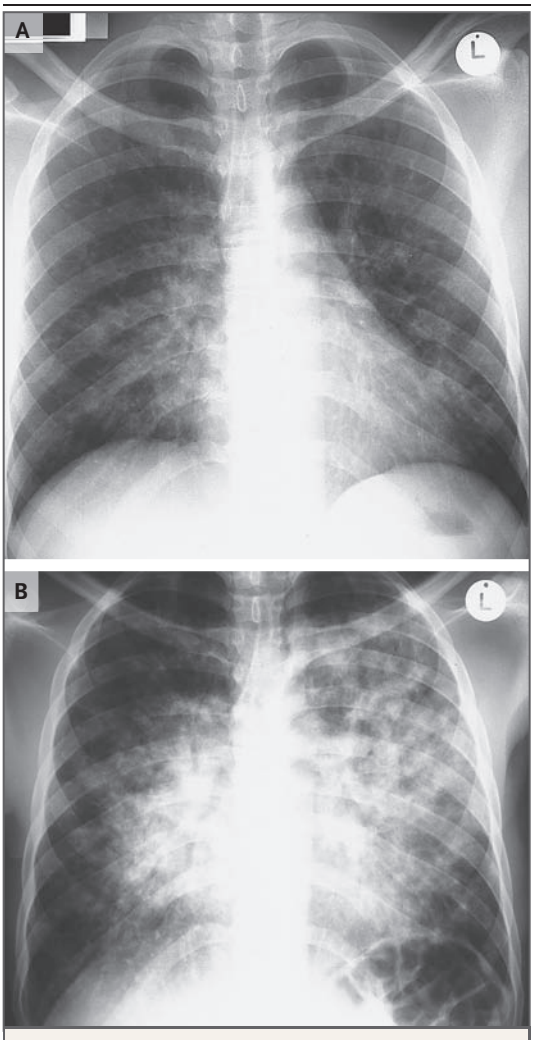

Figure 2. Chest Radiographs.

A chest radiograph obtained 14 weeks before admission (Panel A) shows bilateral reticular and ill-defined micronodular opacities in the middle and lower zones, with peribronchovascular and perihilar predominance. Bilateral peribronchial cuffing is present. Partial opacification and air bronchograms are apparent in the right lower zone, and the right border of the heart is obscured, indicating pathology in the right middle lobe. In the lingular segment of the left upper lobe, there is poorly marginated opacification, and the left border of the heart is partially obscured. No mediastinal lymphadenopathy or pleural effusions can be seen. A chest radiograph obtained on admission (Panel B) shows marked progression of the previous findings, with extensive central perihilar and peribronchovascular coalescent consolidation and irregular borders. There is a marked increase in size and profusion of the reticulonodular opacities.

2 cm below the costal margin, and the spleen tip was palpable. Violaceous skin lesions were present on the legs, arms, torso, palate, and left eyelid. There was lymphadenopathy in the cervical and axillary regions, with a draining lymph node and a groove sign (visible separation of enlarged inguinal and femoral lymph nodes by the inguinal ligament) in the left groin.

The blood levels of electrolytes, bilirubin, phosphorus, magnesium, alkaline phosphatase, and alanine aminotransferase were normal, as were the platelet count, red-cell indexes, and results of renal-function tests. The results of screening tests for hepatitis A and B viruses were consistent with immunity from previous exposure, and the results of screening for hepatitis C virus were negative; other results are shown in Table 1.

Dr. Naidoo: A chest radiograph showed marked progression of previous radiographic findings (Fig. 2B). There was extensive central perihilar and peribronchovascular confluent consolidation. Irregular nodular opacities were seen in the periphery of both lung fields, with some in the left upper lobe showing possible cavitation or air bronchograms. There were no pleural effusions.

Given this constellation of radiographic findings in an immunocompromised patient with cutaneous Kaposi's sarcoma, the differential diagnosis includes lymphoma, Kaposi's sarcoma, and Kaposi's sarcoma–associated immune reconstitution inflammatory syndrome (IRIS). Atypical tuberculosis and *Pneumocystis jirovecii* infections could be further considerations.[1-3]

Dr. Wong: Gram's staining of a sputum specimen revealed scanty gram-positive cocci, and a culture grew normal respiratory flora; Ziehl–Neelsen and auramine staining, direct fluorescence antibody testing for *P. jirovecii*, and a mycobacterial culture were negative. The administration of antiretroviral and antituberculous medications was continued, and doxycycline, trimethoprim–sulfamethoxazole, prednisone, and oxygen (40%, administered through a nonrebreather face mask) were added.

Diagnostic procedures were performed.

DIFFERENTIAL DIAGNOSIS

Dr. Gerald H. Friedland: Although the differential diagnosis of progressive pulmonary disease in a person with HIV-1 infection is broad, several clues in this case will allow me to focus on relatively few entities. The patient's CD4 T-lymphocyte count at presentation, the tempo of disease progression, the organ systems involved, and geography should all be considered when formulating a differential diagnosis.

Table 1. Laboratory Data.*

Variable	Reference Range, Adults†	On Admission
Hematocrit (%)	40–50	34.5
Hemoglobin (g/dl)	13.0–17.0	11.9
White-cell count (per mm^3)	4000–10,000	10,030
Differential count (%)		
Neutrophils	40–75	69.90
Lymphocytes	20–45	20.40
Monocytes	2–10	8.10
Eosinophils	1–6	1.10
Basophils	0–1	0.50
Erythrocyte count (per mm^3)	4,500,000–5,500,000	3,930,000
Absolute CD4 T-lymphocyte count (per mm^3)	500–2010	533
CD4 percentage of total lymphocytes	28.0–58.0	23.5
HIV RNA by PCR (copies per ml)	<40	<40
Prothrombin time (sec)	10–14	11.4
International normalized ratio for prothrombin time	0.8–1.2	1.1
Protein (g/liter)		
Total	60–78	70
Albumin	35–52	26
Globulin	15–35	44
Calcium (mmol/liter)	2.15–2.55	2.57

* HIV denotes human immunodeficiency virus, and PCR polymerase chain reaction. To convert the values for calcium to milligrams per deciliter, divide by 0.250.
† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at the 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.

This patient presented with localized Kaposi's sarcoma and an initial CD4 T-cell count of 330 per cubic millimeter. A subsequent CD4 T-cell count was 268 per cubic millimeter, before the initiation of ART. Despite a brisk rise in the count to 533 cells per cubic millimeter after the initiation of therapy, the disease progressed clinically and radiographically. Because the CD4 T-cell count was higher than the counts typically associated with the common opportunistic infections that are seen in persons with the acquired immunodeficiency syndrome (AIDS), I will focus my differential diagnosis on entities that occur in persons with higher CD4 T-cell counts. Kaposi's sarcoma and other cancers, as well as certain bacterial infections, most notably tuberculosis, are the illnesses that most often occur at this stage of infection. I find it useful to think of the timing of the appearance of complications of HIV disease as inversely related to the virulence of the infecting agent. Earlier complications typically occur with more virulent organisms and continue with increasing frequency throughout the remaining course of the natural history of HIV disease, whereas less virulent agents begin to appear as the immune system becomes increasingly weakened. Given this patient's progressive decline at a relatively high CD4 T-cell count, I will consider diseases that occur early with an aggressive presentation.

The progression of this patient's disease, from subacute to chronic, may also provide a diagnostic clue. The illness appears to have progressed over a period of 5 months, from discovery of the skin lesions of Kaposi's sarcoma to a more rapid acceleration of severe systemic disease. This pattern is consistent with progressive Kaposi's sarcoma, although other cancers, tuberculosis, and other slowly progressive infectious diseases remain possibilities.

This patient's presentation is characterized by cutaneous and pulmonary disease. Although he

may have had multiple concurrent conditions, if we attempt to explain his presentation with a single, unifying process, we must focus our differential diagnosis on entities that cause systemic disease with involvement of both the skin and lungs.

Last, the geographic context of the patient's illness is of great diagnostic value. This patient is from South Africa, a country experiencing the world's most severe HIV–AIDS epidemic and concurrent tuberculosis epidemics. We should attempt to fit this patient's clinical disease within the context of disease entities most frequently seen in South Africa.

What specific diagnoses would have these features? The one already known in this patient is Kaposi's sarcoma, initially diagnosed by the appearance of a few characteristic, violaceous, raised cutaneous lesions and confirmed on biopsy. What other diagnoses should we consider?

AIDS-RELATED LYMPHOMA

AIDS-related lymphomas, including large-B-cell lymphoma and Burkitt's lymphoma, should be considered in this case. Symptoms and signs depend on the site of involvement and the stage of the disease, which can be variable. As with Kaposi's sarcoma, B-cell lymphomas occur with increased frequency in persons with HIV infection and may occur in persons with higher CD4 T-cell counts, and the clinical progression of the disease at presentation is usually subacute.[4] Most patients present with constitutional B symptoms such as fever, weight loss, and night sweats. Skin involvement is unusual, and visceral disease predominates, particularly in the gastrointestinal tract and central nervous system. Pulmonary disease, which this patient had, is less frequent. Minimal hematologic abnormalities and the absence of prominent visceral lymphadenopathy also argue against lymphoma. These features of the patient's illness make AIDS-related lymphoma possible but unlikely.

TUBERCULOSIS

Tuberculosis must be highest on our list of diagnoses. Tuberculosis is the most common cause of HIV-associated illnesses and death worldwide.[5] In areas of the world and in specific populations with a high prevalence of both HIV and *M. tuberculosis*, epidemics of tuberculosis commonly emerge. In South Africa, the incidence of tuberculosis approaches 1000 persons per 100,000 population,[5] in contrast with 3 to 4 per 100,000 population in the United States. In the province of KwaZulu-Natal, where this patient resided, rates exceed 1000 persons per 100,000. In the rural Zulu population, the presence of tuberculosis often leads to the diagnosis of HIV infection, and it is commonly said that "TB is the mother of AIDS."

This patient has many features of tuberculosis. The risk of active tuberculosis begins at higher CD4 T-cell counts and increases progressively as the CD4 T-cell count declines. The tempo of disease progression is subacute, and chronic cough, fever, night sweats, and weight loss are characteristic. Although tuberculosis is high on our diagnostic list, the presence of severe dyspnea on exertion, atypical radiologic findings, and the negative results of mycobacteriologic testing reduces the likelihood. The sputum smear is often falsely negative in patients coinfected with tuberculosis and HIV, as a result of the paucibacillary disease in the lungs and pulmonary secretions. PCR testing is more sensitive, with positivity rates as high as 75% in coinfected patients.[6] In this case, PCR testing was performed and was negative. Culture for *M. tuberculosis* remains the standard and was negative on two occasions. Extrapulmonary tuberculosis is also common in patients with tuberculosis and HIV coinfection. Diagnostic tests performed in this case could not rule out extrapulmonary tuberculosis, but the patient's predominant involvement of the visceral organ system was pulmonary, and I believe results of the sputum examination were adequate to make this diagnosis unlikely.

The patient was placed on empirical antituberculous therapy with no improvement over a 2-month period, which reduces the likelihood that he had tuberculosis, unless he had drug-resistant tuberculosis. He did not have a history of previous exposure to antituberculous medications; therefore, the origin of drug-resistant tuberculosis would have been through recent transmission from another person in a health care or community setting,[7,8] which is a well-documented and frequent occurrence in South Africa. However, his negative sputum cultures make this unlikely.

KAPOSI'S SARCOMA

Kaposi's sarcoma appears to fit well within the contextual framework of the CD4 T-cell count,

tempo of disease progression, localization of organ-system involvement, and geography. When this patient presented, his CD4 T-cell count was well above 200 per cubic millimeter. The disease changed from localized and indolent to subacute, with a few characteristic skin lesions rapidly increasing in number, with mucosal involvement; it progressed to fever, weight loss, night sweats, and extensive pulmonary involvement, with severe dyspnea on exertion. This all occurred in sub-Saharan Africa in the context of a rising incidence of Kaposi's sarcoma associated with the epidemic of HIV disease.

In resource-privileged settings, the incidence of Kaposi's sarcoma has decreased dramatically with the availability of ART. In contrast, in sub-Saharan Africa, where the HIV–AIDS epidemic and associated immunosuppression is on the rise and ART availability is limited, the incidence of Kaposi's sarcoma has accelerated dramatically. This is particularly so in geographic regions that have a prevalence of both HHV-8, the causative agent of Kaposi's sarcoma, and HIV-1.[9,10] Among persons with HIV infection, the risk of Kaposi's sarcoma is 10,000 times as great as the risk among persons without HIV infection[11]; Kaposi's sarcoma has become one of the most common cancers in sub-Saharan Africa. Pulmonary manifestations of Kaposi's sarcoma are well described and include progressive infiltrates and dyspnea, as seen in this patient.[12,13]

Could this patient's clinical course be explained by the presence of both Kaposi's sarcoma and tuberculosis, given the high rates of both diseases, their geographic overlap, and the clinical characteristics as noted? This is certainly possible. Coexistence of Kaposi's sarcoma and tuberculosis is common in patients with HIV in sub-Saharan Africa. In a descriptive study performed in a major referral hospital in Durban, one third of 152 consecutive patients in whom Kaposi's sarcoma was diagnosed were shown to have an additional opportunistic infection, most commonly tuberculosis.[14]

Kaposi's Sarcoma–Associated Immune Reconstitution Inflammatory Syndrome

One of the striking features of the patient's clinical course was the deterioration in his condition after the initiation of highly active ART. ART alone may ameliorate and even reverse the lesions of Kaposi's sarcoma, but not invariably and often very slowly.[14,15] A likely additional event that could explain the patient's worsening condition is Kaposi's sarcoma–associated IRIS.[16,17] This entity is not uncommon and can be serious or even fatal.[14]

There is no laboratory test to confirm the diagnosis, and other entities need to be ruled out, as was done for tuberculosis in this case. However, both the timing of the deterioration of the patient's condition after the start of ART and the clinical expansion of the existing lesions of Kaposi's sarcoma are most consistent with the diagnosis of Kaposi's sarcoma–associated IRIS. Treatment with antiinflammatory agents, particularly glucocorticoids, can ameliorate the disease process. The diagnostic procedure that would confirm the diagnosis is a bronchoscopy, with inspection for bronchial lesions and consideration of transbronchial biopsy if no lesions are seen.

Dr. Rajesh T. Gandhi: Dr. Moosa, what was your impression when you evaluated this patient?

Dr. Mahomed-Yunus S. Moosa: When I evaluated this 32-year-old man with HIV infection, I was concerned about the fairly rapid evolution of his pulmonary symptoms. On the basis of his known diagnosis of cutaneous Kaposi's sarcoma, we believed that pulmonary involvement with Kaposi's sarcoma was the most likely explanation for the rapid disease progression. However, given that *P. jirovecii* pneumonia and tuberculosis are so common, we could not dismiss these diagnoses without more definitive testing. In addition, the temporal relationship between his clinical deterioration and the initiation of ART made IRIS a likely possibility. IRIS is considered a manifestation of immune dysregulation.[18] ART-induced HHV-8–specific inflammatory response may result in an increase in proinflammatory cytokines and chemokines that up-regulate expression of angioproliferative and tumorigenic factors.[19] This in turn may result in a paradoxical worsening of preexisting HIV–Kaposi's sarcoma (paradoxical Kaposi's sarcoma–associated IRIS). Criteria for the diagnosis of pulmonary Kaposi's sarcoma–associated IRIS include biopsy-proven Kaposi's sarcoma at an extrapulmonary site with an otherwise unexplained worsening chest radiograph, mucocutaneous lesions consistent with Kaposi's sarcoma that occur in temporal association with successful ART, or both. This patient had biopsy-proven Kaposi's sarcoma of the skin and a dramatic worsening of findings on the chest radiograph. We elected to perform bronchoscopy for a

more definitive diagnosis of Kaposi's sarcoma–associated IRIS.

CLINICAL DIAGNOSIS

Pulmonary Kaposi's sarcoma complicated by the immune reconstitution inflammatory syndrome.

DR. GERALD H. FRIEDLAND'S DIAGNOSES

Cutaneous and visceral (pulmonary) Kaposi's sarcoma.

Kaposi's sarcoma–associated immune reconstitution inflammatory syndrome.

PATHOLOGICAL DISCUSSION

Dr. Bilal Abdool-Gafoor: Bronchoscopic inspection is considered the most sensitive method of diagnosis of pulmonary Kaposi's sarcoma because of the tendency of this condition to progress from the subepithelial layer to invasion of the mucosal surfaces. We performed bronchoscopy, and our first finding was multiple, macular red lesions parallel to the tracheal rings (Fig. 3A). Multiple

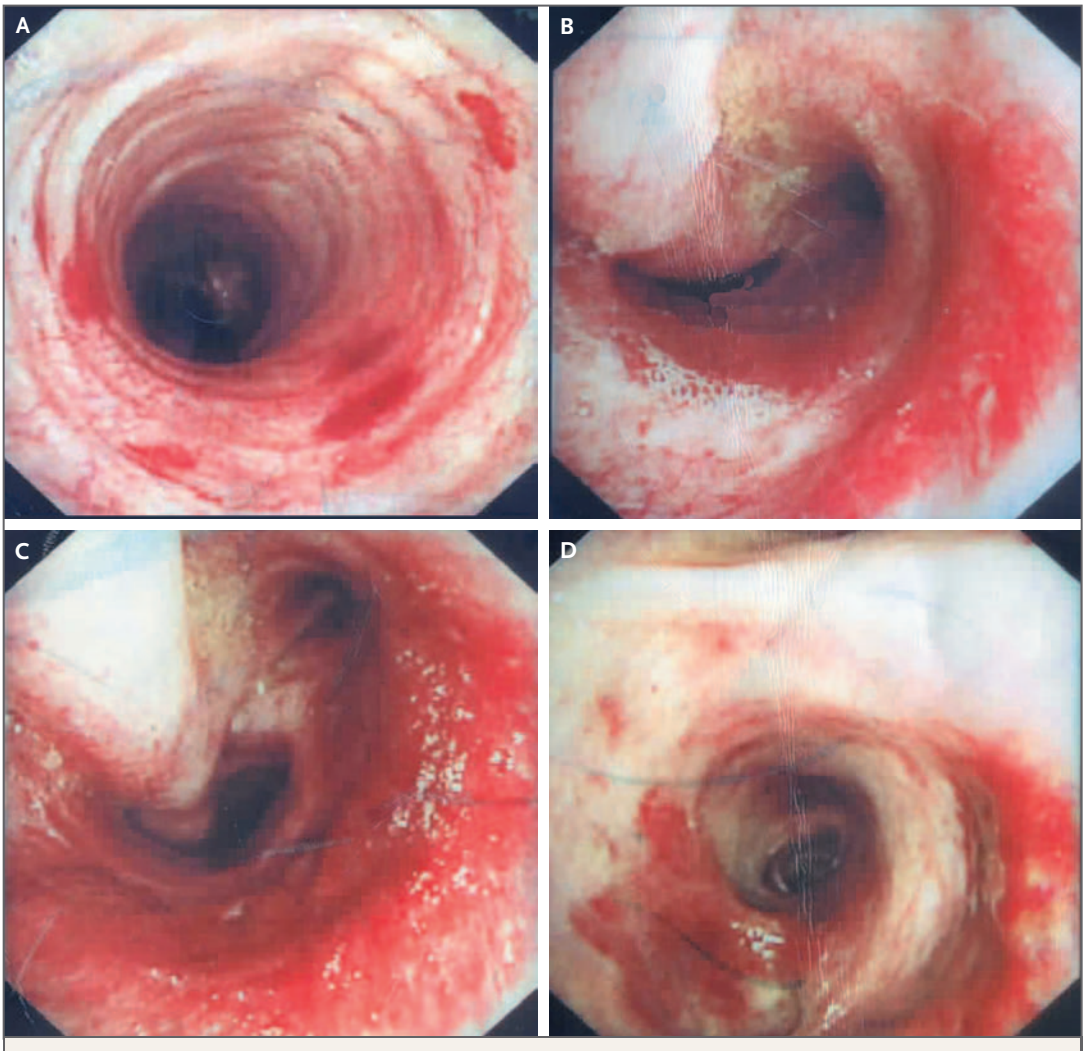

Figure 3. Bronchoscopic Evaluation of the Airways.

Shortly after admission, bronchoscopic evaluation of the airways was performed. Images from the procedure show macular red lesions parallel to the tracheal rings (Panel A). The lesions are concentrated at the tracheal carina (Panels B and C) and the left main bronchus (Panel D). The appearance of these lesions is consistent with a diagnosis of Kaposi's sarcoma.

maculopapular lesions that were concentrated at the tracheal carina (Fig. 3B and 3C) and the left main bronchus (Fig. 3D) were also noted. The carina was splayed, suggesting subcarinal lymphadenopathy. Endobronchial lesions of Kaposi's sarcoma are characteristically maculopapular, reddish-purple in color, concentrated at airway bifurcations, and parallel to the tracheal rings. Collectively, these features increased our clinical suspicion of pulmonary Kaposi's sarcoma.

We did not perform a biopsy because it is usually not indicated in lesions typical of Kaposi's sarcoma. A biopsy carries a 30% risk of clinically significant hemorrhage, and the diagnostic yield from bronchoscopic biopsies ranges from 26 to 60%, because of the patchy submucosal involvement.[20] On the basis of the characteristic bronchoscopic appearance of the lesions, in combination with the diagnosis of cutaneous Kaposi's sarcoma, our clinical diagnosis was pulmonary Kaposi's sarcoma, probably complicated by IRIS.

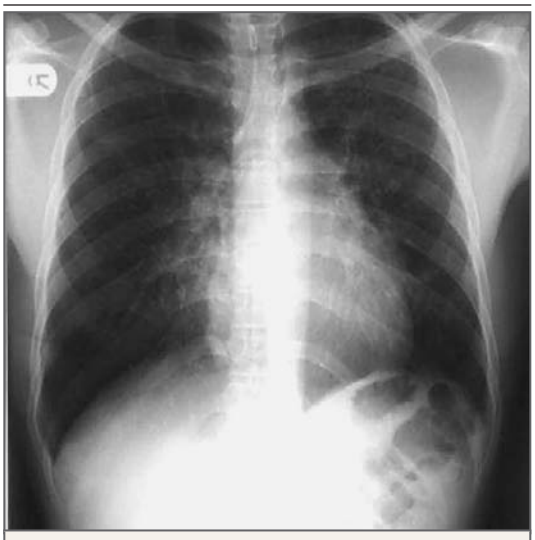

Figure 4. Chest Radiograph, 25 Weeks after Admission.
There is marked improvement, with almost complete resolution of the perihilar and peribronchovascular opacification. Bilateral reticular opacities in the upper and middle lung zones represent areas of fibrosis.

MANAGEMENT

Dr. Gandhi: The mainstays of treating widespread Kaposi's sarcoma in a patient with HIV infection, such as this patient, are ART and chemotherapy. All patients infected with HIV who have Kaposi's sarcoma should receive ART. After the initiation of ART, plasma HHV-8 levels decline because of an increase in HHV-8–specific immune responses.[16,21,22] The effect of ART on HHV-8, and thereby on tumorigenesis, most likely accounts for the dramatic drop in the incidence of Kaposi's sarcoma in the United States since effective ART was introduced there.[23] However, although ART alone may lead to regression of Kaposi's sarcoma, at times lesions may worsen, as seen in this case. Moreover, pulmonary Kaposi's sarcoma continues to be associated with a high mortality rate, even in the era of effective ART.[24]

Because the Kaposi's sarcoma in this patient worsened while he was receiving ART, additional therapy was clearly needed. Chemotherapeutic options include pegylated doxorubicin, liposomal daunorubicin, or paclitaxel.[25] Since these drugs are often not available in resource-limited settings, alternative agents are sometimes used, such as a combination of doxorubicin, bleomycin, and vincristine (as in this case) or oral etoposide.[26] Although anti–HHV-8 therapy with ganciclovir seems to protect patients with AIDS from the development of Kaposi's sarcoma,[27,28] there is no apparent role for such treatment once Kaposi's sarcoma occurs,[29] perhaps because HHV-8 is mainly in a latent form by the time the tumor is established.

A combination of ART and chemotherapy has an important role in some patients with HIV-associated Kaposi's sarcoma. The overall rate of survival among patients with Kaposi's sarcoma who receive ART alone is similar to the rate among those who receive ART plus chemotherapy. However, combination therapy has a higher response rate and progression-free survival rate than does ART alone.[14] Moreover, the rate of death among patients with Kaposi's sarcoma–associated IRIS is particularly high. Because of the widespread disease, symptomatic visceral involvement, and evidence of IRIS in this patient, a combination of ART and chemotherapy would be appropriate.

Dr. Moosa, would you tell us what happened with this patient?

Dr. Moosa: After the negative findings on microbiologic examination of the bronchoalveolar-lavage fluid, treatment for pneumocystis and tuberculosis was discontinued. The patient was started on chemotherapy with doxorubicin, bleomycin, and vincristine. He had a dramatic im-

provement in the first 3 days of chemotherapy. He was subsequently referred to another hospital for ongoing oncologic care. The patient continued to receive ART and maintained an undetectable viral load. The skin lesions began improving soon after the initiation of chemotherapy, with complete resolution by the sixth cycle (approximately 16 weeks after commencement).

Another chest radiograph obtained 25 weeks after chemotherapy was begun showed a return to baseline (Fig. 4). However, 7 weeks after completing the sixth cycle of chemotherapy (22 weeks after commencing chemotherapy), new skin lesions appeared on the right side of the chest anteriorly and on the right foot, with swelling of the left eyelid. The patient did not have any respiratory symptoms, and the chest radiograph remained normal. He was referred for further chemotherapy.

Within a month after recommencement of chemotherapy, all the lesions regressed. To date, the patient has received a total of nine cycles of chemotherapy and remains well, with no skin lesions. His last outpatient visit was approximately 9 months after presentation.

ANATOMICAL DIAGNOSIS

Kaposi's sarcoma complicated by the immune reconstitution inflammatory syndrome.

Rajesh T. Gandhi, M.D., was the guest editor for this case, which was presented at the Sixth Annual Workshop on Advanced Clinical Care–AIDS in Durban, South Africa (and organized by Drs. Henry Sunpath, Mahomed-Yunus S. Moosa, Francois Venter, and Rajesh T. Gandhi). The workshop was sponsored by the Harvard University Center for AIDS Research (NIH P30 AI060354), McCord Hospital (Durban), the University of KwaZulu-Natal, the South African HIV Clinicians Society, and the Department of Health, KwaZulu-Natal.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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