

Case Records of the Massachusetts General Hospital



Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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Case 5-2000

PRESENTATION OF CASE

A 35-year-old man was admitted to the hospital because of a painful abdominal mass and fever.

The patient was a native of West Africa who had traveled to the United States several times during the previous three years. He had been generally well except for an episode of typhoid fever five years before admission and multiple bouts of malaria over a number of years; the most recent bout occurred three months before admission. Thirty days before admission, he returned to this country. Three or four days later, fever developed, and his temperature rose to 39.4°C, with shaking chills and a vague headache, followed by constant pain in the left lower abdominal quadrant. Suspecting recurrent malaria, he began to take sulfadoxine–pyrimethamine and acetaminophen, but the pain worsened after another week, and he consulted a physician. A stool examination revealed no ova or other evidence of intestinal parasites; blood smears were negative for malaria. A computed tomographic (CT) scan of the abdomen showed extensive abdominal lymphadenopathy, with thickening of the wall of the adjacent small bowel.

The patient had no knowledge of a previous tuberculin skin test or of a test for the human immunodeficiency virus (HIV). He was referred to this hospital.

The patient had initially been a farmer but more recently had worked as a teacher. He had had unprotected heterosexual intercourse once five years before admission. His appetite was reduced, and he had lost 10 kg in weight during his illness. He did not have a history of use of alcohol or recreational drugs, tuberculosis or exposure to it, night sweats, cough, hemoptysis, homosexual intercourse, venereal infection, or use of non-Western medicine.

TABLE 1. HEMATOLOGIC LABORATORY VALUES.*

VARIABLE	VALUE
Hematocrit (%)	34.3
Mean corpuscular volume (μm^3)	76.0
White-cell count (per mm^3)	4,800
Differential count (%)	
Neutrophils	76
Band forms	17
Lymphocytes	2
Monocytes	4
Eosinophils	1
Platelet count (per mm^3)	475,000
Prothrombin time	Normal
Partial-thromboplastin time	Normal
Iron ($\mu\text{g}/\text{dl}$)	16.0
Iron-binding capacity ($\mu\text{g}/\text{dl}$)	280
Ferritin (ng/ml)	449†

*To convert the values for iron and iron-binding capacity to micromoles per liter, multiply by 0.1791.

†The normal range is 30 to 300 ng per milliliter.

TABLE 2. BLOOD CHEMICAL VALUES.*

VARIABLE	VALUE
Urea nitrogen	Normal
Creatinine	Normal
Protein (g/dl)	7.4
Albumin	2.4
Globulin	5.0
Bilirubin	
Total	Normal
Conjugated	Normal
Glucose (mg/dl)	163.0
Calcium (mg/dl)	8.1
Phosphorus (mg/dl)	2.5
Sodium (mmol/liter)	133.0
Potassium (mmol/liter)	3.9
Chloride (mmol/liter)	98.0
Carbon dioxide (mmol/dl)	25.5
Aspartate aminotransferase (U/liter)	82
Alanine aminotransferase	Normal
Lactate dehydrogenase (U/liter)	350.0
Alkaline phosphatase	Normal
Amylase	Normal
Lipase	Normal

*To convert the value for glucose to millimoles per liter, multiply by 0.05551. To convert the value for calcium to millimoles per liter, multiply by 0.250. To convert the value for phosphorus to millimoles per liter, multiply by 0.3229.



Figure 1. Radiograph of the Chest Showing Normal Findings.

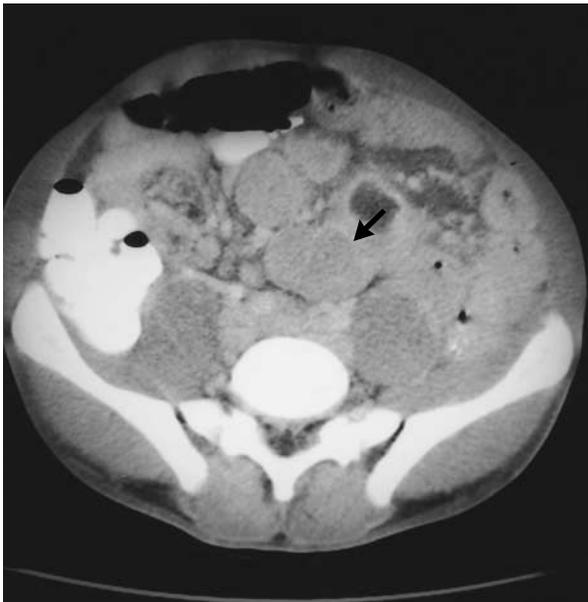


Figure 2. Abdominal CT Scan Showing an Enlarged Mesenteric Lymph Node with Low Attenuation at Its Center (Arrow).

The temperature was 37°C, the pulse was 80, and the respirations were 20. The blood pressure was 130/70 mm Hg.

On physical examination, the patient appeared well. Palpation revealed shotty submental, cervical, axillary, and inguinal lymph nodes, which had reportedly been

palpable for many years. No thrush was seen. The lungs were clear. A grade 2 systolic murmur was heard at the left sternal border and apex. On abdominal examination, a vaguely outlined, firm mass, 8 cm in diameter, was palpated to the left of the umbilicus; it was immobile, tender, and lobulated. A stool specimen was negative for occult blood.

The urine was positive (+) for urobilinogen and positive (trace) for protein. Laboratory tests were performed (Tables 1 and 2).

A radiograph of the chest (Fig. 1) showed no abnormalities. A CT scan of the abdomen (Fig. 2) showed multiple, enlarged mesenteric lymph nodes, several of which had centers of low attenuation. There was mild-to-moderate thickening of the wall of the small bowel but without evidence of obstruction.

A diagnostic procedure was performed.

DIFFERENTIAL DIAGNOSIS

DR. JOHANNA P. DAILY*: May we review the imaging studies?

DR. RONALD S. ARELLANO: The film of the chest (Fig. 1) shows no abnormalities. The abdominal CT scan obtained at this hospital (Fig. 2) shows enlarged mesenteric lymph nodes, many of which have central areas of low attenuation. There is slight thickening of the small-bowel wall but without evidence of obstruction. The liver, spleen, pancreas, and genitourinary system appear normal.

DR. DAILY: It is critical to rule out life-threatening infections in a febrile person who has lived or traveled in the tropics. Malaria, typhoid fever, meningococcal infection, rickettsial disease, and hemorrhagic fever, among other infections, require timely diagnosis and treatment. Travelers should be questioned about exposure to animals and bodies of water, the quality of their water and food, and ingestion of unpasteurized products. Vaccination and prophylaxis against malaria may alter the differential diagnosis, although malaria can develop despite prophylaxis. Finally, the prevalence of a disease among persons who travel to the tropics may differ from the prevalence among residents of the tropics, who have a longer period of exposure. This patient had lived in West Africa most of his life, and we can assume that he had been exposed to tuberculosis, which remains endemic in many parts of Africa. He became febrile shortly after his return from the tropics, and his initial nonspecific symptoms are consistent with the presence of malaria. If a person with such symptoms remains febrile, blood cultures should be performed to rule out bacteremia, and blood smears for malaria should be repeated.

The diagnosis is particularly challenging in patients from the tropics, since they may be infected with

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multiple pathogens. Many of these agents are rarely or never found outside the tropics. Coinfection with HIV, which may alter or accelerate the course of concomitant diseases, should be considered in this case because of the high prevalence of HIV infection in parts of Africa. It has been estimated that more than 20 million HIV-infected people live on the African continent.¹ Until recently, the rates of HIV infection were lower in West Africa than in other parts of Africa, where an estimated 25 percent of the adult population is infected. However, infection rates have been increasing in West Africa; in parts of Nigeria, for example, an estimated 4.1 percent of adults are infected.²

The most striking feature of this patient's illness is the extensive abdominal lymphadenopathy. Before focusing on the differential diagnosis, I shall consider the possibility of concomitant disease, which is suggested by the lymphopenia and chronic, diffuse, shotty lymphadenopathy, and its relation to the illness for which the patient sought medical care.

Many disorders can result in lymphopenia. In a study that antedated the HIV epidemic,³ a review of 178 cases of lymphopenia (defined as a lymphocyte count of less than 1000 per cubic millimeter) showed that the most common underlying disease was cancer (in 42 percent of cases), primarily colon cancer or lymphoma, for which some patients were receiving cytotoxic or radiation therapy. No underlying disease was detected in 22 percent of the patients. Infections and collagen vascular diseases were encountered less frequently than cancer. Tuberculosis can sometimes result in marked lymphopenia, with a specific decrease in CD4+ and CD8+ T cells. In three patients with active tuberculosis and lymphocyte counts of less than 900 per cubic millimeter, the lymphopenia resolved completely after the administration of antituberculosis therapy alone.⁴ These patients had negative serologic tests for HIV type 1 (HIV-1), HIV type 2 (HIV-2), and human T-cell lymphotropic virus type I (HTLV-I); both CD4+ and CD8+ T-cell counts were low, with the preservation of a normal ratio of CD4+ to CD8+ T cells. In contrast, in patients with HIV infection, this ratio becomes inverted.

The profound lymphopenia in this patient suggests the presence of HIV-1 infection, which is the most prevalent retrovirus in parts of West Africa, such as Nigeria. Other retroviruses predominate in other areas.⁵ For example, HIV-2 is the predominant strain in areas of Guinea-Bissau.⁶ HIV-1 group O is found primarily in West Africa, but its prevalence is low, and unlike other HIV-1 groups and HIV-2, it is not detected with standard assays. HIV-1 group O infection also results in a reduced number of CD4+ T cells and the development of opportunistic infections. Specialized testing is required to identify this group of viruses.⁵

The natural history and complications of HIV-1 infection have been studied extensively in Western countries, but much less is known about those aspects of

HIV infection in tropical areas. In a study of HIV-infected patients in rural Uganda, the wasting syndrome was the most common manifestation of late-stage disease (in 46 percent of patients), followed by esophageal candidiasis (in 33 percent), chronic herpes simplex virus infection (in 13 percent), and Kaposi's sarcoma (in 13 percent).⁷ Other studies have shown a strong association between HIV infection and tuberculosis, probably because of the high prevalence of tuberculosis in Africa.^{8,9} Patients who have tuberculosis alone may present with a wasting disease, and antituberculosis therapy is often given to such patients.¹⁰ In a prospective study of abdominal pain in patients in South Africa who had HIV infection and a CD4+ T-cell count of less than 200 per cubic millimeter,¹¹ disseminated tuberculosis was diagnosed most frequently (in 32 percent of the patients). Abdominal lymphadenopathy, ascites, and abscesses were strongly associated with tuberculosis. Most of the patients did not have other coexisting opportunistic infections; only 5 percent had atypical mycobacterial infection. In Africa, unlike the United States and Europe, *Pneumocystis carinii* pneumonia has only rarely been reported as a complication of HIV infection.⁷

Infection with HIV-2, which is found predominantly in West Africa, may also result in lymphopenia. HIV-2 infection causes a slower depletion of CD4+ T cells than does HIV-1 infection, with less effect on morbidity and mortality.^{12,13} In some studies, however, HIV-2 infection has been closely associated with active tuberculosis and the opportunistic infections to which hospitalized patients are susceptible.^{9,14}

Although it is unclear whether this patient's chronic generalized, peripheral, shotty lymphadenopathy was caused by a pathologic process, infection with HIV-1, HIV-2, or HTLV-I could account for this finding. Patients infected with HTLV-I are typically asymptomatic, but in rare cases, the virus results in leukemia, lymphoma, or tropical spastic paraparesis.¹⁵ In Africa, its seroprevalence rates vary widely according to the region. The prevalence in adults is estimated to range from 0.5 to 1 percent in most African countries and up to 12 percent in specific locations in West Africa. In one very small, population-based cohort study in West Africa, HTLV-I infection did not affect survival during a follow-up period of six years.¹⁶

Other causes of peripheral lymphadenopathy in West Africa, reported before the HIV epidemic began, include reactive hyperplasia, metastatic cancer, lymphoma, tuberculosis, and toxoplasmosis; Hodgkin's disease and filarial granulomas have also been reported.¹⁷ One of the most common extrapulmonary manifestations of tuberculosis is peripheral lymphadenopathy.

HIV infection is associated with an increase in cases of active tuberculosis and, in some parts of the world, with increased lymph-node involvement.¹⁸ To assess the effect of the HIV epidemic on superficial

lymph nodes, a study conducted in Lusaka, Zambia, reviewed the histologic findings in specimens from all lymph-node biopsies performed in 1981, as compared with those performed in 1990; in addition, a cohort of patients undergoing lymph-node biopsy in 1990 was tested for HIV infection.¹⁹ The 1990 specimens were much more likely than the 1981 specimens to show evidence of tuberculous lymphadenitis, and in the group of patients who underwent HIV testing, 88 percent of those with tuberculous lymphadenitis had positive tests. Also, findings suggestive of the diagnoses of HIV lymphadenopathy and Kaposi's sarcoma of the lymph nodes were more common in 1990 than in 1981.

The most striking finding in this patient is marked abdominal lymphadenopathy, which is probably due to either cancer or infection. If the correct diagnosis is cancer, the extensive lymphadenopathy and the absence of evidence of a primary tumor elsewhere suggest either lymphoma or Kaposi's sarcoma. In a review of cases of lymphoma reported between 1979 and 1988 in Nigeria, non-Hodgkin's lymphoma and Hodgkin's lymphoma accounted for 68 and 32 percent of the cases, respectively. Painless peripheral lymphadenopathy, particularly involving the cervical lymph nodes, was the most frequent clinical presentation. Burkitt's lymphoma was diagnosed primarily in children, who typically presented with an abdominal or pelvic tumor.²⁰ In another study from Nigeria, Burkitt's lymphoma was the most common diagnosis, followed by lymphosarcoma, leukemia, and Hodgkin's disease.²¹ Burkitt's lymphoma was originally described in African children who presented with large facial tumors. It is an aggressive tumor of B-cell lineage, has a characteristic t(8;14) translocation, and is related to the Epstein-Barr virus. Cases are generally found in a restricted geographic distribution in Africa that correlates with the regions of holoendemic malaria.²²

Lymphomas related to HIV infection in Western countries are typically high-grade non-Hodgkin's lymphomas of B-cell lineage. Large abdominal lymph nodes are frequently seen, often with associated constitutional symptoms. Extranodal disease, particularly bowel involvement, is common.²³ Splenomegaly may also be present. In a review of patients who had lymphoma in association with the acquired immunodeficiency syndrome (AIDS), 90 percent of the patients with Hodgkin's disease and 84 percent with non-Hodgkin's lymphoma had splenomegaly.²⁴ In a case-control study conducted in South Africa between 1992 and 1995, there was a strong association between HIV infection and non-Hodgkin's lymphoma, although it was not as strong as that reported in the United States.²⁵ Patients with rapidly growing lymphoma may have lymph nodes with low-density centers.

Kaposi's sarcoma, which is associated with human herpesvirus 8 infection, can also cause bulky lymphadenopathy. This tumor was initially reported in elderly

men living along the Mediterranean Sea who had indolent skin lesions on their legs, with a minimal effect on their survival. A more aggressive form, known as the endemic or African variant, involves lymphadenopathy, in which there is painless replacement of lymph nodes by tumor. Lymphadenopathic Kaposi's sarcoma predominantly affects children, who often have no skin lesions, unlike young adults with the disease.²⁶

Epidemic Kaposi's sarcoma, which is associated with HIV infection, is similarly aggressive, often involves the lymph nodes and viscera,²⁷ and can result in marked mesenteric and retroperitoneal lymphadenopathy. However, the enlarged lymph nodes do not have focal low-density areas.²⁸ HIV-related Kaposi's sarcoma typically involves the skin, although it can be confined to the viscera.²⁹ Also, Kaposi's sarcoma is the most common form of HIV-related gastrointestinal neoplasia, and a combination of gastrointestinal and lymph-node disease is not unusual. The tumor can develop in any part of the gastrointestinal tract and typically causes thickening of the bowel wall.³⁰

I shall limit my discussion of infections causing bulky lymphadenopathy to mycobacterial and fungal infections. Disseminated histoplasmosis may occur in immunocompromised hosts and often involves the gastrointestinal tract; oral ulcers are the most common manifestation. Distal to the oropharynx, the terminal ileum and proximal colon are the most common sites of involvement. Abdominal lymph nodes are often enlarged, and in patients with acute disseminated disease, they may be markedly enlarged.³¹ Gastrointestinal histoplasmosis differs from other forms of disseminated histoplasmosis in that pulmonary symptoms and fever may be absent. In a review of 77 cases, only 31 percent of the patients had fever, and only 32 percent had peripheral lymphadenopathy.³¹ In a review of CT findings in 16 patients with HIV infection and disseminated histoplasmosis, 12 patients had enlarged abdominal lymph nodes, with central areas of low density in 5. The predominant pulmonary radiographic findings were diffuse nodular or reticulonodular infiltrates, although seven patients had normal findings.³² In contrast to the high incidence of disseminated histoplasmosis in HIV-1-infected patients in parts of the United States and Latin America, few cases of coinfection have been reported in African patients.^{33,34} This distribution may reflect differences between *Histoplasma* var. *duboisii*, which is found in Africa, and *H. capsulatum*, which is endemic in areas surrounding the central river valleys of the Western hemisphere. In rare cases, cryptococcal infection can give rise to bulky lymphadenopathy.³⁵ Other disseminated fungal infections, such as coccidioidomycosis, blastomycosis, and paracoccidioidomycosis, have been reported in HIV-infected patients, and they may cause abdominal lymphadenopathy, but the pathogens are more likely to be found in parts of the world other than Africa.

Finally, extrapulmonary mycobacterial disease, particularly tuberculosis, must be considered because of the patient's residence in an area where it is endemic. The prevalence of intestinal tuberculosis has decreased since the beginning of the 20th century. In an early study, gastrointestinal involvement was found in 69 percent of persons with fatal pulmonary tuberculosis.³⁶ The subsequent decline in extrapulmonary mycobacterial disease may be related to public health measures, including the routine pasteurization of milk, or to earlier diagnosis and treatment. One mechanism of mycobacterial bowel infection is ingestion of the organisms. *Mycobacterium bovis* infects many animals, including cattle, and can be present in their milk, causing primary intestinal tuberculosis in humans who ingest it. Widespread pasteurization of milk has virtually eliminated this disease. Ingestion of sputum containing *M. tuberculosis* or hematogenous seeding during primary infection can also cause gastrointestinal disease. Although tuberculosis can affect any portion of the gastrointestinal tract, the ileocecal region is involved most frequently, possibly because of the concentration of lymphoid tissue in that area.

Mesenteric lymphadenitis has been reported as the principal manifestation of tuberculosis. In a study conducted before the HIV epidemic, 10 of 59 patients in South Africa who had gastrointestinal tuberculosis presented with mesenteric lymphadenitis. None of the patients had pulmonary involvement; seven had palpable masses.³⁷ In a review of 182 cases of abdominal tuberculosis in India,³⁸ only 42 percent of the patients had fever, and 11 percent presented with mesenteric lymphadenopathy. Masses were detected in patients with hyperplastic ileocecal tuberculosis, mesenteric lymphadenopathy, and strictures of the small or large intestine. Of the 86 patients for whom chest radiographs were available, only 24 had evidence of active or inactive pulmonary disease. Thus, the absence of abnormalities on a chest film does not eliminate tuberculosis as a possible diagnosis. A CT scan may demonstrate enlarged mesenteric lymph nodes with low-density centers, as well as mesenteric thickening, omental masses, and ascites.³⁹ Pulmonary disease, fever, weight loss, and abdominal pain are often absent in patients with gastrointestinal tuberculosis, making it difficult to establish the diagnosis.^{38,40}

HIV infection has contributed to the increase in cases of active tuberculosis in many parts of the world. Coinfection varies greatly according to the geographic location. For example, in Nigeria only 6.1 percent of patients with tuberculosis were infected with HIV, as compared with 80 percent in other parts of Africa.^{41,42} CT findings in coinfecting patients included central necrosis of lymph nodes in 31 of 32 HIV-positive patients with abdominal tuberculosis; in contrast, ascites and peritoneal and omental thickening were more prominent in HIV-negative patients. The extensive

mesenteric, omental, and peripancreatic lymphadenopathy seen in this patient has also been reported in coinfecting patients; other findings have included splenomegaly, hepatomegaly, ascites, bowel involvement, and intrasplenic and intrahepatic masses.⁴³

Infection with *M. avium* complex can give rise to bulky abdominal lymphadenopathy late in the course of HIV infection, when the CD4+ T-cell count has dropped to less than 50 per cubic millimeter.⁴⁴ Dissemination of *M. avium* complex infection may involve the blood, liver, spleen, and lymph nodes,⁴⁵ with symptoms of fever, weight loss, and less often, diarrhea. Laboratory markers of the infection include severe anemia and in many cases an elevation of the alkaline phosphatase level. CT scans may also show enlarged lymph nodes with low-density centers.²⁴ In the United States, infection with *M. avium* complex occurs in up to 43 percent of patients who have a marked reduction of CD4+ T cells,⁴⁶ but the infection is rare in Africa. In a series of 50 HIV-infected patients in Uganda who had severe illness with chronic weight loss, none had blood cultures that were positive for *M. avium* complex.⁴⁷

Although there are similarities in the manifestations of *M. avium* complex infection and tuberculosis, some features differ. Disseminated tuberculosis occurs earlier in the course of CD4+ T-cell depletion in HIV-infected patients than does infection with *M. avium* complex. In a review of patients with HIV infection and mycobacterial disease, all the patients infected with *M. avium* complex had an AIDS-defining illness at or before the time that infection with *M. avium* complex was diagnosed. In contrast, only 34 percent of those with tuberculosis had an AIDS-defining illness when the tuberculosis was diagnosed. The two groups had similar symptoms and physical findings, but CD4+ T-cell counts were lower in the patients infected with *M. avium* complex.^{48,49}

In summary, I favor the diagnosis of tuberculous lymphadenitis because of its prevalence in this patient's native country. Although tuberculosis alone can account for the findings, I would test for HIV infection because of the high frequency of coinfection. A definitive diagnosis has to be made rapidly to allow early initiation of therapy. I would recommend a CT-guided, percutaneous needle biopsy of an enlarged lymph node for histopathological examination, special stains, and mycobacterial and fungal cultures.

DR. NANCY L. HARRIS: Does the disease cause diarrhea or other bowel symptoms?

DR. DAILY: Surprisingly few patients have a change in their bowel habits.

DR. ROBERT H. SCHAPIRO: As a gastroenterologist who saw this patient, I was struck by the extensive lymphadenopathy, which resulted in a confluent mass in the left side of the abdomen. I favored the diagnosis of lymphoma over that of tuberculosis.

CLINICAL DIAGNOSIS

? Lymphoma involving the abdominal lymph nodes.

DR. JOHANNA P. DAILY'S DIAGNOSES

Tuberculous lymphadenitis.

? Coinfection with the human immunodeficiency virus.

PATHOLOGICAL DISCUSSION

DR. SAHA SADEGHI: A specimen from a fine-needle aspiration biopsy of the abdominal mass revealed aggregates of histiocytes with foamy, granular eosinophilic cytoplasm on a background of fibrous tissue and scattered mononuclear cells (Fig. 3). An acid-fast stain revealed abundant, variably beaded acid-fast bacilli within the histiocytes (Fig. 4). There were no well-formed granulomas, which are typically absent in patients with AIDS, indicating a poor immunologic response to the mycobacteria.⁵⁰ Culture of the specimen grew *M. avium* complex (Fig. 5). A serologic test for HIV was positive; the result was confirmed by a Western blot assay. The ratio of CD4+ to CD8+ T cells was inverted (0.03), with a CD4+ count of 2 cells per cubic millimeter.

M. avium complex is a complex of two closely related organisms, *M. avium* and *M. intracellulare*. *M. avium* was reported to infect chickens in 1890 and was referred to as the avian tubercle bacillus.⁵⁰ *M. intracellulare* was first cultured in 1969 from the sputum of patients with tuberculosis at the Battey State Hospital in Rome, Georgia; it became known as the Battey bacillus.⁵⁰ *M. avium* complex organisms are ubiquitous; they have been isolated throughout the world from soil, house dust, freshwater plants, animal feed and bedding, chickens, and other birds. Human infection occurs mainly through the ingestion of contaminated water or food or the inhalation of aerosols. Human-to-human transmission appears to be minimal. *M. avium* complex organisms grow slowly and are nonphotochromogenic; they form smooth, cream-colored colonies (Fig. 5).⁵¹ In contrast, *M. tuberculosis* organisms form flat, dry, rough colonies (Fig. 6). The more virulent strains of *M. avium* complex, however, tend to be rough, and increasingly yellow colonies have been reported in patients with AIDS.⁵²

In contrast to other nontuberculous mycobacteria, *M. avium* complex can possess plasmids, which may contribute to their virulence.⁵⁰ Almost all *M. avium* complex strains isolated from patients with AIDS have plasmids.⁵⁰

A single positive blood culture is considered diagnostic of disseminated *M. avium* complex infection.⁴⁵ Positive cultures of bone marrow or abdominal fluid also indicate dissemination of disease.⁴⁵ Positive cultures of respiratory tract or gastrointestinal specimens, however, are not diagnostic of dissemination and may reflect colonization by the mycobacteria.

Since the drug regimen used for *M. avium* complex

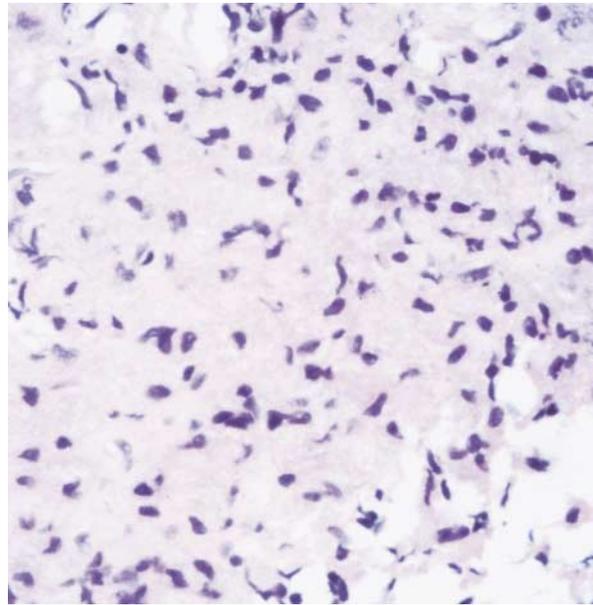


Figure 3. Specimen of the Abdominal Mass Containing Aggregates of Histiocytes with Foamy, Granular Eosinophilic Cytoplasm (Hematoxylin and Eosin, $\times 250$).

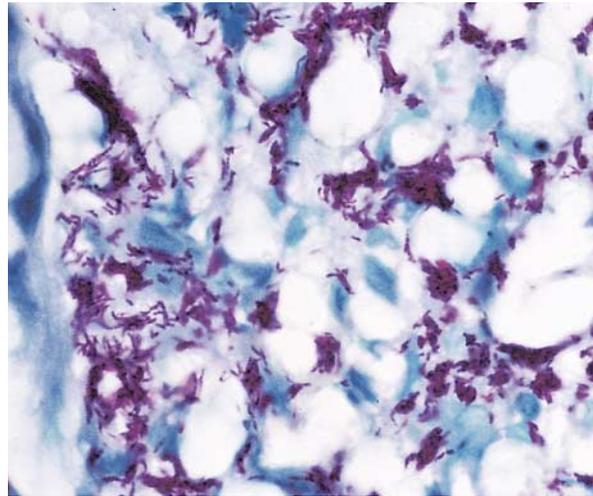


Figure 4. Histiocytes Packed with Acid-Fast Bacilli (Acid-Fast Stain, $\times 500$).

infection differs from that used for *M. tuberculosis* infection, newer, faster techniques for culture and species identification have been developed, reducing the turnaround time from the usual 5 to 10 weeks to 2 to 4 weeks.

DR. EUGENE J. MARK: After the diagnosis was made, this patient was seen by Dr. Basgoz.

DR. NESLI BASGOZ: The patient received clarithromycin, ethambutol, and clofazimine for *M. avium*

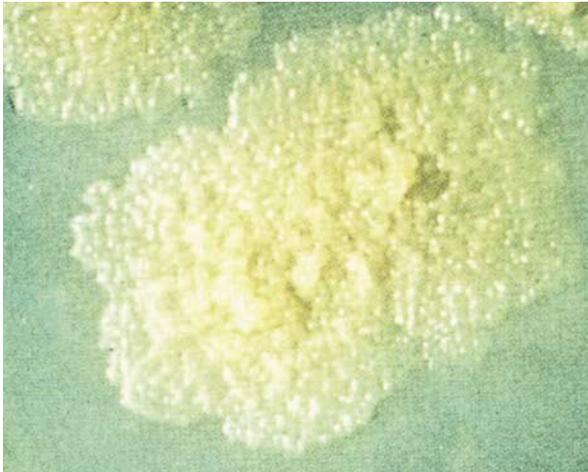


Figure 5. Smooth, Cream-Colored Colonies of *Mycobacterium avium* Complex.

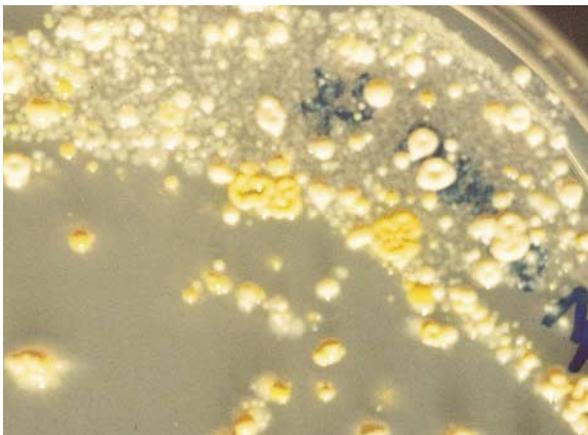


Figure 6. Flat, Dry, Rough Colonies of *Mycobacterium tuberculosis* in a Specimen from Another Patient.

complex infection. Highly active antiretroviral therapy was not given at this time because of concern about additional toxicity and clinical worsening during the phase of acute immune reconstitution that occurs rapidly with this regimen. The patient's condition improved, and he was discharged. Subsequent examination in the outpatient clinic revealed diminished tenderness and a very slow decrease in the size of the mass. Six weeks after he began the mycobacterial therapy, his blood cultures were negative, and his HIV RNA level had fallen from 750,000 copies per milliliter at the time of the diagnosis to 62,000 copies. Two weeks later, he began receiving stavudine, lamivudine, and indinavir for his HIV infection. Within two weeks after starting these drugs, he had increased abdominal pain and tenderness in the region of the mass. However, he did not have a fever, and

there was no obvious increase in the size of the mass. Therefore, both types of therapy were continued. The patient has since returned to his native country.

Dr. Daily, if you had seen the patient after the detection of mycobacteria but before the identification of *M. avium* complex, how would you have treated him?

DR. DAILY: This question highlights the importance of rapid identification of the mycobacterial species. Some clinical laboratories can identify mycobacterial species on the basis of polymerase-chain-reaction testing of pathological specimens, and I would have pursued this approach. Alternatively, a five-drug regimen of isoniazid, rifampin, pyrazinamide, ethambutol, and clarithromycin would adequately cover both *M. tuberculosis* infection and *M. avium* complex infection pending the results of culture. Rifabutin would be the preferred type of rifamycin to administer if protease-inhibitor therapy were also started. I agree with the delay of highly active antiretroviral therapy, since it would certainly have worsened the lymphadenitis.

DR. MARK: Dr. Daily, does the extensive lymphadenopathy in this case indicate a poor prognosis?

DR. DAILY: The burden of mycobacterial disease is a less important prognostic indicator than the patient's ultimate response to antiretroviral therapy. It is critical that the maximal antiretroviral effect be achieved to allow immune reconstitution.

ANATOMICAL DIAGNOSES

Disseminated *Mycobacterium avium* complex infection.

Acquired immunodeficiency syndrome.

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