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# **REVIEW ARTICLES**

# Cavitary Pulmonary Lesions in Patients Infected with Human Immunodeficiency Virus

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The differential diagnosis of cavitary pulmonary lesions in individuals infected with human immunodeficiency virus (HIV) is broad, especially in patients with advanced disease. In patients with *Pneumocystis carinii* pneumonia, cavitation is an uncommon manifestation of a common disease. It is unusual in patients with pulmonary cryptococcosis, coccidioidomycosis, and histoplasmosis but occurs frequently in patients with invasive pulmonary aspergillosis. In patients with pulmonary tuberculosis, cavities are more common during earlier stages of HIV disease, when cellular immunity is relatively preserved. *Mycobacterium avium* complex is an uncommon cause of lung disease and infrequently produces cavities. However, *Mycobacterium kansasii*, is often associated with cavitation. Cavities can complicate any bacterial pneumonia and are especially common with pneumonia due to *Pseudomonas aeruginosa*, *Nocardia asteroides*, and *Rhodococcus equi*. Noninfectious causes of cavitary lesions are rare, but cavitary lesions caused by pulmonary Kaposi's sarcoma and non-Hodgkin's lymphoma have been reported. Because of the broad differential diagnosis is essential.

HIV infection results in a progressive cellular and humoral immunodeficiency that leads to the development of a wide variety of opportunistic infections and malignancies. Pulmonary complications—including opportunistic infections, malignancies, and idiopathic processes—are a prominent feature of HIV infection. Up to 65% of AIDS-defining illnesses are diseases involving the lung [1]. The variability and nonspecificity of the clinical and radiographic manifestations of HIV-associated pulmonary processes frequently complicate the diagnosis of HIV-associated lung disease.

Cavitation can occur as a result of numerous HIV-associated pulmonary complications. Pathologically, a pulmonary cavity is a gas-filled space, with or without fluid, contained within a zone of pulmonary consolidation or within a mass or nodule that is produced by the expulsion of a portion of the lesion via the bronchial tree [2]. It is the end result of a pathological process leading to tissue necrosis. Cavitation is rarely detectable by physical examination but is discovered on chest roentgenograms, where it is manifested by a translucency within the lung parenchyma that is surrounded by a complete wall. Important radiographic features include location, shape, size,

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© 1996 by The University of Chicago. All rights reserved. 1058–4838/96/2204–0012\$02.00 wall thickness, presence or absence of fluid or other contents, presence of satellite lesions, and appearance of the surrounding lung tissue. These features are helpful, but not diagnostic, in determining the cause of the cavity. For example, the cavity created by a lung abscess typically has a thin, smooth wall and contains a fluid level, while a bronchogenic tumor tends to form a more eccentric-shaped cavitation with a thicker, irregular wall [3]. Cavities should be distinguished from cystic changes; cystic changes are produced by progressive rupture of the alveolar walls, which creates abnormally large air spaces [4]. Pulmonary cysts have thin walls, the rupture of which may result in pneumothorax.

The differential diagnosis of acquired cavitary lesions in immunocompetent individuals includes neoplasms, both primary and metastatic; infections, including those caused by bacteria, mycobacteria, fungi, and parasites; collagen-vascular diseases, such as Wegener's granulomatosis; traumatic processes; and vascular entities, such as a pulmonary embolus with infarction [5]. While HIV-infected individuals may have any of the conditions known to cause cavities in immunocompetent hosts, certain infections and malignancies are made more likely by HIV infection. The following is a review of the disease processes causing cavitary changes in patients with HIV infection.

# **Protozoal Infections**

# Pneumocystis carinii

*P. carinii* is discussed here under its traditional category as a protozoan, although recent data suggest that it may be

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taxonomically closer to a fungus [6]. Despite the widespread use of prophylaxis, P. carinii remains the most common serious opportunistic pathogen in HIV-infected patients. In the Multicenter AIDS Cohort Study [7], P. carinii pneumonia (PCP) was the AIDS-defining diagnosis for 43% of patients. Patients often present subacutely with progressive fever, nonproductive cough, dyspnea, and weight loss, and abnormalities in gas exchange are common [8]. The radiographic manifestations of PCP vary widely. Although diffuse bilateral reticulonodular infiltrates are the most common finding, patients may also present with localized alveolar infiltrates, cystic lesions, and spontaneous pneumothoraces [9-12]. These latter two findings appear to be associated with aerosolized pentamidine prophylaxis [13-15]. Normal chest radiographs have been described for as many as 39% of patients with PCP [10]. A number of atypical pathological manifestations of PCP have been described, including diffuse alveolar involvement, bronchiolitis obliterans, localized granulomas, and cavities [16].

Atypical manifestations of PCP, including cavitation, were recognized even before the AIDS era [17, 18]. Though uncommon, there have been reports of cavitary nodules in HIVinfected patients with PCP, including patients with cavities in the setting of diffuse infiltrates [19, 20], patients with nodular infiltrates that subsequently became cavitary [21], and patients with isolated cavities without surrounding infiltrates [22]. Solitary cavities are more common than multiple cavities and are distinguished from PCP-associated cysts by the presence of thicker walls [23]. Ferré and colleagues [24] reviewed 23 cases of PCP with cavitation that were reported over the past 10 years and reported an additional six cases. Upper-lobe cavities were present in 21 of the 29 patients, and in 10 of these cases, stains of bronchoalveolar lavage (BAL) specimens were negative for P. carinii. They concluded that the presence of a cavitary lesion should lower the threshold for performing transbronchial biopsy in addition to BAL. As with cystic lesions, the presence of cavities in patients with PCP may increase the risk of pneumothorax due to spontaneous rupture [25].

Although it is an infrequent manifestation of pneumocystic infection, a cavitary infiltrate should prompt consideration of PCP, since it continues to be such a common problem in HIVinfected individuals. Atypical radiographic manifestations of PCP, including cavitary lesions, have been associated with aerosolized pentamidine prophylaxis [13–15, 20], which has also been associated with a lower diagnostic yield of both examination of an induced sputum specimen and BAL in some series [26, 27]. Therefore, while examination of an induced sputum specimen is appropriate as a first diagnostic procedure, bronchoscopy, usually with both BAL and transbronchial biopsy, may frequently be necessary to make the diagnosis when cavities are present.

#### Toxoplasma gondii

T. gondii, an obligate intracellular protozoan, is the most common cause of CNS mass lesions in patients with AIDS as well as a cause of opportunistic pneumonia [28, 29]. The geographic variation in the prevalence of *T. gondii* infection and in the incidence of toxoplasmosis is considerable. In France, where exposure to *T. gondii* is widespread, seven (4%) of 169 HIV-infected patients undergoing bronchoscopy were found to have pulmonary toxoplasmosis [30]. In contrast, only one of 441 patients with AIDS-related pneumonia was found to have toxoplasmosis in a study carried out in the United States [31].

Patients with toxoplasmic pneumonitis typically present with dyspnea, nonproductive cough, and fever [32]. The most common radiographic findings for patients with toxoplasmic pneumonia are bilateral interstitial infiltrates or coarse nodular infiltrates [29, 32]. Although cavitation has been described in a patient without underlying illness [32], to date cavitary infiltrates have not been described in HIV-infected patients with pulmonary toxoplasmosis [28, 32-34].

# **Fungal Infections**

# Cryptococcus neoformans

Cryptococcosis, a common late manifestation of HIV infection, usually presents with meningitis; however, the lungs represent one of the most common sites of extraneural involvement. Approximately one-quarter to one-third of patients with cryptococcal disease present with pulmonary complaints, and as many as two-thirds of patients without CNS infection present with cough and dyspnea [35, 36]. Only 18% of patients with documented meningitis have pulmonary symptoms due to *Cryptococcus* [36]. Because the portal of entry of *C. neoformans* is the lung, a far greater number of patients probably have clinically silent pulmonary infection.

Cryptococcal pneumonitis in immunocompetent patients or patients who are immunocompromised from causes other than HIV infection typically presents with poorly defined masses or consolidated infiltrates [37–40]. Cavitation, which is present in 10% to 22% of patients in some series, occurs most frequently in patients who are immunocompromised secondary to glucocorticoid administration or chemotherapy [37–39, 41].

In contrast, HIV-infected patients typically present with an ill-defined interstitial infiltrate resembling that associated with PCP [36, 42]. Other radiographic manifestations include alveolar infiltrates, solitary lobar infiltrates, mediastinal masses, and pleural effusions [43–45]. Cavitation is uncommon [42, 46] but has been described in small numbers of patients in several series and case reports [19, 36, 42, 47–49].

Most AIDS-related cases of cryptococcosis are caused by *C. neoformans* variety *neoformans* (serotypes A and D). An HIV-infected individual was found to have a cavitary pulmonary nodule due to *C. neoformans* variety *gattii* (serotype B), a variant of *C. neoformans* associated with Australian eucalyptus trees [50].

#### Histoplasma capsulatum

Histoplasmosis is an opportunistic complication of HIV infection; it occurs as a result of new infection or reactivation of latent infection with *H. capsulatum*, which is usually acquired in the valleys of the Ohio and Mississippi Rivers (the areas of the highest level of endemicity in the United States). In immunocompetent hosts acute histoplasmosis is usually a benign, self-limiting illness. Chest roentgenograms of symptomatic patients may even be normal. More commonly, single or multiple areas of pneumonitis are seen, usually in the lower lobes, often with ipsilateral hilar adenopathy. Patients with underlying chronic lung disease may have progressive pulmonary histoplasmosis, which typically presents with clinical and radiographic manifestations similar to those of pulmonary tuberculosis. Upper-lobe cavitary lesions are common [51, 52].

Individuals with advanced HIV infection and histoplasmosis frequently present with widespread dissemination and multisystem involvement. In fact, most cases of disseminated histoplasmosis today occur in HIV-infected individuals [53, 54]. Although HIV-infected patients with disseminated histoplasmosis frequently have radiographic evidence of pulmonary involvement, constitutional symptoms are usually more prominent than respiratory complaints [54]. Patients with pulmonary involvement typically present with diffuse infiltrates, which can be nodular or interstitial, although localized infiltrates also occur. Cavitary infiltrates can occur [55] but are uncommon. In three series involving 155 HIV-infected patients with disseminated histoplasmosis [54, 56, 57], none of the patients had cavitary infiltrates.

#### Coccidioides immitis

Coccidioidomycosis, a fungal disease endemic to the southwestern United States, occurs most frequently in immunocompetent individuals and usually produces a self-limited or subclinical lower respiratory tract illness [58]. Lobar consolidation and nodular or patchy infiltrates are the most common findings for patients with radiographic manifestations. Residual asymptomatic pulmonary lesions, usually nodules or thin-walled cavities, persist in ~5% of patients [59]. Ninety percent of the cavities are single, and 70% are found in the upper lobes. Cavitary disease is a prominent feature of chronic pulmonary coccidioidomycosis, which occurs more frequently in diabetics and immunocompromised patients [60].

In immunocompromised patients, including those with HIV infection, coccidioidomycosis may be more severe, and extrathoracic dissemination is common. Patients typically present with diffuse pulmonary disease, often with a reticulonodular pattern [61, 62]. Cavitary disease occurs but is not a common presentation. In a review of 77 cases of HIV-infected patients with coccidioidomycosis by Fish and colleagues [63], 51 patients (66%) presented with pulmonary disease. Of those 51 patients, 31 had diffuse infiltrates, and 20 had focal involvement. Only three patients had radiographic evidence of cavitation. In a prospective cohort analysis of HIV-infected individuals living in an area of endemicity [64], 13 (7.6%) of 170 patients had coccidioidomycosis over a median follow-up time of  $\sim 1$  year. Of the 11 patients with pulmonary infection, 5 had diffuse, reticulonodular infiltrates and 6 had focal pulmonary infiltrates; none of the patients had cavitary disease.

#### Aspergillus Species

Aspergillosis is a common complication of immunodeficiency or neutropenia due to chemotherapy. Immunocompromised patients without HIV infection who have invasive pulmonary aspergillosis typically present with single or multiple pulmonary nodules. Progressive disease occurs in one of three patterns: cavitation of existing nodules; enlargement of the nodules that produces single or multiple areas of homogeneous consolidation; or the development of large wedge-shaped, pleura-based lesions, which sometimes cavitate [65].

Although aspergillosis was once believed to be a rare opportunistic infection in patients with AIDS [66, 67], it is now being recognized with greater frequency. Cavitation is common, occurring in 36% to 42% of HIV-infected patients with invasive pulmonary aspergillosis [68-71]. The cavities can be single or multiple, are usually thin-walled, and tend to occur in the upper lobes. Other radiographic features of invasive pulmonary aspergillosis include focal or multifocal alveolar opacities that often mimic bacterial pneumonia. In addition to the nonspecific symptoms of fever, cough, and dyspnea, patients with cavitary aspergillosis are more likely to experience chest pain and hemoptysis than are patients with other radiographic presentations [68]. As in patients without HIV infection, patients with preexisting cavities caused by other infections, such as PCP, may have aspergillomas; cultures of sputum from these patients are likely to be positive for Aspergillus [72].

Growth of *Aspergillus* species in cultures of respiratory specimens may represent contamination or colonization [73, 74]. In the setting of compatible clinical findings, especially upper-lobe cavitary lesions, multiple positive cultures may be suggestive of invasive aspergillosis; however, the diagnosis requires histologic confirmation or a positive culture of a transthoracic aspirate.

# Other Fungi

Blastomycosis, a systemic fungal disease seen in areas of endemicity in the midwestern and southwestern United States, is an uncommon infection in patients with AIDS [75]. To our knowledge, there have been no large series describing the clinical and radiological features of blastomycosis in the setting of HIV infection. In the general population patients typically present with alveolar infiltrates with consolidation [76]. Other radiographic patterns include masslike infiltrates and interstitial infiltrates. In one series [76] cavitation within pulmonary infiltrates was demonstrated for 37% of patients with pulmonary blastomycosis. In other series [77–79] the frequency of cavitation has been somewhat lower. Cavitation also occurs in patients with HIV-related pulmonary blastomycosis, although the frequency is not known [75, 80]. In the largest series [75], involvement of the lungs and pleura was demonstrated for seven of 15 patients. Of those seven patients, three had focal lobar infiltrates, three had miliary or diffuse interstitial changes, and one had bilateral nodules. Only one patient presented with cavitary disease.

Candidal pneumonitis is uncommon in immunocompromised hosts, including individuals with HIV infection. When *Candida* is isolated from sputum or bronchial specimens, it usually represents oropharyngeal contamination. Most cases of true pulmonary candidiasis have been diagnosed at autopsy and have reflected disseminated disease, often due to an intravascular focus of infection. Regardless of the cause of immunosuppression, cavitation is rare in patients with candidal pneumonitis [81, 82].

Disseminated infection with the dimorphic fungus *Penicil-lium marneffei* has been described in HIV-infected patients in Southeast Asia [83–86]. The most common presenting symptoms are fever, anemia, weight loss, and papular skin lesions. Cough is also common, and in the largest series [86], chest roentgenograms revealed abnormalities in six of 21 patients. Radiographic findings included diffuse reticulonodular infiltrates in three patients, localized interstitial infiltrates in two, and localized alveolar infiltrates in one. Although *P. marneffei* has been reported to cause cavitary lung lesions in patients without known HIV infection [87], cavitary disease due to this organism has not been described in HIV-infected patients.

A case of cavitary pulmonary mucormycosis due to *Absidia* corymbifera has been reported [88]. The development of pulmonary involvement was preceded by long-standing pharyngeal ulcerations that were subsequently discovered to be caused by the same organism.

### **Mycobacterial Infections**

# Mycobacterium tuberculosis

The AIDS epidemic has led to a rise in the incidence of tuberculosis not only in developing countries but also in the United States, where the incidence had previously been declining steadily [89]. Because *M. tuberculosis* is more virulent than many of the other HIV-associated opportunistic pathogens, it often causes disease at an earlier stage of HIV infection and is frequently the initial manifestation [90]. The incidence of tuberculosis is higher among populations with an increased likelihood of prior exposure to *M. tuberculosis*, such as injection drug users, African-Americans, Hispanics, and individuals from developing countries.

The natural history of *M. tuberculosis* infection is altered dramatically by HIV infection. Among individuals with latent *M. tuberculosis* infection who acquire HIV infection, the risk

of reactivation is 2% to 8% per year [91]. Among HIV-infected persons who acquire new M. tuberculosis infection, the risk of progressive primary tuberculosis is extremely high [92]. Clinical features of tuberculosis in HIV-infected patients vary depending on the degree of immunosuppression. In patients with mild-to-moderate depression of the CD4 cell count who present with reactivation tuberculosis preceding the diagnosis of AIDS, the presentation is similar to that seen in other populations [93-97]. Most of these patients have disease confined to the lungs, with nodular or cavitary infiltrates in the apical and posterior segments of the upper lobes and the superior segments of the lower lobes. Cavities are often irregularly shaped, with thin or thick walls, and air-fluid levels are relatively uncommon [5, 98]. However, patients in whom tuberculosis develops at a more-advanced stage of HIV infection often have atypical radiographic findings, which sometimes mimic those of primary tuberculosis. Cavitary disease is uncommon in such individuals, and lower-lobe infiltrates or miliary patterns occur frequently [99-101]. Intrathoracic adenopathy and extrapulmonary dissemination are also common.

In recent years multidrug-resistant tuberculosis has emerged as a significant public health problem, especially in immunocompromised individuals. In a case-control study comparing HIV-infected patients with multidrug-resistant tuberculosis (cases) with patients with tuberculosis due to single-drug-resistant or susceptible strains (controls), Fischl and co-workers [102] found that patients with multidrug-resistant tuberculosis were more likely to have alveolar infiltrates (76%) and cavities (18%) than were controls (49% and 3%, respectively). Interstitial infiltrates occurred more frequently in controls than in cases. Cases with interstitial infiltrates were more likely to have a reticular pattern, while a miliary pattern was more common in controls. It was suggested that the differences in the radiographic presentation reflected the more-fulminant nature of multidrug-resistant tuberculosis and the immune status and host reaction of the patients.

#### Mycobacterium avium Complex

Disseminated disease due to *M. avium* complex (MAC) is the most common systemic bacterial infection in patients with AIDS in the United States [103]. It tends to occur late in the course of AIDS, usually after the CD4 cell count has fallen to  $<50/\text{mm}^3$ , and at the time of diagnosis, it is usually widely disseminated [103–105].

Pulmonary MAC infection primarily occurs in elderly patients with underlying chronic lung disease [106]. In this population the disease may resemble tuberculosis, with progressive upper-lobe cavitary pneumonia [106–108]. In HIV-infected patients, however, clinically significant lung disease is uncommon, despite the frequent isolation of the organism from respiratory secretions [109]. Pulmonary MAC infection has been described in patients with [110] and without [99, 111] disseminated disease. Endobronchial lesions have also been described [112, 113].

Although cavitary infiltrates are common in patients without AIDS, to date only 13 HIV-infected patients with cavitation as a result of pulmonary MAC infection have been described [99, 114-116]. In a series of 200 patients with AIDS and disseminated MAC infection [116], five (2.5%) had pulmonary MAC infection as defined by (1) the isolation of MAC from at least two respiratory tract specimens or a single lung biopsy sample, (2) the presence of a pulmonary infiltrate, and (3) the absence of other identified pulmonary conditions. Four additional patients without evidence of dissemination met criteria for pulmonary disease. Cavities were present in one of the patients without disseminated MAC infection and in two of the patients with pulmonary disease in the setting of dissemination. In the first patient the CD4 cell count was 162/mm<sup>3</sup> at the time of presentation, and pulmonary MAC infection was the first manifestation of AIDS. In all three cases smears of sputum samples or BAL specimens were positive for acid-fast bacilli, and cultures were positive for MAC. All patients in the series responded clinically and radiographically to drug therapy directed against MAC. The cavitary infiltrates resolved after 2 to 12 months of therapy.

Because cavitation is an uncommon manifestation of pulmonary MAC infection, which is itself uncommon in HIV-infected individuals, it should not be assumed that cavitary infiltrates are caused by MAC when the organism is isolated from respiratory specimens. It is important to look for other pulmonary pathogens or malignancies in such patients, usually by means of BAL and/or transbronchial biopsy. Those patients in whom no other pulmonary process is identified should be treated for MAC infection, usually with a combination of clarithromycin and at least one other agent with activity against MAC (such as ethambutol) [117]. The presence of acid-fast bacilli on smears of sputum or BAL specimens increases the likelihood that MAC is a true pathogen, but patients with such findings should be treated presumptively for tuberculosis until culture results are available.

### Other Mycobacteria

Mycobacterium kansasii is a cause of serious pulmonary disease in patients with advanced HIV infection. Pulmonary disease appears to be considerably more common than disseminated infection, which is an AIDS-defining condition [118, 119]. In some series [119, 120] *M. kansasii* was isolated more frequently than *M. tuberculosis* from HIV-infected patients.

In a review of 19 cases of *M. kansasii* infection at The Johns Hopkins Hospital (Baltimore) [118], 17 patients had pulmonary disease. The clinical features and response to therapy resembled those of patients with pulmonary tuberculosis. Radiographic features included diffuse interstitial or apical infiltrates. Thinwalled cavities were present in nine patients (53%); of these patients, five had diffuse infiltrates, and four had disease confined to the upper lobes. The presence of thin-walled cavities was thought to be an important diagnostic clue in patients with pulmonary disease and advanced HIV infection. In contrast, no cavities were seen in the six patients with pulmonary *M. kansasii* infection in a series at Parkland Memorial Hospital (Dallas) [119]. Radiographic findings in that series included nodular, interstitial, or diffuse parenchymal infiltrates, and one patient had a pleural effusion.

In a series of 28 HIV-infected patients with disease due to *M. kansasii* [121], the organism was isolated from a pulmonary source from 17 patients, and both pulmonary and extrapulmonary isolates were recovered from an additional five. Respiratory symptoms were common, and all but one patient had pulmonary infiltrates. Four patients had cavitary lung disease. In a recent series of 49 HIV-infected patients with *M. kansasii* infection [122], chest radiographs revealed abnormalities in 45. Cavities were present in nine of the 32 patients with disseminated infection. In patients with HIV infection, *M. kansasii* disease is associated with a greater degree of immunosuppression than is tuberculosis. In most series of HIV-associated *M. kansasii* disease [118, 119, 122], the median CD4 cell counts have been <50/mm<sup>3</sup>.

*Mycobacterium xenopi*, an occasional cause of pulmonary disease in elderly patients with chronic lung disease [123], rarely causes disease in HIV-infected individuals. Cases of both disseminated disease [124–126] and pulmonary disease [127, 128] have been reported, however. One patient presented with constitutional and respiratory symptoms and was found to have a perihilar cavitary infiltrate. Examination of sputum smears demonstrated acid-fast bacilli, and *M. xenopi* was isolated from multiple respiratory specimens as well as from fluid from a peritracheal abscess. Although pulmonary colonization with *M. xenopi* appears to be much more common than true disease [111, 126], the organism may be an occasional cause of pulmonary disease, including cavitary infiltrates, in HIV-infected individuals.

Cavitary pulmonary infiltrates in HIV-infected patients have been attributed to *Mycobacterium simiae* [129] and *Mycobacterium scrofulaceum* [130]. Although infections with *Mycobacterium haemophilum* usually involve skin, bone, or joints, pulmonary disease has been described in HIV-infected patients [131, 132], including cavitary disease in at least one report [133].

# **Bacterial Infections**

HIV-infected individuals are at increased risk for community-acquired pneumonia, which frequently occurs with mildto-moderate immunosuppression before the onset of other opportunistic conditions. The risk of bacterial pneumonia appears to be higher for injection drug users [134–136]. The most common causative organisms are *Streptococcus pneumoniae* and *Haemophilus influenzae* [136–138]. As in immunocompetent individuals, the radiographic features in HIV-infected pa-

tients typically include localized segmental or lobar consolidation, especially in those with pneumococcal pneumonia [137, 139-141]. Radiographic manifestations of H. influenzae pneumonia are more variable and may include the diffuse bilateral infiltrates characteristic of PCP [137]. Bacterial pneumonia in patients with HIV infection may be more severe; the incidence of multilobar involvement is higher, and the response to antibiotics is less rapid [141]. Community-acquired pneumonia caused by S. pneumoniae or H. influenzae is rarely complicated by cavitation. However, cavity formation was described in three of 15 HIV-infected patients with pneumococcal pneumonia in one series [142], and other local complications of pneumococcal infection, such as effusion, empyema, and abscess, may be more common in HIV-infected individuals [143]. Cavitary pneumonia caused by H. influenzae has also been described [144] but is uncommon.

There has been a growing number of reports of *Pseudomonas* aeruginosa causing both community-acquired and nosocomial pneumonia in patients with advanced HIV infection [145–148]. In one review of 16 cases of HIV-infected patients with *P. aeruginosa* pneumonia [146], 15 (94%) were thought to be community-acquired. Cavitary infiltrates were present in 11 patients (69%) at some point during the course of their illness. In a series of 58 patients with 73 episodes of *P. aeruginosa* infection [148], there were 25 cases of pneumonia, six of which were cavitary. Patients with cavitary pneumonia appeared to have a less-fulminant illness than did those without cavities.

Nosocomial pneumonia in patients with AIDS is also caused by other gram-negative bacilli and by *Staphylococcus aureus* [137, 149, 150]. As for other hospitalized patients, risk factors include neutropenia, the use of broad-spectrum antibiotics, and the presence of central venous catheters. Nosocomial pneumonia is associated with higher rates of morbidity and mortality than is community-acquired pneumonia [149].

Cavitation is not uncommon in immunocompromised individuals with legionellosis [151–156] but is unusual in immunocompetent hosts [157, 158]. Although they are infrequently pathogenic in HIV-infected individuals, both *Legionella pneumophila* [159, 160] and *Legionella micdadei* [161] have been reported to cause cavitary pneumonia in patients with AIDS. Cavitary pneumonia has also been attributed to *Salmonella typhimurium* in HIV-infected individuals [162].

Although not specifically related to HIV infection, pulmonary abscesses may occur with increased frequency in some HIV-infected populations. Intravascular infections should always be considered in the differential diagnosis of cavitary pulmonary lesions, especially in injection drug users or individuals with central venous catheters. Septic pulmonary emboli, which may become cavitary, are frequent complications of tricuspid valve endocarditis, especially that caused by *S. aureus* [163, 164]. Anaerobic lung abscesses may occur in HIV-infected drug abusers following aspiration of oropharyngeal contents, which is the most common cause of lung abscess [165]. The gingivitis and periodontitis often observed in HIV-infected patients [166] may also increase the risk of lung abscess.

#### Nocardia asteroides

Nocardia, a gram-positive aerobic actinomycete, is an uncommon human pathogen. Nocardial infection occurs most commonly in immunocompromised hosts, frequently causing cavitary pulmonary infiltrates that can mimic tuberculosis or aspergillosis [167, 168]. Despite its predilection for individuals with defects in cell-mediated immunity, nocardiosis is relatively uncommon in patients with HIV infection. In most cases disease occurs in patients with advanced immunodeficiency (CD4 cell counts of <200/mm<sup>3</sup>) [169]. Patients typically present with an indolent course and nonspecific constitutional complaints. Pulmonary symptoms, such as cough or dyspnea, may also be present. As in patients without HIV infection, the lung is the most common site of disease in HIV-infected patients, although dissemination is common. Roentgenographic changes include nodules, cavities, and diffuse or focal infiltrates [169-172]. In a review by Javaly et al. [169], four of 18 previously described HIV-infected patients for whom chest roentgenograms revealed abnormalities due to nocardiosis had definite or probable cavitary lesions. In a subsequent series of 30 HIV-infected patients with nocardiosis [173], 22 had pulmonary involvement. Of those 22 patients, 14 had alveolar infiltrates, 2 had reticulonodular patterns, and 6 had a mixed pattern. Cavitation was a prominent feature in four of the patients, and cavitating lesions developed in an additional 14.

The diagnosis of nocardiosis is suspected when filamentous, beaded, branching, gram-positive, acid-fast rods are seen on gram stains or modified acid-fast stains of sputum or other respiratory specimens [169, 172]. Because of the slow growth of the organism, cultures should be held for 4 weeks when nocardiosis is suspected. Culturing sputum for mycobacteria and fungi improves the chances of isolating *Nocardia*.

#### Rhodococcus equi

Rhodococcus equi is an aerobic, weakly acid-fast, grampositive bacillus most commonly causing disease in domestic animals; however, it is now also recognized as an infrequent cause of pneumonia in patients with AIDS. It was first reported as a human pathogen in 1967, when it caused a lung abscess [174], and was first reported to cause pneumonia in an HIVinfected patient in 1986 [175]. In immunocompromised individuals *R. equi* infection is typically manifested by pulmonary disease, whereas immunocompetent patients are more likely to have isolated extrapulmonary infection [176]. Bacteremia is also more common in immunocompromised hosts. The presentation of *R. equi* pulmonary infection is typically subacute and is associated with fever, productive or nonproductive cough, fatigue, pleuritic chest pain, and weight loss [176]. Patients with AIDS frequently present with cavitary lung lesions, which may be associated with pleural effusion or empyema [176–178]. In one review [179] seven of the 12 described patients presented with cavitary infiltrates. Numerous other reports have substantiated the high frequency of cavitation in HIV-infected patients with *R. equi* infection [176, 180–183]. Because cavities are less likely to develop in patients who have pulmonary tuberculosis or other mycobacterial infections with advancing immunosuppression, *R. equi* should always be considered as a potential pathogen in any patient with AIDS and cavitary pneumonia, especially if gram-positive coccobacilli or acid-fast organisms are isolated from respiratory secretions or blood.

# **Neoplasms and Idiopathic Conditions**

#### Kaposi's Sarcoma

Kaposi's sarcoma was the first neoplasm to be described in association with AIDS, and it remains the most common HIVassociated tumor (especially in homosexual men), although the prevalence appears to be declining among all groups [184, 185]. Extracutaneous Kaposi's sarcoma is not uncommon, and the lungs are the most common site of visceral involvement, especially in patients with CD4 cell counts of  $<100/\text{mm}^3$  [186]. The radiographic presentation is highly variable, with bilateral infiltrates occurring in four major patterns: interstitial, alveolar, mixed, and nodular [187]. A diffuse reticulonodular pattern is seen in approximately one-third of patients [188]. Interstitial infiltrates mimicking the radiographic appearance of PCP are especially common [186–189]. Hilar lymphadenopathy is present in approximately one-half of cases [187], and pleural effusions are also common [186–188, 190].

There has been one report of an HIV-infected patient who presented with diffuse reticulonodular infiltrates and bilateral lower-lobe cavitary lesions that were determined by CT-guided needle aspiration to be caused by Kaposi's sarcoma [191]. We recently described a patient with known pulmonary Kaposi's sarcoma who had extensive nodular infiltrates and a large cavitary lesion at the time of his death [192]. Postmortem examination of the lungs revealed the presence of both Kaposi's sarcoma and non-Hodgkin's lymphoma at the site of the cavity. Histologic examination of a tissue section demonstrated that the tumors were adjacent to each other, forming what has been termed a *collision tumor*. To date we know of no other cases in which cavitary disease has been described in the setting of pulmonary Kaposi's sarcoma.

# Non-Hodgkin's Lymphoma

As with Kaposi's sarcoma, non-Hodgkin's lymphoma involving extraneural sites does not require severe immunodeficiency. Most of these lymphomas are B cell malignancies and are typically characterized by widespread involvement of extranodal sites at the time of diagnosis [193, 194]. The most common sites of involvement are the gastrointestinal tract, the CNS, the bone marrow, and the liver. Pulmonary involvement is uncommon, occurring in <10% of cases [194, 195]. In those individuals with pulmonary involvement, respiratory symptoms rarely dominate the clinical picture. The chest roentgenogram usually shows a nonspecific interstitial or alveolar pattern with hilar and/or mediastinal adenopathy and pleural effusions [196]. Pulmonary lesions may have a more sharply marginated appearance and are usually more rapidly progressive than the infiltrates of Kaposi's sarcoma. Cavitation is rare. In addition to our report of a cavitary collision tumor involving Kaposi's sarcoma and non-Hodgkin's lymphoma [192], we know of only one report of non-Hodgkin's lymphoma presenting with pulmonary cavitation [196].

### **Bronchogenic Carcinoma**

There have been numerous case reports and series describing HIV-infected patients with bronchogenic carcinoma [197–202]. In most cases there has been a history of intravenous drug use and cigarette smoking; however, the previously described patients were younger than would be expected for patients with lung cancer, and their survival was shortened significantly. In many cases patients present with advanced-stage lung cancer, often despite asymptomatic or mildly symptomatic HIV infection. The radiographic features are similar to those seen in other populations and include the presence of cavitary nodules. The nature of the association, if any, between HIV infection and bronchogenic carcinoma is not understood.

### **Idiopathic Conditions**

Lymphocytic interstitial pneumonia is an idiopathic process in which lymphocytes and plasma cells accumulate in the pulmonary interstitial space. It occurs most commonly in children with AIDS but can also occur in adults. Patients present with diffuse or focal reticular interstitial infiltrates, which are often indistinguishable from those of PCP [1, 203]. Although nodular densities and cystic changes have been reported, lymphocytic interstitial pneumonia is not a cause of cavitary lung disease [204, 205]. Other idiopathic processes involving the lungs of HIV-infected individuals include lymphocytic alveolitis and nonspecific pneumonitis, neither of which causes cavitation [206–208].

# Conclusions

In summary, the differential diagnosis of cavitary pulmonary lesions in HIV-infected individuals is extensive, and the appearance of the chest radiograph may not be helpful in making a specific diagnosis. In patients with a compatible clinical presentation who have a reasonably preserved immune function (e.g., CD4 cell count of >200/mm<sup>3</sup>), pulmonary tuberculosis should be strongly considered. As cellular immunity wanes, however, the likelihood that cavitary lesions are caused by While examination of an expectorated or induced sputum sample is an appropriate first step, further studies and procedures are often required, including CT, BAL, and transbronchial or percutaneous biopsy. In most cases the evaluation of cavitary pulmonary lesions in HIV-infected patients will lead to the diagnosis of treatable opportunistic infections.

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