



## Radiology of pulmonary *Mycobacterium avium-intracellulare* complex

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Infection with nontuberculous mycobacteria is an increasingly important cause of pulmonary disease. Of the nontuberculous mycobacteria, *Mycobacterium avium-intracellulare* complex (MAC) is the most common pathogen [1]. In the immunocompetent patient, pulmonary infection likely results from the inhalation of aerosolized water droplets containing MAC. In the immunocompromised host, pulmonary infection typically reflects spread of the disease from a gastrointestinal source [2]. This article will discuss the radiographic appearance of pulmonary MAC in both the normal host and the immunocompromised patient.

### Pulmonary MAC in the immunocompetent host

The radiographic appearance of pulmonary MAC in the immunocompetent host can be variable. For this article, however, the radiographic presentation can be described as being either classic or atypical. These two presentations are distinct radiographically and often occur in different patient populations. Much of the data on the radiographic appearance of pulmonary MAC comes from studies that evaluated nontuberculous mycobacterial (NTMB) infections in general. These studies failed to find substantial differences in the radiographic appearance between the various species of NTMB infection [3,4]. Additionally, though there are a number of NTMB that can cause disease, MAC along with *M kansasii* account for the bulk of NTMB pulmonary infection [2]. As such, the radiographic appearance of pulmonary MAC and other NTMB infections are grouped together in this article. Though

the radiographic appearance may be more suggestive of a specific type of mycobacterial infection, it is important to remember that a correlation needs to be made with both the clinical and laboratory features of the disease in each patient.

### Classic appearance

The classic radiographic appearance of pulmonary MAC is indistinguishable from that of pulmonary tuberculosis (Figs. 1–3). It is seen most commonly in white males [5,6] and is often associated with other diseases, especially chronic pulmonary disease. Dutt and Stead [6] reviewed 85 cases of pulmonary MAC. One or more associated medical problems were present in 76% of patients. Previously diagnosed or suspected *M tuberculosis* was present in 31 patients; chronic obstructive pulmonary disease (COPD) was present in 15 patients; and other pulmonary diseases (bronchiectasis, histoplasmosis, blastomycosis, silicosis, sarcoidosis, and pulmonary fibrosis) were present in 9 patients. A variety of nonpulmonary diseases were also seen, such as rheumatoid arthritis, nonpulmonary malignancy, diabetes mellitus, and alcoholism, with each present in six patients. Heart disease and partial gastrectomy were each present in five patients. Christensen et al [5] found radiographically evident COPD in 52% of their patients, with bullous emphysema present in 24%. Other studies have found a smaller frequency of predisposing disease. In Albelda's series [3], only one-fourth to one-third of the patients had pre-existing pulmonary disease. Of the 40 patients reviewed by Woodring et al [7], only 13 (33%) had a predisposing factor. Eleven of those patients had COPD, and two had non-AIDS-related immunosuppression.

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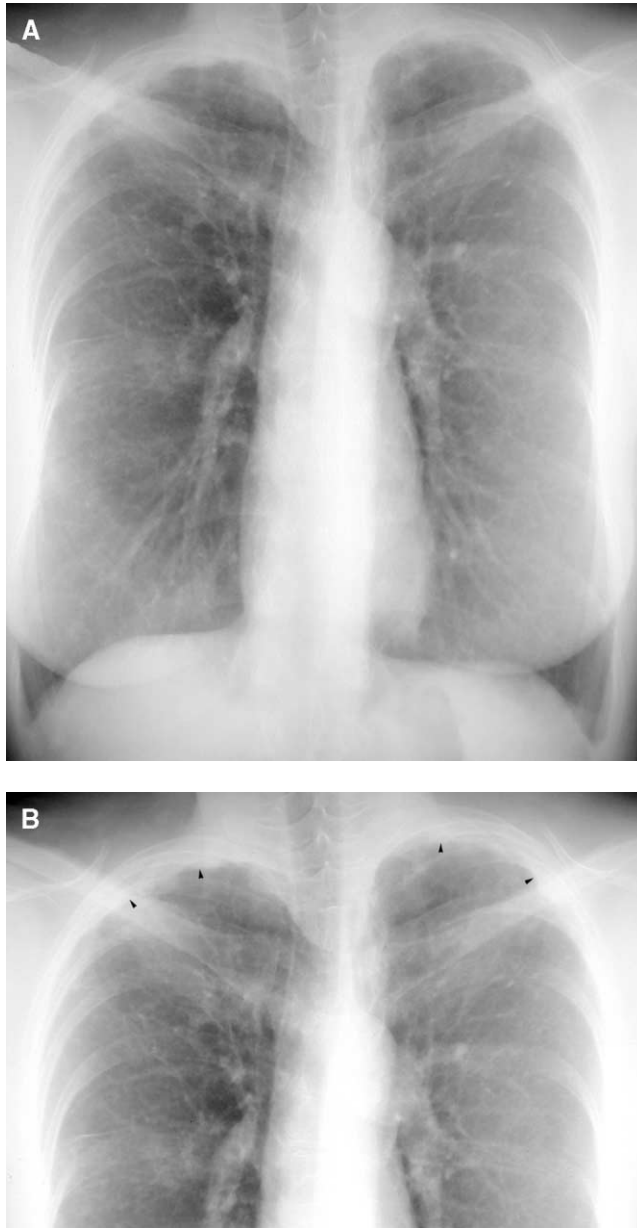


Fig. 1. (A) Frontal radiograph and close up (B) of 43-year-old female patient with pulmonary *M avium-intracellulare* complex. Faint biapical parenchymal opacities are present along with pleural thickening (arrowheads, B).

#### *Parenchymal disease*

Christensen and colleagues [5] reviewed 114 cases of pulmonary MAC documented between 1959 and 1977. Seven of these patients had no evidence of radiographic disease despite repeated positive sputum cultures. Another seven patients had “reticulonodular appearing” disease without a well-defined focus. The remaining 100 patients had an identifiable focus that

was felt to be the initial site of parenchymal infection (progenitive focus). The apical or posterior portion of the upper lobes was the site of the progenitive focus in 92% of those patients. Seventy percent of the patients with upper lobe progenitive foci had scarring with volume loss. Pleural thickening adjacent to the upper lobe foci of disease was present to some degree in 56% of cases, with 16% having pleural thickening greater

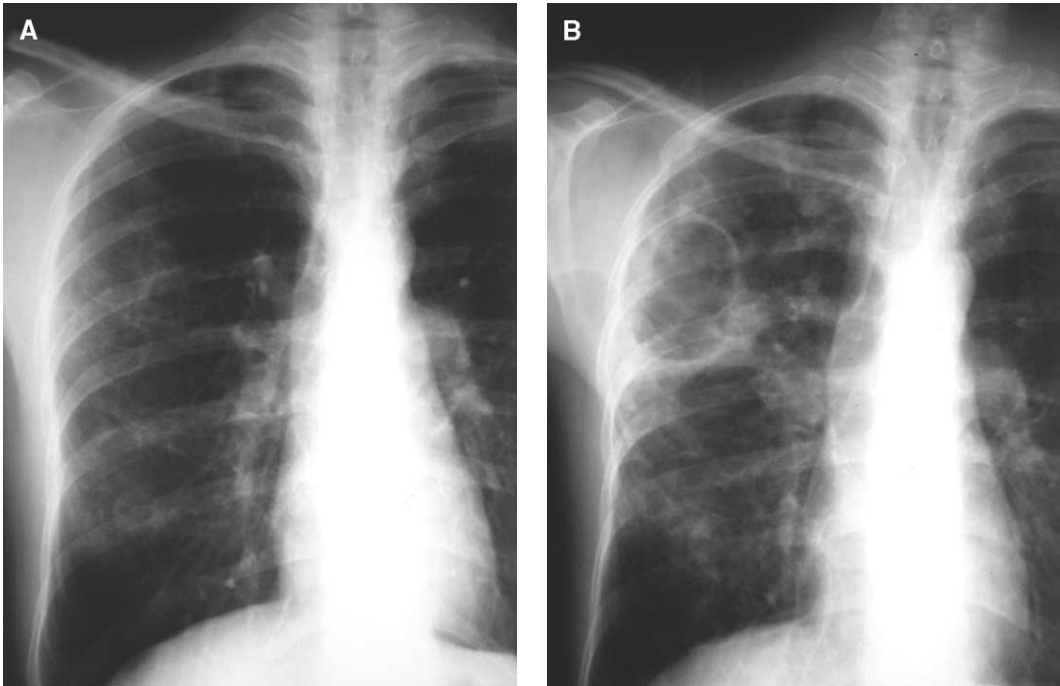


Fig. 2. Frontal radiographs of a 47-year-old female patient with pulmonary *M avium-intracellulare* complex. (A) The initial radiograph demonstrates subtle right mid- and upper-lung opacities. (B) A subsequent radiograph obtained 3 years later demonstrates interval development of a large cavity with increasing parenchymal disease throughout the right lung.

than 2 cm. Atypical locations for the progenitive focus included superior segment of right lower lobe, lingula, middle lobe, anterior segment of left upper lobe, and basilar segments of right lower lobe. Widespread disease was common and was present in 76% of patients at presentation. This was felt to reflect an endobronchial spread of disease from the initial site of infection. Of the 100 patients with a clearly defined focus of infection, 53% had disease involving three or more lobes.

Though the radiographic appearances of pulmonary MAC were similar to those seen with *M kansasii*, bilateral disease was more common with pulmonary MAC (65% versus 41% respectively). *M kansasii* infection was more likely to be extensive and more likely to be associated with radiographic evidence of COPD. These patients were typically younger and more likely to be male.

Albelda and colleagues [3] reviewed 35 patients with NTMB infection and compared their radiographic features with those observed in 29 patients with *M tuberculosis*. Of the patients with NTMB, 23 patients had pulmonary MAC, 7 had infection with *M kansasii*, 4 with *M scrofulaceum*, and 1 with *M gordonae* infection. One of the 35 patients had an unclear immunodeficiency state and demonstrated a miliary

pattern of disease. Of the remaining 34 patients, 17 had disease that was radiographically similar to that seen with *M tuberculosis*. Seven patients had a single upper lobe focus, and three patients had multiple upper lobe foci of disease. Three patients had a solitary focus of disease not within the upper lobe. Twelve patients had diffuse disease without a dominant parenchymal focus within the upper lobe.

Woodring and colleagues [7] reviewed the radiographs of 40 patients with NTMB. Of these, 34 individuals had pulmonary MAC, 5 had *M kansasii* infection, and 1 was infected with *M fortuitum*. All patients had clinical signs and symptoms of active disease. Pulmonary parenchymal disease was present in 39 of the 40 patients (98%). The most common abnormality was a mixture of linear opacities and small nodules, which was termed a fibroproductive pattern. This was present in 25 of the 40 cases and was felt to reflect postprimary infection or disease of indeterminate phase. The apical and posterior segments of the upper lobes were most commonly involved (87%). Disease within two or more pulmonary segments was seen in 72% of patients. No patient had disease limited to the anterior segments of the upper lobes, and disease limited to the basal segments of the lower lobes was seen in only 6% of patients. In 6



Fig. 3. Frontal radiograph of a 77-year-old male patient with pulmonary *M avium-intracellulare* complex. Widespread parenchymal disease is present. Of note, there is a moderate thoracic scoliosis (arrowheads identify the lateral aspect of the spine).

of the 25 cases, the disease was minimal and in 12 cases disease was considered extensive. In 5 of the 40 patients, the parenchymal disease consisted primarily of 1 or more foci of homogeneous consolidation. This pattern was seen with both suspected primary and postprimary infection. In the remaining nine patients, there was a mixture of fibroproductive nodules and alveolar consolidation. A marked fibrotic response with upper-lobe volume loss and hilar retraction was present in 12 patients.

This case series also points to the difficulties in the radiographic evaluation of patients with pulmonary MAC. In no case was the diagnosis of an atypical mycobacterial infection initially considered. In 13 of the 40 patients, *M tuberculosis* was suspected. Mycobacterial infection of any type was not suspected, however, for the remaining 27 patients. In many of these patients, the fibroproductive lesions were either overlooked or were interpreted as reflecting inactive scarring. The slow progression of disease seen was one of the major factors for the failure to consider mycobacterial disease. In two thirds of the patients, it took an average of 6 years to demonstrate radiographic progression. In one case, radiographic

progression did not occur until 12 years after the onset of pulmonary symptoms.

#### Cavitory disease

Cavitory disease is commonly seen with the classic appearance of pulmonary MAC; however, its frequency is variably reported. Christensen et al [5] reported cavitory disease in 88% of their patients with an identifiable progenitive focus, and cavitory disease was felt to be the dominant abnormality in 60% of the cases. The cavities were multiple in 79% of patients. Most of the cavities were less than 4 cm in size, with nearly half of cavities being between 2 and 4 cm in diameter. Other investigators report cavitation less frequently. Reich and Johnson [8] identified cavitation in 13 of 23 patients (56%) with the classic radiographic appearance of pulmonary MAC. Woodring [7] identified cavitation in 38% of patients with NTMB. In Albelda's series [3], cavitation was present in 15 of the 34 patients (44%) with NTMB. Seven of those 15 patients had cavities with a wall thickness less than 1 mm. The cavities seen with NMTB were generally smaller than those seen with *M tuberculosis*. In the NMTB group, the cavities ranged from

0.5–7 cm in diameter, with an average diameter of 2.5 cm. For *M tuberculosis*, the cavities ranged from 2–10 cm in diameter with an average of 6 cm. Thus, the finding of a large or thick-walled cavity favored *M tuberculosis*. Unfortunately, the converse is not necessarily true. Though thin-walled cavities were two and one-half times more common in individuals with pulmonary MAC or *M kansasii* than in individuals with *M tuberculosis* (10% versus 4%), the increased incidence of tuberculosis far outweighs this. As such, a thin-walled cavity is also more likely to be caused by *M tuberculosis*.

#### *Thoracic cage abnormalities*

Iseman et al [9] reviewed 67 patients with pulmonary MAC and compared the incidence of thoracic cage abnormalities with a control group of 55 patients with pulmonary tuberculosis. Seventy percent of patients with pulmonary MAC had either scoliosis or abnormal narrowing in the anterior-posterior dimension. Abnormal narrowing was considered to be a minimum distance from the anterior border of the vertebral bodies to the posterior surface of the sternum of less than 10.2 cm for males or less than 9.2 cm for females. These abnormalities were significantly more common in patients with pulmonary MAC than in the group with tuberculosis or the general population. A decrease in the anterior-posterior (AP) diameter of the chest was present in 27% of patients with pulmonary MAC versus 9% of patients with tuberculosis and 2.4% of the general population. Scoliosis was present in 52% of patients with pulmonary MAC versus 13% of patients with tuberculosis and 1% of the general population.

In other findings, pleural effusions are relatively infrequent and are reported in 5–15% of patients with pulmonary MAC [5,7]. Mediastinal and/or hilar adenopathy also are uncommon, seen in roughly 5% of cases [5].

#### *Computed tomography*

Lynch and colleagues [1] reviewed the chest radiographs and computed tomography (CT) examinations of 55 patients with pulmonary MAC and compared them with those obtained from 15 patients with pulmonary tuberculosis (TB). The CT examination in this study consisted of both 10-mm thick and high-resolution CT images. None of the patients had a history of AIDS, other immunodeficiency, or malignancy. Patients with pulmonary tuberculosis were significantly more likely to have pleural calcification (33% versus 7%). Diffuse bronchiectasis, involving four or more lobes, was seen only in subjects with pulmonary MAC, whereas focal bronchiectasis was

more common in patients with pulmonary TB (40% versus 15%). No significant differences were found between the two groups in the prevalence of pleural thickening or effusion, calcified or noncalcified lymphadenopathy, cavity formation, pulmonary nodules, airspace disease, or bronchial wall thickening. Nodules were present in 49 patients with pulmonary MAC, with airspace disease present in 44 patients. Cavities were seen in 36 of 55 patients, with upper lobe cavities present in 25 patients. The data for the cavities were reported by lobe. Twenty-one lobes had cavities less than 1 cm in diameter, 12 had cavities 1–2 cm in diameter, and 48 lobes had cavities >2 cm in diameter.

CT was more effective at identifying specific disease features, such as bronchiectasis, pulmonary nodules, and lymphadenopathy. Importantly, the CT examination often added significant new information. Eight of the sixteen subjects with diffuse bronchiectasis on CT examination were initially felt to have bronchiectasis limited to only one lobe on plain film.

#### *Atypical manifestations*

Though there are many atypical presentations of pulmonary MAC, two deserve specific attention: the combination of bronchiectasis and small nodules (Lady Windermere syndrome), and focal mass-like opacities (Figs. 4–6). Both of these presentations are associated almost exclusively with pulmonary MAC and are typically seen in patients with no predisposing conditions [2].

#### *Lady Windermere syndrome*

Prince and colleagues [10] reported 21 patients with pulmonary MAC and no predisposing factors. Of these patients, 81% were females with a mean age of 66 years. The vast majority of patients presented with chronic productive cough or purulent sputum. Within this group, the most common radiographic pattern was that of either diffuse or localized pulmonary nodules. Although upper lobe disease predominated, there typically was involvement of the lower lobes as well. The presence or absence of bronchiectasis was not described. Radiographic progression was slow, often with a minimum time of 2–3 years.

Reich and Johnson [8] reviewed 29 cases of pulmonary MAC identified over a 12-year period from a nonreferral setting. Of these, six patients had isolated lingular or middle lobe disease (Fig. 4). All six of these patients were elderly women, and none had radiographic features typical of classic pulmonary MAC infection. The authors considered this to be a distinct clinical syndrome and used the term “Lady Windermere Syndrome” to describe these

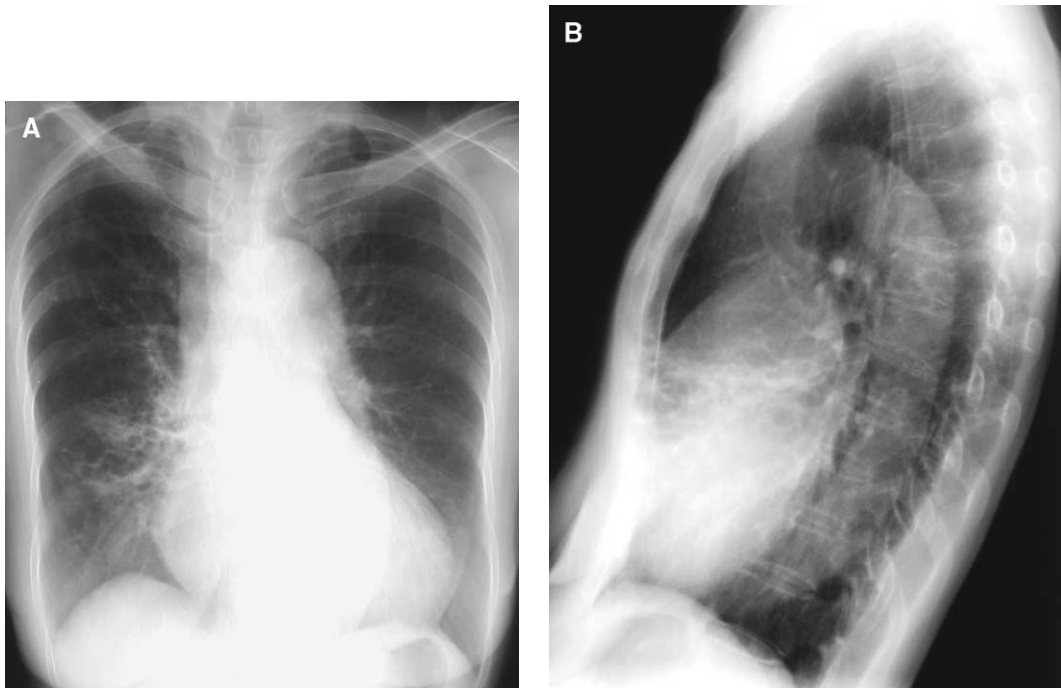


Fig. 4. Frontal (A) and lateral (B) radiographs of a 69-year-old female patient with pulmonary *M avium-intracellulare* complex. Isolated bronchiectasis and bronchial wall thickening is present within the right middle lobe.

findings [11]. Reich and Johnson hypothesized that habitual, voluntary cough suppression might be responsible for the clinical and radiographic features of this disease. The name of the syndrome was taken from the Oscar Wilde play, *Lady Windermere's Fan*, because of the fastidious nature of its main character. Subsequently, there have been case reports of the Lady Windermere syndrome in women who have had a history of voluntary cough suppression [12,13].

Hartman and colleagues [14] identified a similar group in a review of CT examinations in patients with pulmonary MAC. They retrospectively reviewed studies performed in 62 patients with documented MAC infection. Thirty patients had conventional CT performed, while 32 patients had either a dedicated high-resolution CT study or had both conventional and high-resolution images. Of the 62 patients, there was a group of 35 with small nodular infiltrates (predominantly nodules less than 5 mm in size) and primarily cylindrical bronchiectasis. The nodules and bronchiectasis were often present within the same lobe, with the middle lobe most frequently involved. Of the 35 patients, 83% were female with an average age of 66 years (range, 43–86 years). These findings led to a retrospective review of 100 outpatient chest CT scans read prospectively as having bronchiectasis

[15]. Of those, 24 patients also had nodules present and 22 of these patients were female. In the majority of patients, these nodules appeared to represent discrete parenchymal nodules, as opposed to foci of distal mucoid impaction. In 21 of the 24, the nodules were predominantly less than 5 mm in diameter. In 19 of the 24, the lung nodules were in the same lobe as the bronchiectasis. Of the 24 patients with nodules, 15 patients had cultures performed for MAC with 8 positive cultures (53%). Of the 76 patients without nodules, 48 had cultures performed for MAC, and only 2 of these cultures were positive. The combination of bronchiectasis and parenchymal nodules had an overall sensitivity of 80% and a specificity of 87% for positive MAC culture.

Bronchiectasis is commonly seen on CT with both pulmonary MAC and pulmonary tuberculosis. Lynch and colleagues [1] found bronchiectasis in 73% of patients with pulmonary MAC and 67% of patients with tuberculosis. But bronchiectasis involving four or more lobes was seen only in subjects with pulmonary MAC. The combination of middle lobe and lingular bronchiectasis was also seen exclusively with MAC infection. As in Hartman's study, the patients with diffuse bronchiectasis typically had associated nodules and these nodules commonly had a centri-

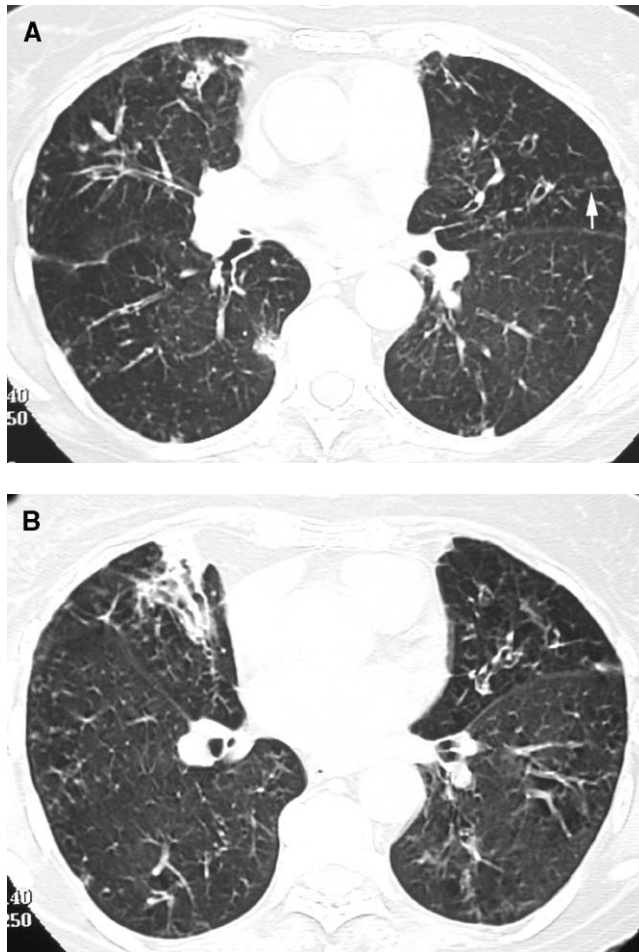


Fig. 5. CT images of an 82-year-old female patient with pulmonary *M avium-intracellulare* complex. Bronchiectasis is present primarily within the right middle lobe and lingula. Scattered, small foci of consolidation are also present. A cluster of centrilobular nodules is present within the lingula (arrow, A).

lobular distribution. Importantly, the findings of diffuse bronchiectasis and nodules were not necessarily associated with a positive sputum culture for MAC at the time of the CT examination. This suggests that further work-up would be warranted even if the initial sputum cultures were negative, given a typical CT appearance of pulmonary MAC.

#### *Focal masses*

Focal mass-like opacities are an uncommon presentation of pulmonary mycobacterial infection. Typically, these are asymptomatic, and the diagnosis is often made at resection for suspected malignancy [2]. Gribetz and colleagues [16] reported 20 solitary nodules caused by mycobacterial infection collected over a 10-year period. Of these, 12 were caused by

pulmonary MAC infection. The nodules ranged in size from 1.1 to 5 cm in the largest diameter. There was no definite predilection for a specific lobe. All of the nodules were discovered as an incidental finding. In Woodring et al's study [7], focal masses were present in 3 of the 40 patients studied. These were often accompanied by surrounding fibroproductive (satellite) lesions. When multiple nodules are present as a result of pulmonary MAC infection, they are usually of similar size and are often clustered [2].

#### **Pulmonary MAC in the immunocompromised host**

Pulmonary infection with MAC is commonly seen in the immunocompromised patient (Fig. 7).

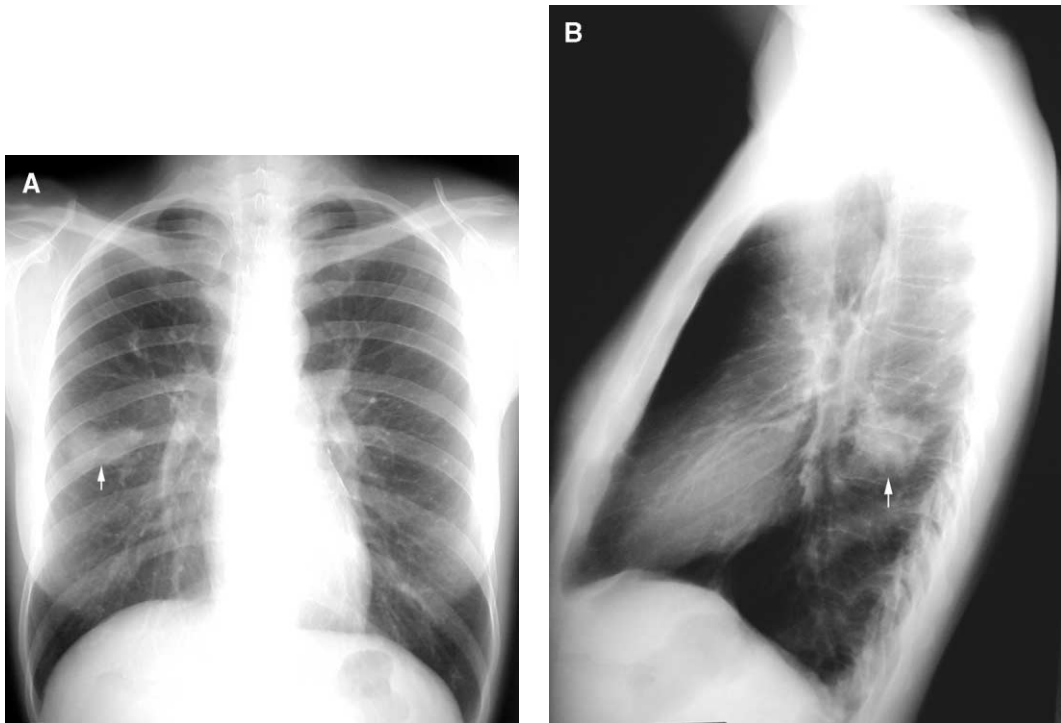


Fig. 6. Frontal (A) and lateral (B) radiographs of a 33-year-old female patient with pulmonary *M avium-intracellulare* complex. A solitary 3 × 5 cm mass is present within the superior segment of the right lower lobe (arrows).

Pulmonary MAC is usually associated with marked immunosuppression, often with a CD4 lymphocyte count less than 10, and disseminated infection is a significant cause of death among patients with AIDS [17]. For patients with AIDS, the lifetime risk of infection with MAC is approximately 10–20% [18]. In general, the radiographic features are similar, regardless of the underlying cause of the immunosuppression [2].

Modilevsky and colleagues [19] reported the clinical and radiographic features of mycobacterial infection in 94 patients with HIV infection. Of these patients, 55 were infected with MAC and 39 were infected with *M tuberculosis*. Pulmonary infection was present in 56% of the patients with MAC and in 74% of the patients with *M tuberculosis*. Unlike tuberculosis, however, isolated pulmonary involvement was uncommon with MAC infection and was identified in only 1 of the 55 patients. Of the patients with pulmonary MAC, the majority of patients had alveolar or interstitial infiltrates that were either diffuse or were not focal to the upper lobes. Only one-fourth of the patients had the classic radiographic appearance seen in immunocompetent patients. Twenty-one percent of the patients with pulmonary MAC had normal chest

radiographs. Similar findings were reported by Marinelli and colleagues [17] in their review of the radiographic findings in nine patients with AIDS and pulmonary MAC. Four of these patients had other, concurrent pulmonary diseases. The five patients with isolated MAC infection had diverse radiographic findings. Diffuse airspace opacities were seen in one patient, isolated mediastinal adenopathy in another patient, and focal pneumonia in still another. Two of the patients had normal radiographs. No cavitary or miliary disease was seen.

### Summary

Although the radiographic appearance of pulmonary MAC infection in the immunocompetent host can be varied, there are several generalizations that can be made. The classic radiographic appearance is indistinguishable from that of pulmonary tuberculosis. The classic form is seen most commonly in males and is typically associated with other predisposing diseases, especially chronic obstructive pulmonary disease. Most patients have upper lobe disease with associated pleural thickening. Widespread disease is



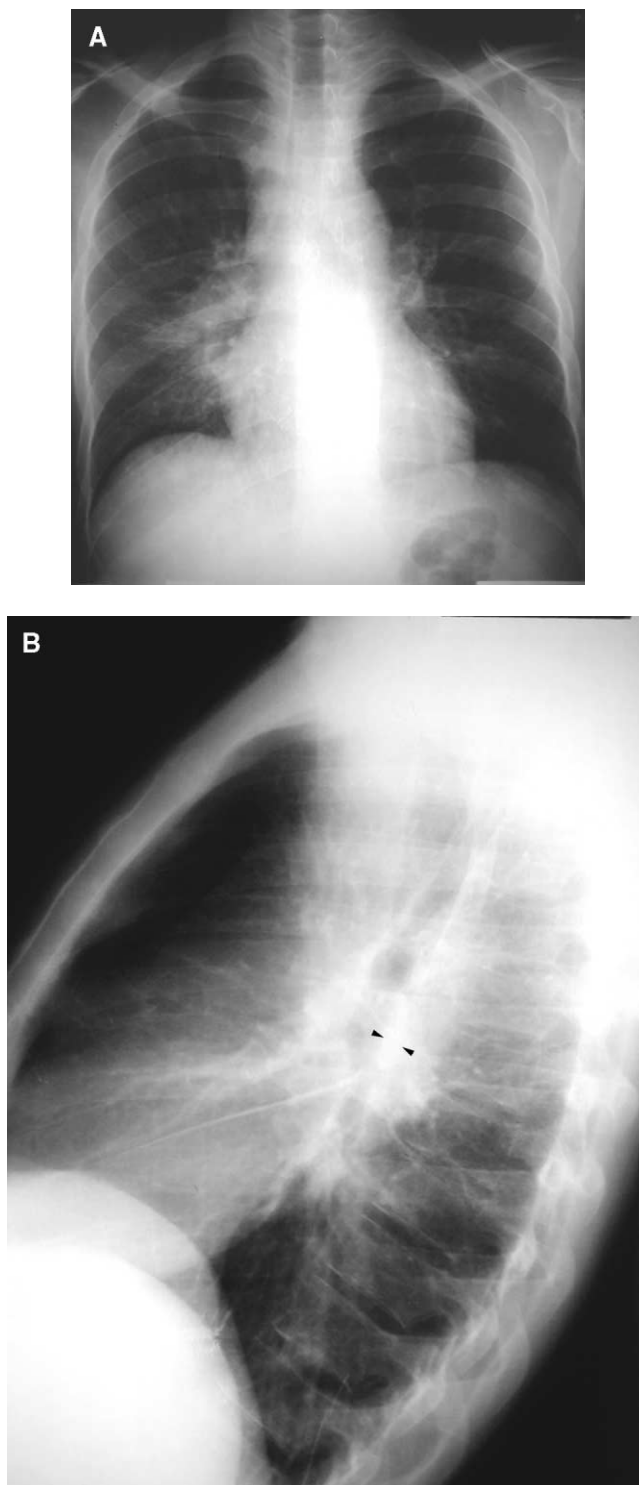


Fig. 7. Frontal (A) and lateral (B) radiographs of a 36-year-old male patient with pulmonary *M avium-intracellulare* complex and AIDS. Marked mediastinal and hilar adenopathy is present. Note thickening of the posterior wall of the bronchus intermedius (B, arrowheads).

common, as is cavitation. Pleural effusions and adenopathy are uncommon.

The Lady Windermere syndrome is a special form of pulmonary MAC seen primarily in middle-aged and elderly women. The radiographic findings are bronchiectasis and small nodules, predominately located within the middle lobe and lingula. The combination of bronchiectasis involving exclusively, or primarily, the right middle lobe and lingula is highly suggestive of pulmonary MAC, even in the face of negative sputum cultures.

Pulmonary infection with MAC in the immunocompromised patient generally reflects a widespread systemic disease. As such, the radiographic appearance is highly variable. Diffuse pulmonary opacities and adenopathy are common features. Plain radiographs are frequently normal despite active pulmonary infection.

Regardless of the clinical situation, pulmonary MAC infection is often omitted from the radiographic differential even when the appearance is characteristic. In general, when pulmonary abnormalities are identified that are consistent with a granulomatous infection, pulmonary MAC needs to be considered along with tuberculosis and fungal infection. Especially with pulmonary MAC, radiographic stability over several years does not exclude active disease. The radiographic appearance may be suggestive of the diagnosis of pulmonary MAC, but correlation with the clinical and microbiological data is necessary to confirm the diagnosis.

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