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Atypical Mycobacterial Infection in the Lung: CT Appearance[1]

The author examined computed tomographic (CT) scans of the chest from 40 patients with cultures positive for atypical mycobacteria. Common manifestations included bronchiectasis, air-space disease, nodules, and scarring and/or volume loss. Less commonly observed signs were cavities, lymphadenopathy, and pleural disease. Serial scans were obtained in 10 patients and showed new areas of bronchiectasis and progression of existing bronchiectasis, suggesting that the bronchiectasis was not a preexisting condition but resulted from infection. The anatomic distribution of the above findings was diffuse, not strongly favoring any lung zone. The identification of multifocal coexistent bronchiectasis, air-space disease, and nodules at CT should raise the possibility of atypical mycobacterial lung disease, even in an otherwise healthy patient.

Index terms: Lung, infection, 60.2031 • Mycobacteria, 60.2031

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PULMONARY disease caused by atypical mycobacterial infection has traditionally been believed to occur only in specific risk groups, such as patients with chronic lung disease or patients with deficiencies in cell-mediated immunity due to human immunodeficiency virus (HIV) infection or other causes. Recent data suggest that these infections are increasing in frequency (1) and may occur in otherwise healthy subjects, particularly elderly women (2,3). In many instances, such infections present a diagnostic and therapeutic challenge because the diagnosis is usually not initially considered, findings at chest radiography may be nonspecific and very slowly progressive, and, even if a positive culture is obtained, colonization may be difficult to distinguish from invasive pulmonary disease.

The plain radiographic appearance of pulmonary nontuberculous mycobacterial infection has been described by many authors. Christensen and colleagues (4,5) concluded that the usual appearance of pulmonary nontuberculous mycobacterial infection was upper lobe cavitary disease indistinguishable from *Mycobacterium tuberculosis*. Woodring et al (6) and Woodring and Vandiviere (7) emphasized fibroproductive disease with a potential for cavitation and a slow rate of change. Albeda and colleagues (8) concluded that cavitation was less common than with *M tuberculosis* infection and noted nodularity and lower lung zone disease. Albeda et al also noted a patchy nodular pattern associated with small cavities, which was believed to resemble, but not represent, true bronchiectasis. Spitz and Wiot (9), however, indicated that bronchiectasis could be seen in *M avium-intracellulare* infection. The discrepancies between the findings of these various studies may be explained by the different clinical, bacteriologic, radiologic, and skin testing criteria used for patient selection, as well as the limited visualization of parenchymal detail on plain radiographs.

To my knowledge, no series has been published describing the computed tomographic (CT) appearance of pulmonary atypical mycobacterial infection.

MATERIALS AND METHODS

All cultures positive for atypical mycobacteria obtained from a pulmonary source at a large city hospital between February 1988 and April 1991 were determined with examination of mycobacteriology laboratory records. Within this group, all patients who had also undergone chest CT were identified. Clinical information was obtained in this group, and all patients with a known disease process that might be expected to involve the lungs (eg, primary or metastatic malignancy, concomitant tuberculosis, other known lung disease) were eliminated from consideration, as were patients with HIV and patients whose scans were unretrievable.

Data were collected on each patient, including age, sex, known underlying diseases, date of CT, source of positive culture(s), date of collection, date of isolation, and species of positive culture(s). If only one positive sputum culture was found in laboratory records, positive cultures from other sources were recorded.

The CT scans were reviewed by a chest radiologist experienced in CT. For purposes of localizing the disease, each patient's lungs were divided into 10 zones, as depicted in Figure 1. The zones were chosen to reflect known patterns of involvement in *M tuberculosis* infection. Each zone was scored with reference to presence of bronchiectasis, air-space disease, and nodules. The presence of scarring and/or volume loss, hilar or mediastinal nodes greater than 1 cm in diameter, pleural thickening or fluid, and any other findings was also noted.

Each focus of bronchiectasis was graded

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Abbreviations: AIDS = acquired immunodeficiency syndrome, HIV = human immunodeficiency virus.

as mild (diameter of the bronchus was slightly larger than that of the accompanying vessel), moderate, or severe (diameter of the bronchus was at least two times larger than that of the vessel or there were cystic bronchiectatic changes). Air-space disease was categorized as an area of ground-glass attenuation or patchy or dense consolidation. The size of nodules was noted (< 5, 5–10, > 10 mm). If thin-section CT scans had been obtained, this was noted. In patients in whom serial scans were obtained, each scan was graded separately and any changes were noted.

RESULTS

Clinical Data

Forty-four patients satisfied the inclusion criteria. Four patients were eliminated because they had normal CT scans and, therefore, colonization was suspected. The resulting study population was composed of 40 patients (26 women and 14 men). The mean age of the women was 67.8 years, and the mean age of the men was 62.9 years. Most subjects were outpatients referred for specialized pulmonary medicine or thoracic surgery consultations because of progressive pulmonary disease. Atypical mycobacterial infection had already been diagnosed in some patients. Because the screening criteria excluded patients with certain underlying diseases, most patients were in otherwise good health. CT was performed with GE 9800 (GE Medical Systems, Milwaukee, Wis), Technicare 1440, or Technicare 2060 (Technicare, Cleveland, Ohio) scanners. The time between CT and a positive culture ranged from 0 to 6.5 months (mean, 1 month).

Thin-section CT scans were available in 29 patients. These scans had been performed either at arbitrarily chosen levels or to clarify abnormal areas. These 1.5- or 2-mm-thick sections were reconstructed by using high-spatial-frequency algorithms, but the scans were not targeted. Ten patients had two to four serial CT scans (total, 31 scans), with follow-up ranging from 2.5 to 42 months (mean, 12.4 months). Reports of findings from previously obtained CT scans were available for three additional patients, with maximum follow-up of 58 months.

Source(s) of positive cultures included sputum culture in 19 patients (one to 10 positive cultures per patient), bronchial washing in nine, tissue from open lung biopsy in five, needle aspiration biopsy in three, both bronchial washing and sputum culture in two, both needle aspiration biopsy and sputum culture in one, and bronchial brushing in one.

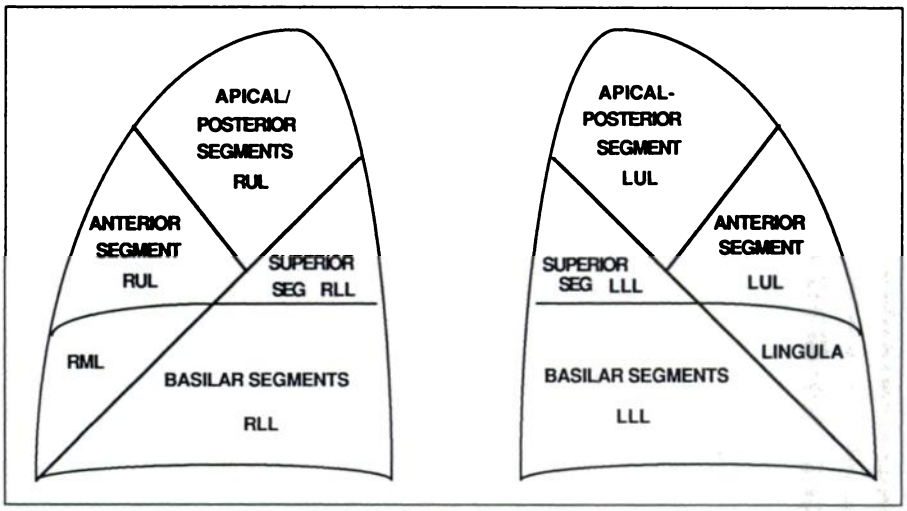


Figure 1. Illustration of the 10 lung zones used for CT analysis. The two lungs are depicted as though opened like a book. *LLL* = left lower lobe, *LUL* = left upper lobe, *RLL* = right lower lobe, *RML* = right middle lobe, *RUL* = right upper lobe, *SEG* = segment.

Table 1
Summary of CT Findings

Finding	Group A (n = 33)	Group B (n = 7)	Total (n = 40)
Bronchiectasis	79 (26)	86 (6)	80 (32)
Air-space disease	76 (25)	57 (4)	73 (29)
Nodules	76 (25)	43 (3)	70 (28)
Cavities	21 (7)	14 (1)	20 (8)

Note.—Data are given as percentages. Numbers in parentheses are numbers of patients.

Thirty-three patients with positive cultures obtained from invasive procedures or two or more sputum samples were analyzed as a group (group A). Seven patients with one positive sputum culture were considered possible cases and analyzed separately (group B). The frequencies of bronchiectasis, air-space disease, nodules, and cavities in the two groups were compared by using the Fisher exact test.

Species cultures included *M avium* complex (n = 34), *M fortuitum* (n = 2), *M terrae* (n = 1), *M xenopi* (n = 1), an unidentified non-*avium* Runyon group III species (n = 1), and a combined infection with *M avium* complex and *M chelonae* (n = 1). Slides from three surgical specimens (all from patients in group A) were available for review and correlation with CT findings.

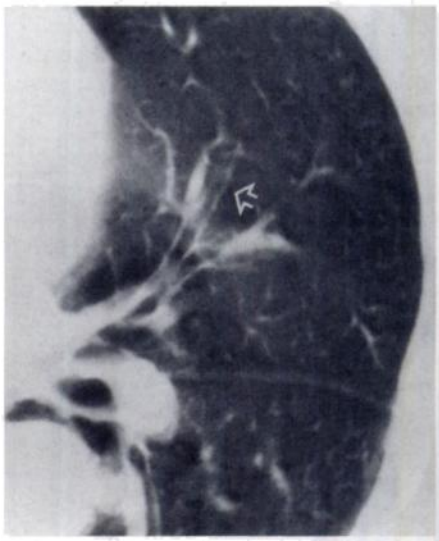
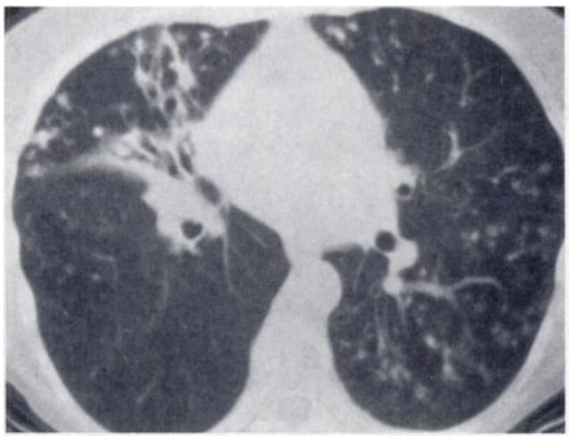


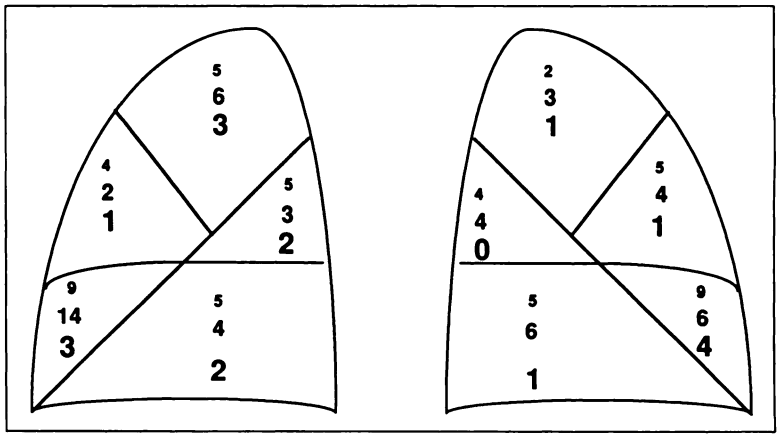
Figure 2. CT scan of mild lingular bronchiectasis (arrow), with the caliber of the bronchus slightly exceeding that of the accompanying vessel.

CT Appearance

Sixty-one scans were available in the 40 patients. CT findings encountered in the two patient groups are summarized in Table 1. There was no significant difference in the frequencies of bronchiectasis (P > .99), air-space disease (P > .99), nodules (P > .99), or cavitation (P > .99) between group A and group B.

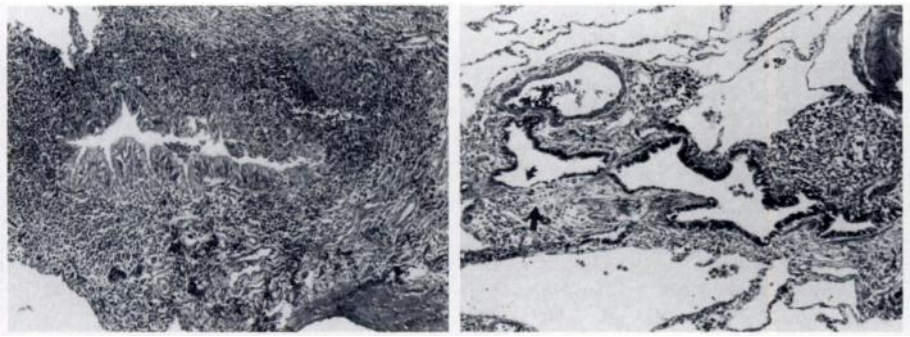
Bronchiectasis.—The most commonly encountered CT finding was





3. 4.

Figures 3, 4. **(3)** Severe bronchiectasis in the right middle lobe. The caliber of the bronchus is two times larger than that of the vessel. Note also nodular changes in the left lung. **(4)** Distribution of mild (small numbers), moderate (medium-size numbers), and severe (large numbers) bronchiectasis in the 10 lung zones. (Data are displayed on a per patient basis [40 patients, 61 scans].)



5. 6.

Figures 5, 6. **(5)** Extensive peribronchial mononuclear cell inflammatory infiltrate surrounds a bronchus in a patient with *M intracellulare* infection. **(6)** Photomicrograph obtained from another patient who, despite undergoing wedge resection of right middle lobe bronchiectasis and the presence of a normal follow-up scan, experienced recrudescence of bronchiectasis in that lobe. The original surgical specimen demonstrates marked thinning of the bronchial mucosa and extensive fibrosis adjacent to these regions (arrows).

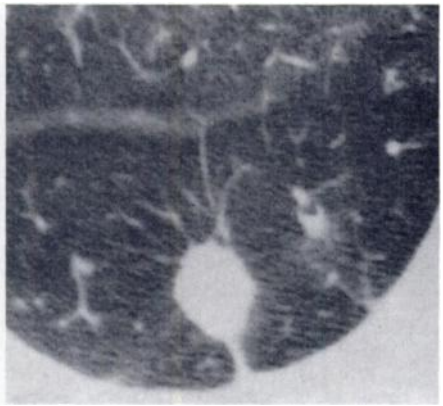
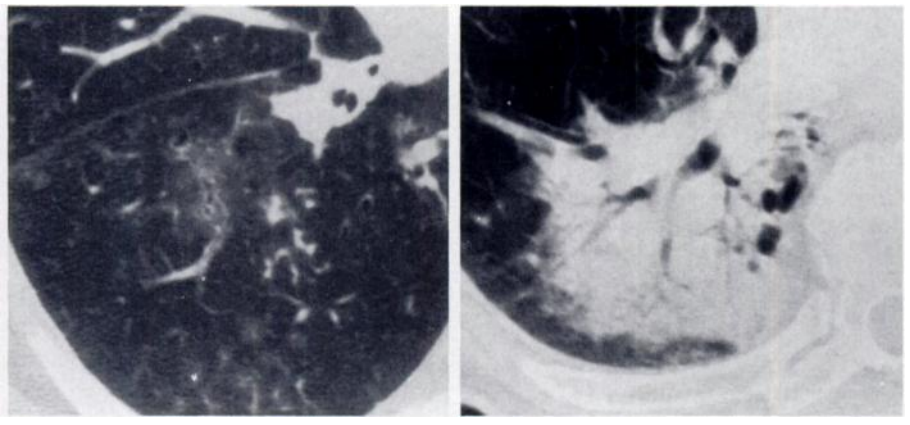


Figure 9. CT scan shows a nodule caused by *M avium* complex infection, which was diagnosed by means of needle aspiration lung biopsy. This nodule demonstrates pleural and fissural tags.



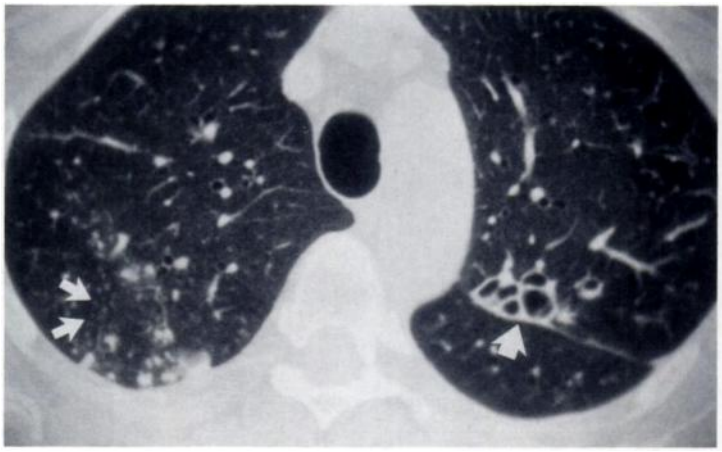
7. 8.

Figures 7, 8. **(7)** CT scan shows air-space disease appearing as an area of ground-glass attenuation in the right lower lobe. **(8)** CT scan shows dense right lower lobe consolidation and air bronchograms.

bronchiectasis, occurring in 26 (79%) of the 33 patients in group A and six (86%) of the seven patients in group B. Mild and severe bronchiectasis are demonstrated in Figures 2 and 3. The lung zone distribution of mild, moderate, and severe bronchiectasis for both patient groups is depicted in Figure 4. Although seen in all lung zones, bronchiectasis was most common in the middle lobe and lingula. In some cases, mucus plugs were present within the dilated bronchi. Most bronchial walls appeared thickened in the affected areas.

In two patients, pathologic specimens that correlated with areas of bronchiectasis seen on CT scans demonstrated inflammatory mononuclear cell infiltrates surrounding bronchial structures (Fig 5). In some areas, marked thinning of the bronchial mucosa was noted associated with scarring in the peribronchial tissues, thought to represent residua of previous inflammation (Fig 6).

Air-space disease.—Air-space disease was observed in 25 (76%) of the 33 patients in group A and four (57%) of the seven patients in group B. Nineteen cases (75%) of air-space disease appeared as patchy consolidation, with the remainder evenly divided between areas of ground-glass attenuation (Fig 7) and dense consolidation



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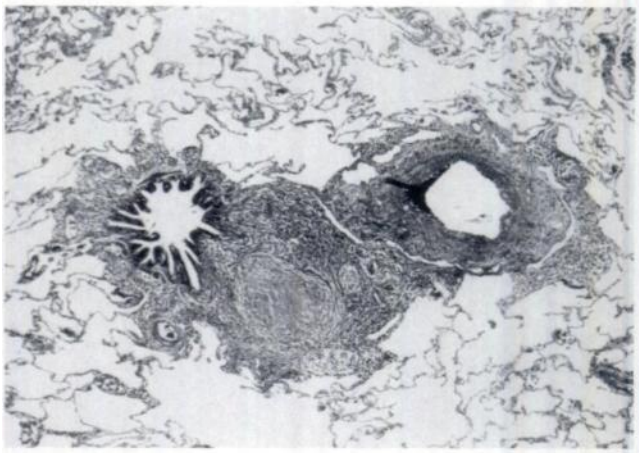


11.

Figures 10, 11. **(10)** CT scan shows nodules of various sizes in the right upper lobe. Note the tree with leaves appearance of transbronchial spread (small arrows). Note also cystic bronchiectasis in the left upper lobe (large arrow). **(11)** Photomicrograph shows a 1-mm discrete granuloma in the region of a bronchovascular bundle. Also note a mononuclear cell infiltrate around the bronchus and pulmonary artery branch.

(Fig 8). Overall, air-space disease showed a slight predominance in the lower lung zones and apices.

Two pathologic specimens from areas showing patchy air-space disease were available. These specimens showed areas of inflammatory thickening of alveolar walls, loosely grouped granulomas, and/or coalescent inflammatory infiltrates and fibrosis completely replacing normal alveoli.

Nodules.—Twenty-five (76%) of the 33 patients in group A and three (43%) of the seven patients in group B had parenchymal nodules. These included well-circumscribed nodules with smooth borders (generally less than 1 cm in diameter), larger masses with ill-defined borders, and spiculated nodules with or without pleural tagging (Fig 9). Relatively well-defined tiny nodules were usually clustered in a "tree with leaves" centrilobular pattern, suggestive of a transbronchial spread of disease (Fig 10).

Resected specimens showing this pattern demonstrated discrete granuloma formation, usually in the peribronchial tissues (Fig 11). Larger discrete nodules consisted of larger, usually caseating, granulomas or a contiguous grouping of multiple granulomas (Fig 12).

Nodules were relatively evenly distributed among the 10 lung zones in the 40 patients analyzed. Forty-two zones contained one or more nodules smaller than 5 mm in diameter, 25 contained nodules 5–10 mm in diameter, and 24 contained nodules larger than 10 mm in diameter.

Cavitation.—Parenchymal cavities were observed in seven (21%) of the 33 patients in group A and one (14%) of the seven patients in group B. Cavities had relatively thick walls, were without air-fluid levels, and ranged in size from 1.5 to 3 cm (Fig 13). The overall distribution of cavities is depicted in Figure 14. Resected cavities were not available for examination.

Other findings.—Overall, 11 (28%) of the 40 patients demonstrated evidence of substantial volume loss or scarring. These findings were usually accompanied by other parenchymal abnormalities, such as air-space disease, bronchiectasis, or nodules.

Hilar or mediastinal nodes larger than 1 cm in diameter were present in seven (18%) of the 40 patients. None of these nodes contained calcification. Pleural effusion and/or pleural thickening was observed in three (8%) of the 40 patients. Unilateral bullous emphysema, mild interstitial fibrosis, and pericardial effusion were seen in one patient each.

Coexistence of air-space disease, nodules, and/or bronchiectasis.—Of the 400 lung zones examined in the 40 patients, 159 zones showed nodules, air-space disease, and/or bronchiectasis at some point in the clinical course. Eighty-one lung zones demonstrated only one of these three findings. Sixty-five lung zones demonstrated two of these three findings. Twelve lung zones demonstrated all three findings. Thirty-nine patients showed nodules, air-space disease, and/or bronchiectasis at some time in the clinical course. Nine patients had only one of these three findings, 10 had two of these three findings, and 20 had all three findings.

Findings on Serial Scans

Ten patients (all from group A) had serial CT scans available for review. Of the 100 possible lung zones, new

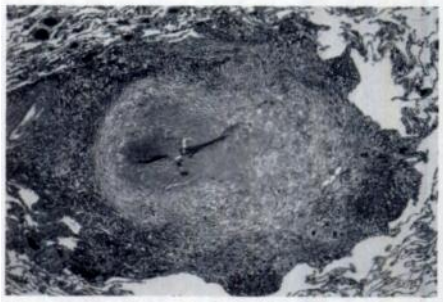


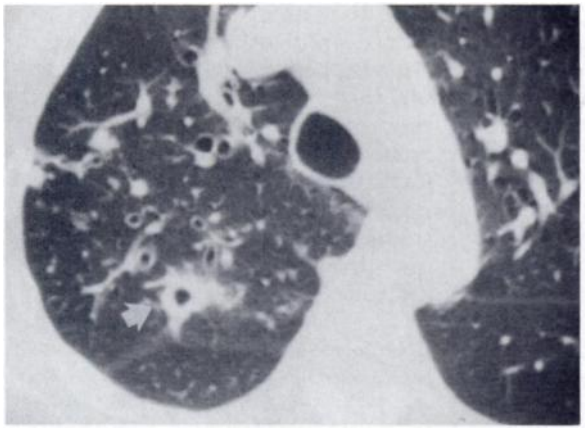
Figure 12. Photomicrograph shows one of a cluster of 5–10-mm nodules showing central caseating necrosis. Note also adjacent areas of inflammatory infiltration of the alveolar walls.

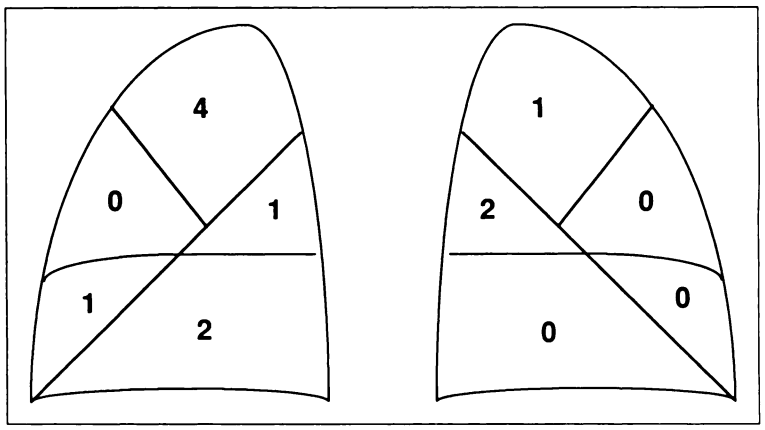
involvement of previously normal lung zones occurred in 12 zones. New bronchiectasis appeared in 10 zones, preceded by nodules in three zones and by surgically resected bronchiectasis in one (Fig 15). Bronchiectasis, eventually present in all 10 patients with serial scans, became more severe in six zones and less severe in one.

The new appearance of nodules in a given zone occurred in 10 of the 100 zones, three of which had preexisting bronchiectasis. Six zones with previous nodular disease cleared or showed improvement.

New air-space disease appeared in nine zones, preceded by nodules and/or bronchiectasis in four. Five zones showed new cavities, preceded by bronchiectasis and/or nodules in two. One zone showed resolution of a previous cavity.

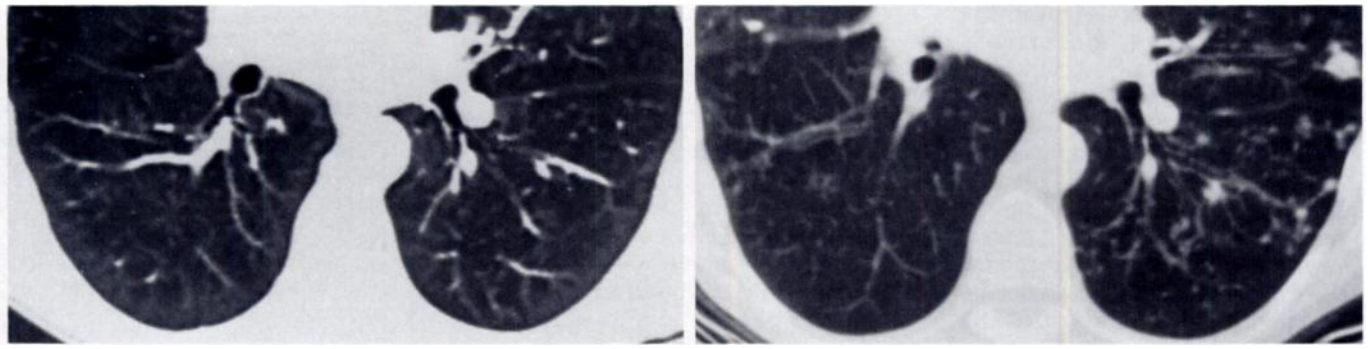
Nine of the 10 patients demonstrated overall progression of disease; one patient (with a 3-month follow-up period) was clinically stable. In three additional patients in whom only reports from previously obtained





13. 14.

Figures 13, 14. **(13)** CT scan shows cavitary nodule with relatively thick walls (arrow) in the right upper lobe. Note the fissural tag. **(14)** Distribution of cavitary disease in the 10 lung zones. (Data are displayed on a per patient basis [40 patients, 61 scans].)



a. b.

Figure 15. Baseline CT scan (5-mm-thick sections) **(a)** and technically similar image obtained at the same level 39 months later **(b)** demonstrate the development of bronchiectasis and nodules. Ten sputum cultures positive for *M avium* and/or *M chelonae* were obtained during the study period.

Table 2
Nontuberculous Mycobacteria That Cause Pulmonary Disease in Humans

Runyon Group	Species of Mycobacteria
I. Photochromogens	*M kansasii*
	M simiae
	M asiaticum
II. Scotochromogens	*M scrofulaceum*
	M xenopi
	M szulgai
	M gordonae
III. Nonchromogens	*M avium/intracellulare*
	M malmoense
	M terrae
IV. Rapid growers	*M fortuitum/chelonae*

CT scans were available for comparison, disease was judged to have progressed in overall severity and/or extent.

DISCUSSION

Within the family of mycobacterial disease, *M tuberculosis* and *M leprae* (leprosy) have long been recognized as human pathogens. Atypical mycobacteria, for years believed to be commensal organisms, have only recently been recognized as responsible for clinically important disease. In 1954, Timpe and Runyon (10) proposed a classification system based on culture characteristics of the different species and emphasized the role of these organisms in human disease. In the Runyon classification system, atypical mycobacteria are separated into four groups on the basis of culture characteristics: Photochromogens produce colored colonies when exposed to light, scotochromogens produce colored colonies regardless of lighting conditions, nonchromogens produce white colonies regardless of lighting conditions, and rapid growers produce colonies rapidly in comparison with the other species. The atypical mycobacteria that may cause pulmonary disease are listed in Table 2. These organisms show substantial geographic variation in both species encountered and the prevalence of infection in the population. The bacteria are found in soil, water, dairy products, and bird droppings.

In the past, patients with chronic diseases such as lung cancer, preexisting chronic lung disease, or immunosuppression have been thought to be the usual hosts of pulmonary atypical mycobacterial infection. More recently, patients with HIV infection have become a recognized risk group. However, in 1989, Prince and colleagues (2) identified a group of patients, predominantly elderly women, with clinically important pulmonary infection caused by *M avium* complex, but without the classic predisposing conditions. These infections were the cause of substantial morbidity and mortality.

Most patients in this study were from the Boston area. During data collection, it was observed that atypical mycobacterial species represented about 80% of the positive cultures for mycobacteria in the hospital laboratory. Isolates of nontuberculous species have increased substantially during the past 10 years in the Boston area (11), and this rise appears to be

due to patients without the acquired immunodeficiency syndrome (AIDS) as well as those with it. This differs from the San Francisco experience, in which patients with AIDS account for the entire observed increase in atypical mycobacterial infections (12). The municipal water supply in the Boston area is known to have a high frequency of contamination by atypical mycobacterial organisms, and infection by inhalation of aerosolized water (eg, during showering) has been postulated (11).

The radiologic diagnosis of atypical mycobacterial infection with plain radiographs may be difficult in the absence of cavitary disease because the findings may be subtle. The high proportion of cavitary disease in a recent national survey suggests that early or noncavitary forms of disease are not easily recognized clinically (1). Patients may present with a variety of nonspecific symptoms such as asthma, cough, dyspnea, or hemoptysis. The relatively slow progression of radiographic findings (often requiring several years to demonstrate changes) may contribute to a delay in diagnosis. Woodring et al (6) noted delays in the diagnosis of atypical mycobacterial infection of up to 16 years in their series, and also noted that in no case did the radiologist suggest the correct diagnosis.

CT of the chest may help suggest atypical mycobacterial infection in many of these patients. As described in this study, the multifocal appearance of bronchiectasis, nodules of varying sizes, and air-space disease should be suggestive of atypical mycobacterial infection, particularly because there are very few disease processes that would be expected to have this unusual constellation of findings. The differential diagnosis would also include *M tuberculosis* and, less typically, bronchiolitis obliterans, sarcoidosis, and possibly fungal disease.

Contrary to popular teaching, the data from serial CT scans in this study strongly suggest that atypical mycobacteria caused bronchiectasis in these cases, rather than being present as a commensal organism colonizing preexisting bronchiectasis. This idea is supported by clear progression of bronchiectasis, both in severity and the involvement of new locations. It is also supported by the presence of nodules and air-space disease preceeding or following the appearance of bronchiectasis and by the presence of bronchiectasis in relatively unusual locations in this group of patients.

These observations regarding the distribution and appearance of parenchymal disease due to atypical mycobacteria are in opposition to some aspects to the official statement regarding nontuberculous mycobacterial disease from the American Thoracic Society adopted in March 1990, that "[nontuberculous mycobacteria] tend to cause thin-walled cavities with less surrounding parenchymal infiltrate, have less bronchogenic but more contiguous spread of disease, are more likely to involve the apical and anterior segments of the upper lobes, and produce more marked involvement of pleura over the involved areas of the lungs [than *M tuberculosis*] . . ." (12). With the advantage of the spatial resolution and precise anatomic localization afforded with CT images, these concepts can be reevaluated. It now appears that the lungs may be diffusely involved, that pleural disease is rare, and that patterns indicative of bronchogenic spread are common.

Many different criteria have been proposed for differentiating between pulmonary atypical mycobacterial infection and colonization. Those presently in use rely on multiple cultures and positive findings at plain radiography. The requirement for numerous positive sputum cultures and clear-cut plain radiographic findings appears to select for the presence of cavitary disease because cavities tend to produce a high percentage of positive cultures and are more obvious on plain radiographs than are, for example, small nodules or bronchiectasis (14). Such criteria may underestimate the numbers of cases of clinically important disease.

Although the cases in group B would generally be regarded as questionable or possibly merely cases of colonization, it is clear from the CT findings that marked, and otherwise unexplained, parenchymal disease was present. This disease was indistinguishable in appearance and degree from those seen in the better-documented cases in group A. In the future, CT may enable more accurate evaluation of the significance of a positive culture for atypical mycobacteria and may suggest in which patients more aggressive diagnostic procedures may be in order. Because the disease tends to be progressive, early identification and treatment is viewed by some as desirable; surgery may be successful in patients with localized disease.

In generalized disease, multiple drugs are administered, although there is a high degree of drug intolerance, particularly in elderly patients. Relapse often occurs after discontinuation of therapy, necessitating indefinite treatment, and disease often progresses despite therapy (15,16). Further study is needed to determine if CT can provide a clinically meaningful evaluation of therapeutic response or failure in this group of diseases, which are often notoriously difficult to treat. ■

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