Mycobacterium avium Complex Pulmonary Disease Presenting as an Isolated Lingular or Middle Lobe Pattern*

The Lady Windermere Syndrome

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Background: Pulmonary disease due to Mycobacterium avium complex (MAC-PD) radiographically resembles that due to tuberculosis; it preferentially affects elderly white men with predisposing pulmonary disorders (PDPD).

Methods: Twenty-nine patients with MAC-PD were identified from a community-based population, and the medical records and chest roentgenograms (CRs) of six with a previously undescribed pattern of MAC-PD were reviewed. The distinctive clinical and demographic features of these six patients were identified and summarized.

Results: All were women who tended to be elderly. None had clinically evident PDPD. The dependent portion of the lingula or its counterpart, the middle lobe, was initially affected. Hilar adenopathy, volume loss, and cavitary disease were uniformly absent.

Conclusions: To account for the distinctive features of this syndrome, we offer the hypothesis that habitual voluntary suppression of cough may have led to the development of nonspecific inflammatory processes in these poorly draining lung regions, upon which MAC-PD engrafted. We offer the term, Lady Windermere's syndrome, to describe this pattern among elderly women and to suggest that their fastidiousness may be its root cause.

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Pulmonary disease due to Mycobacterium avium complex (MAC-PD) radiographically resembles that due to reinfection tuberculosis, initially and predominantly involving the upper lobes.1-5 A less frequent multinodular form has been emphasized by Prince et al.6 The responsible organisms are lower in virulence than M tuberculosis. As a result, they are causative agents of disease principally among persons with clinically apparent predisposing pulmonary disease (PDPD), most often one or more of the following: inactive tuberculosis; bronchiectasis; pneumoconiosis; and chronic obstructive pulmonary disease.7-9 The occurrence of MAC-PD in normal individuals is said to be uncommon,7 although more recent evidence suggests otherwise.6,9,10 For unknown reasons, white and male subjects are affected preferentially.7,11 Possibly because a PDPD is most often manifest prior to the development MAC-PD, the latter occurs at a later age on average than does tuberculosis.7,12

We recently reported a new pattern of presentation of MAC-PD in which, in contrast to the expected radiographic and epidemiologic pattern, the disease was limited at onset to the lingula or middle lobe, PDPD was not clinically evident, and those afflicted were female patients.10 This report expands those clinical and radiographic observations and proposes a mechanism which could account for the distinctive features of what appears to be a clinical syndrome.

Materials and Methods

In a prior report, we described the research setting and the methodology employed to identify and evaluate cases of MAC-PD over a period of 12 yr in a nonreferral population.19 Briefly, all isolates of MAC from pleuropulmonary sources resulted in a medical record review. When indicated, chest roentgenograms (CRs) were reviewed by the senior author. Patients whose CRs were compatible with a diagnosis of mycobacterial disease and from whom MAC was repeatedly recovered in profusion or in whom caseating granuloma were identified in pathologic material from which the organism had previously or subsequently been isolated were considered as cases. Twenty-nine persons (excluding two cases of acquired immune deficiency syndrome) met these criteria, of whom six (21 percent) comprise this report.

Case Reports

Case 1

A 45-yr-old nonsmoking white female office worker developed a nonproductive cough and left submammary pleuritic pain in May 1976. A 3-cm infiltrate involving only the most dependent portion of the lingula was observed (Fig 1). A 1965 CR was normal. The results of fiberoptic bronchoscopy (FB) were normal except for a return of turbid material on washing the lingular bronchus. Fluorescent stain for mycobacteria showed rare organisms. Culture of the washings grew 4 + MAC. Treatment was initiated with isoniazid (INH), ethambutol (EMB), rifampin (RMP), streptomycin (SM), and ethionamide (ETA). Therapy with INH and ETA was discontinued because of intolerable side effects. Cough and pleurisy disappeared after 6 mo of treatment with the three remaining drugs, and a lingulectomy was performed. The lingula was abnormal only in its distal portion, where atelectatic and nodular changes were observed. Microscopic examination revealed numerous caseating granulomata.

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and bronchiectasis. Material for culture was inadvertently discarded. Therapy with RMP and EMB was continued for an additional 6 mo. Continued observation for 9 yr revealed no evidence of recurrence.

**Case 2**

A 70-yr-old nonsmoking white housewife presented in January 1982 with symptoms of cough productive of sparse yellow-green sputum and night sweats. A CR revealed a peripheral middle lobe infiltrate which gradually increased in extent over time. Prior CRs were normal. Failure to respond to therapy with a variety of antibiotics led to the performance of FB, which revealed scattered flecks of purulent material. The middle lobe bronchus appeared normal. Washings showed 1+ with Ziehl-Neelsen stain and 2+ with fluorescent stain. Subsequently, multiple sputum specimens were positive on smear and culture for MAC. In May 1982, treatment was initiated with INH, RMP, ETA, kanamycin (KM), and EMB. The symptoms and radiographic abnormalities resolved completely in 12 mo. The patient was free of relapse 54 mo after therapy was terminated.

**Case 3**

A 76-yr-old nonsmoking white housewife developed a nonproductive cough in February 1986. A CR revealed an infiltrate in the lingula (Fig 2). No prior CRs were available for comparison; FB revealed pus originating in the lingula and the posterior basal segment of the left lower lobe. Washings showed 2+ on Ziehl-Neelsen stain; culture was strongly positive for MAC. Two years of treatment with INH, EMB, and RMP eliminated the cough and halved the extent of the infiltrate.

**Case 4**

A 57-yr-old nonsmoking Asian housewife developed repeated hemoptysis and left pleuritic pain in September 1985. A CR revealed a lingual infiltrate (Fig 3). A 1984 CR was normal. At FB, the lingual orifice was observed to be reddened; the mucosa was edematous and friable. Washings showed 2+ with fluorescent stain, and culture revealed numerous MAC. Therapy consisted of INH, RMP, and EMB for 3 mo; INH and RMP for an additional 3 mo; and bronchiectasis. Material for culture was inadvertently discarded. Therapy with RMP and EMB was continued for an additional 6 mo. Continued observation for 9 yr revealed no evidence of recurrence.

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The radiographic features identified in points 4, 5, and 6 distinguish these cases from "middle lobe syndrome" and primary mycobacterial disease.

**Discussion**

The clinical and radiographic similarities of these six patients appear to comprise a distinct clinical syndrome, the cardinal features of which are (1) initial involvement of the periphery of the lingula or of its counterpart, the middle lobe; (2) absence of clinically evident PDPD; and (3) exclusivity of the features to female patients. These features, which implied a common pathogenetic mechanism peculiar to this group and distinct from that operating in the usual case of MAC-PD, gave rise to the following analysis.

The lingula and its homologue, the middle lobe, have in common long, narrow, and, in the upright position, dependent bronchi. Brock\(^3\) emphasizes the descending direction of the lingular bronchus as a feature predisposing it to infection, particularly bronchiectasis. Because nonspecific inflammatory processes are frequently seen in the dependent portions of these lobes,\(^4\)-\(^6\) they are considered unsuitable sites for open lung biopsy in patients with diffuse lung disease.\(^14\) From these observations, it seems reasonable to infer that these regions of the lung clear secretions less efficiently than their counterparts elsewhere, and also that they may require greater tussive effort to do so. A comprehensive search of the medical literature failed to elicit any information on differential clearance rates of the segmental bronchi.

Female exclusivity led us to consider in what way a gender difference might account for a propensity for developing disease in these regions of the lung. The
medical apothegm, "Ladies don't spit," embodies the idea that female patients are more fastidious and hence more likely to regard expectoration as socially unacceptable behavior. If the regions of the bronchial tree under consideration are more dependent than others upon voluntary expectoration to clear secretions, it follows that voluntary suppression of forceful coughing could lead to the development of postobstructive pneumonitis, pulmonary fibrosis, or focal bronchiectasis in the tips of these lobes. This would provide a locus minoris resistentiae, similar in character to the diffuse PDPD, upon which MAC-PD might secondarily engraft.

Because this hypothesis was engendered by a retrospective case review, no inquiries were made concerning the patients' habits of expectoration. No reports of pulmonary disease either caused or influenced by the mechanism of voluntary suppression of expectoration were found in a comprehensive search of the medical literature. Therefore, two examples, derived from the senior author's pulmonary referral practice, are put in evidence (see appendix).

CONCLUSIONS

A syndrome of MAC-PD which represents a clear departure in both clinical and radiographic features from the anticipated pattern has two important consequences.

1. The correct diagnosis may be delayed or missed in this group of patients unless this unusual pattern is recognized and appropriate diagnostic studies employed. If MAC is isolated in profusion, even in atypical circumstances, it should not be discounted as a comensal.

2. The syndrome implies a different pathogenesis from the usual case. To account for the three distinctive features of this syndrome, we hypothesize that habitual voluntary suppression of expectoration permits the evolution of a nidus of inflammatory disease at the tip of the lingula or middle lobe, upon which MAC becomes engrafted; once initiated, tussive suppression is overcome. We offer the term, Lady Windermere's syndrome, from the Victorian-era play, Lady Windermere's Fan, to convey the fastidious behavior hypothesized: "How do you do, Lord Darlington. No, I can't shake hands with you. My hands are all wet with the roses."17

Support for this hypothesis could come from a variety of sources: recognition of the same or similar syndromes by others; determination of whether non-specific inflammatory processes in the dependent portions of the lingula or middle lobe are more common in female patients; structured psychologic interviews of affected patients; tussive provocation studies; and studies of the differential clearance rates of the bronchial segments.

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APPENDIX A

CASE A

A 34-yr-old nonsmoking woman previously in good health except for benzodiazepine abuse was referred for FB to evaluate hemoptysis and bilobar atelectasis. At high altitude, she had experienced severe posterior epistaxis requiring nasal cauteryization and posterior nasal packing. Large quantities of blood were expectorated at the time of the procedure and small blood clots thereafter. Upon examination ten days after the cauteryization, she reported that she attempted to suppress her cough because of the "repulsiveness" of the material she had expectorated. Examination showed anterior nasal synchia, rightward tracheal deviation, and impaired breath sounds over the posterior right thorax. A CR revealed atelectasis of the middle and right lower lobes (Fig 4). Bronchial obstruction due to retained blood clots was suspected, and the patient was advised to dislodge them by coughing forcefully. A follow-up CR one week later revealed complete resolution.

CASE B

An 89-yr-old nonsmoking retired schoolteacher, known to be tuberculin-positive since childhood, presented with protracted symptoms of fever and cough. Physical examination revealed scattered rhonchi, and a CR demonstrated widespread patchy infiltrative changes affecting predominantly the bases of both lungs (Fig 5). Despite vigorous urging and induction attempts using ultrasonically nebulized hypertonic saline solution, the patient failed to expectorate sputum. At FB, 15 ml of purulent secretions was found widely distributed throughout the bronchial tree and were strongly positive on smear and culture for M tuberculosis. The radiographic pattern of tuberculosis in which the lung bases are affected preferentially was frequently observed in European sanitaria during the preantibiotic era when patients were enjoined to suppress their coughs as a public health measure (Jacques Cretien, M.D., oral communication, May, 1989).

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