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CASE REPORT

The Lady Windermere Syndrome

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Abstract

Lady Windermere syndrome is right middle lobe or lingular segment bronchiectasis due to *Mycobacterium avium intracellulare* infection. In this brief report we describe two cases with contrasting clinical courses and discuss controversies regarding aetiology, pathogenesis and treatment. Hypotheses explaining middle lobe predilection are discussed and an alternative hypothesis is offered.

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Introduction

Lady Windermere syndrome is right middle lobe or lingular segment bronchiectasis due to *Mycobacterium avium intracellulare* infection. We describe two cases with contrasting clinical courses and discuss controversies regarding aetiology and treatment.

Case reports

Patient 1

An 82-year old thin female presented with dry cough and dyspnoea for two years. There was no history of fever, postnasal drip, gastroesophageal reflux, anorexia or weight loss. She did not have any significant travel history nor did she have any contact with pets. She had smoked for about a year and had quit smoking 40 years ago.

On examination, she had rales over the right anterior chest. Examination of the heart and abdomen was unremarkable. Chest radiograph showed right middle zone infiltrates (Figure 1). High resolution CT of the chest revealed multiple nodules in the right upper lobe with right middle lobe bronchiectasis (Figure 1). Bronchoalveolar lavage showed acid fast bacilli, shown to be *Mycobacterium avium intracellulare* by DNA probe analysis. She declined therapy, fearing adverse drug effects. She continues to cough, and has progressively worsened.

Patient 2

A 63-year old female presented with a one-year history of dry cough associated with intermittent low grade fever. The cough was described as being worse on lying down. There was no history of dyspnoea, haemoptysis, anorexia or weight loss. She did not have any symptoms of gastroesophageal reflux, sinusitis or allergies. She had recently traveled to Arizona, Bermuda and the Caribbean. She did not have any pets at home. She was hypertensive and had mitral valve prolapse without regurgitation. She was socially active and had never smoked. She did not take any medications which could induce chronic cough.

Physical examination revealed a thin woman in no apparent distress. Examination of the heart, chest and abdomen was essentially normal. Chest radiograph revealed right middle zone infiltrate which was new compared to a radiograph from seven years ago (Figure 2). High resolution CT of the chest showed right middle lobe bronchiectasis (Figure 2). She had normal spirometry. Bronchoscopy showed purulent secretions from the right middle and lower lobes. There was no endobronchial lesion, and the right middle lobe bronchus orifice was not narrow or acutely angled. Acid fast bacilli were seen in bronchial lavage and brush specimens. DNA probe revealed *Mycobacterium avium intracellulare*. She was treated with azithromycin, rifampin and ethambutol,

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Figure 1. Patient 1: Chest radiograph on left showing bilateral reticular infiltrates and high resolution CT chest on the right showing right middle lobe bronchiectasis.

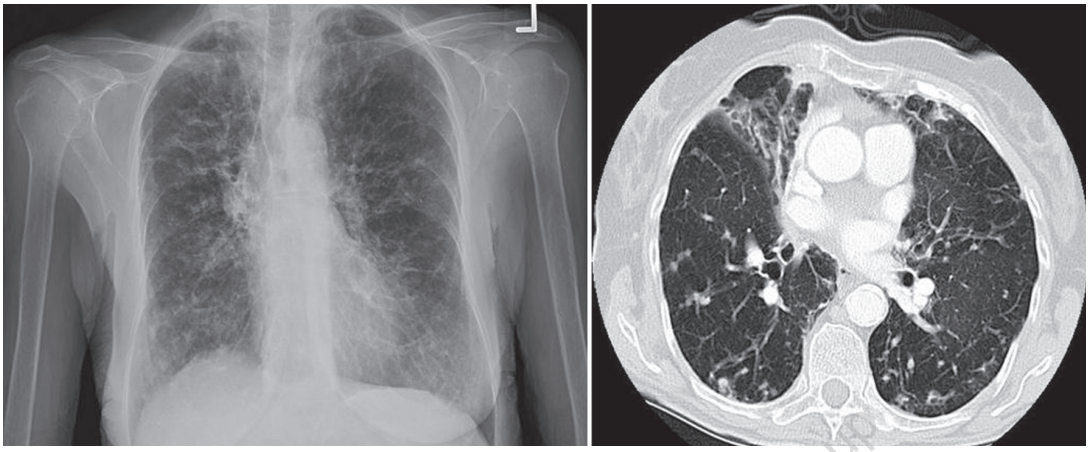
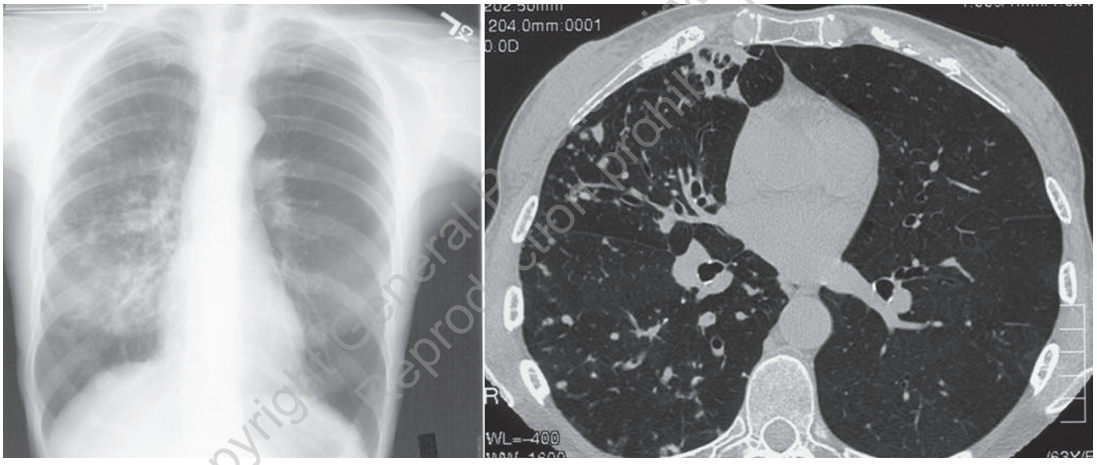


Figure 2. Patient 2: Chest radiograph on left showing right mid zone infiltrates and high resolution CT chest on the right showing nodules and bronchiectasis in the right middle lobe.



which she has taken for one and half years now, tolerated well, and she has responded well.

Discussion

Mycobacterium avium complex (MAC) pulmonary disease has traditionally been seen in the immunocompromised and in patients with pre-existing structural lung disease. This view changed with the recognition of MAC pulmonary disease without the above predispositions,[1] seen predominantly in elderly, otherwise healthy non-smoking women.[2] Increasing awareness has lead to recognition of more such cases, and the American Thoracic Society has formulated criteria for its recognition.[3]

In immunocompromised states, MAC involvement of the lung represents a disseminated disease, is frequently cavitary, and follows an aggressive course. Manifestation in other patients follows three clinico-pathologic and radiologic patterns.[4] The fibrocavitary form is seen in older patients, mostly males, with a history of smoking and underlying pulmonary disease like COPD and bronchiectasis. Hot tub lung disease, seen in the young and middle aged, presents with diffuse interstitial and nodular infiltrates; whether this is due to aerosolised MAC infection or a form of hypersensitivity pneumonitis remains unresolved. In 1992, a new subtype, the Lady Windermere syndrome – defined as a constellation of reticulonodular infiltrates with cylindrical bronchiectasis involving the right middle lobe or lingular segment bronchiectasis due to *Mycobacterium avium intracellulare* infection – was described.[5]

The syndrome is named after a supposedly fastidious character in Oscar Wilde's play *Lady Windermere's Fan*.[5] More cases have subsequently been described, and it appears to be common in thin elderly women who have never smoked and

who have no underlying pulmonary disease. Many also have scoliosis, pectus excavatum, and mitral valve prolapse.[6] Voluntary suppression of cough in these fastidious women is hypothesised to cause reduced clearance of secretions from the right middle lobe and lingular segments which have long and narrow bronchi with relatively acute angulations from the parent bronchi, thus predisposing to MAC infection.[5] However, this has never been proven, and few of the reported cases have a history of voluntary suppression of cough.[7] Other hypotheses explaining the marked predisposition to involvement of the middle lobe have included an interplay of lung and chest anatomy, and personal habits. One such hypothesis suggested that the associated skeletal abnormalities indicated a connective tissue defect and that the predilection to middle lobe and lingular involvement is explained by the rarefaction caused by cardiac motion.[8]

Chronic inflammation due to MAC has been associated with an obstructive pattern on spirometry.[9,10] Middle lobe syndrome has been seen more frequently in asthmatics than in non-asthmatics, suggesting some role for retention of secretions in the middle lobe in patients with dynamic airway obstruction.[11] The right middle lobe is relatively isolated anatomically and has poor collateral ventilation, decreasing the possibility of re-inflation once atelectasis occurs. Patients with bronchiectasis can also have an obstructive pattern on spirometry, but in Lady Windermere syndrome MAC precedes bronchiectasis.[5] We hypothesise that the airway obstruction with or without bronchial wall oedema and inflammation combined with the acute angulation of bronchi in the middle lobes probably accelerates the progression of MAC disease in these lobes, leading to selective or early bronchiectasis.

Histology of removed lung specimens has revealed epithelioid cell granulomas with lymphocytic infiltrations mainly affecting the central bronchiolar walls, occasionally showing polypoid protrusion into the bronchiolar lumen.[12] The bronchial lesions appeared to progress from the peripheral bronchioles towards the central airway, resulting in atrophy of bronchial smooth muscles and consequent bronchiolectasis.[12]

MAC is ubiquitous in soil and water and there is no human-to-human transmission. It tends to progress slowly, taking months to years to manifest. Despite increasing awareness that MAC is a progressive disease and not just a colonising organism, controversies exist in management. Making a diagnosis of MAC disease does not mandate therapy, which is a decision based on weighing the risks and benefits of instituting drugs with potentially severe toxicities in these frail patients. For most patients, a three-times-per-week regimen of clarithromycin (1000mg) /azithromycin (500 mg), rifampin (600 mg) and ethambutol (25 mg/kg) is recommended.[3] It might become necessary to initiate treatment gradually to educe drug toxicity. The therapy should continue till the patients become culture negative on treatment for one year. Sputum for acid fast bacillus smears and culture should be obtained every month. Most patients show clinical improvement within three to six months and become sputum negative within a year. Though surgery is indicated in some selected patients with MAC disease, patients with this syndrome might not tolerate the procedure. The condition is currently non-reportable since it is non-communicable, but there is a need for increased awareness.

Conflicts of interest

All authors declare that we have no actual or potential financial interest or any conflict of interest in relation to this article.

Patient consent

Consent was obtained for these two case histories to be published for the purpose of medical education.

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