

Lady Windermere Syndrome: An Interesting Clinical and Radiological Presentation

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Abstract

Lady Windermere Syndrome is an uncommon pulmonary disease characteristically observed in elderly white females with chronic cough suppression and dyspnea. It is classically associated with *Mycobacterium avium complex* (MAC) species. An 84-year-old female was evaluated for longstanding non-productive cough and intermittent dyspnea. A chest computed tomography scan revealed densities in the right upper lobe and scattered nodular-cystic bronchiectasis. Biopsy was negative for malignancy; however, bronchioalveolar lavage studies showed presence of MAC. Patient was treated with a 12-month course of azithromycin, rifampin and ethambutol resulting in resolution of her symptoms.

Keywords

Lady Windermere Syndrome, Mycobacterium Avium Complex, Dyspnea, Bronchiectasis

1. Introduction

Named after Oscar Wilde's character Lady Windermere, Lady Windermere Syndrome (LWS) is an infrequently encountered pulmonary disease associated with *Mycobacterium avium complex* (MAC). It has been reported in middle-aged and elderly white females who chronically suppress their cough reflex, termed as Volitional Cough Suppression (VCS). This leads to mucous stasis, resulting in localized bronchiectasis and colonization of MAC [1].

Characteristic symptoms include indolent chronic cough and dyspnea. The cough in LWS is described as "intermittent but persistent" [2]. Additional symptoms may include sputum production, night sweats, weight loss, and fatigue [3] [4].

The prevalence of MAC infections in the United States from 2004 to 2006 increased from 1.4 to 6.6 per 100,000 persons. In England, Wales, and Northern Ireland, all MAC infections increased from 0.9 per 100,000 per person in 1995 to 2.9 per 100,000 persons in 2006 [5]. Traditionally, these occur in immunocompromised patients or those with pre-existing lung diseases; however, its association with LWS follows a classic clinical and imaging pattern that we aim to discuss in this report.

We report a case that fits the criteria of LWS, its diagnostic workup, and management.

2. Case Report

An 84-year-old female of Eastern European descent was evaluated for chronic non-productive cough and intermittent dyspnea in the pulmonology clinic. This was accompanied by fatigue; however, she did not have a fever, hemoptysis, night sweats, pleuritic chest pain, weight loss, or wheezing. She was a non-smoker for life. She did not have other comorbidities or genetic diseases except a medical history of well-controlled hypertension. On examination, she was afebrile with a respiratory rate of 20/minute, pulse 88/minute, blood pressure 134/78mmHg, and oxygen saturation of 94% on ambient air. There was no chest deformity and no crackles, wheezing, or crepitations were heard on auscultation of the lungs. Heart sounds were normal with no murmur or gallop, and there was no jugular venous distension or extremity edema. The rest of the systemic examination was unremarkable.

Initial workup, including a chest x-ray and pulmonary functions tests, were unremarkable. Chest computed tomography (CT) revealed 1.5 cm × 1 cm density in the right upper lobe (RUL), right middle lobe (RML) atelectasis and scattered pulmonary nodular infiltrates, as seen in **Figure 1**. A CT-guided biopsy of RUL density was unremarkable for malignancy. Histochemical stains of the tissue showed no evidence of any organisms. Subsequently, symptomatic treatment was provided and was advised to be followed in the clinic.

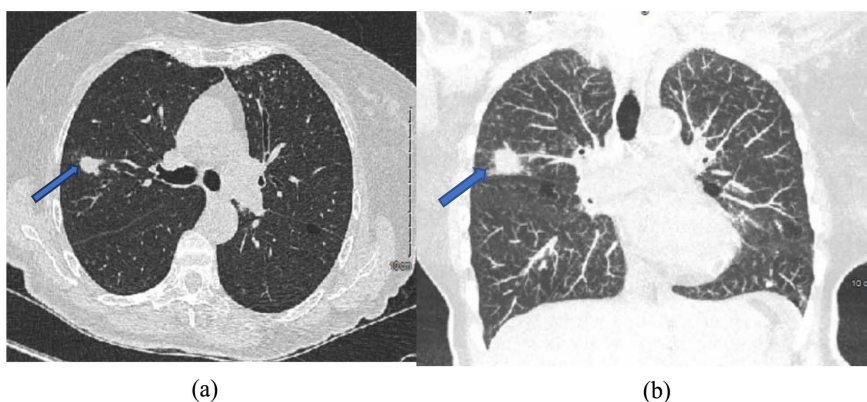


Figure 1. First chest CT shows spiculated density (blue arrow) in the RUL along with nodularity and bronchiectasis seen on both axial (a) and sagittal (b) images.

Eight months later, the patient returned to the office due to persistent symptoms of cough, fatigue and “feeling unwell”. A follow-up chest CT showed RUL nodular density mildly increased in size with new findings including multiple bilateral cysts, bilateral bronchiectasis, and a subtle tree-in-bud pattern in the upper lobes (**Figure 2**). Sputum studies, at this time, including culture, gram stain and acid-fast bacilli (AFB) stain were negative. She was treated with azithromycin for possible pulmonary infection; however, her symptoms did not improve on subsequent follow ups.

The patient continued to have a non-productive cough and reported “feeling congested” at times but “has not been coughing up much” on subsequent follow-ups. A repeat chest CT, 6 months later, revealed worsening RML atelectasis and increasing size (1.8 cm × 1 cm) of RUL nodular density, clearer tree-in-bud pattern, and scattered nodular-cystic bronchiectasis (**Figure 3**). Due to high suspicion for both infection and malignancy, endobronchial ultrasound-guided biopsy (EBUS) of RUL mass and bronchioalveolar lavage (BAL) were performed. Pathology was unremarkable for malignancy; however, BAL fluorescent microscopy

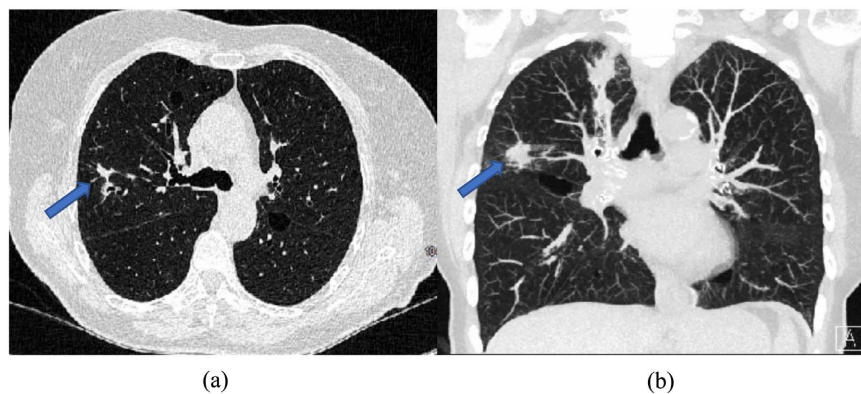


Figure 2. Repeat chest CT shows persistent RUL mass, now increased in size, with extension along the bronchial branches over time (blue arrows) in images (a) & (b). New right apical airspace and nodular foci with air bronchograms not seen previously (b).

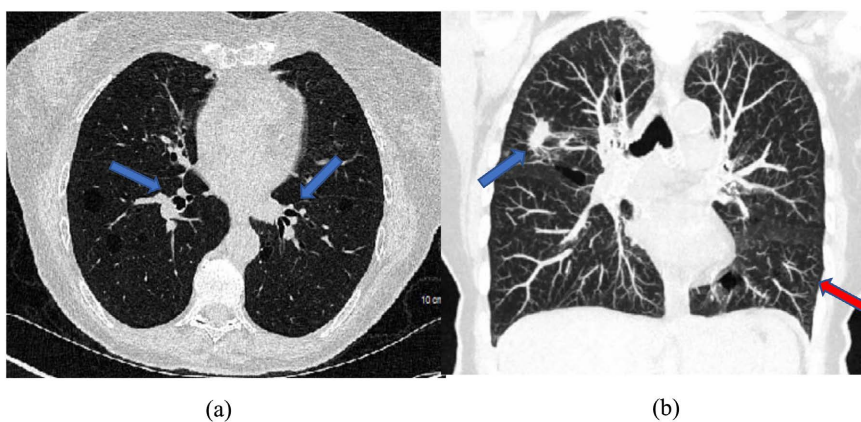


Figure 3. Repeat chest CT 14 months after first CT in **Figure 1** showing bilateral bronchiectasis (blue arrows), air cysts, and bullae. Subtle tree-in-bud pattern is demonstrated on the sagittal image (b) (red arrow).

was positive for AFB, and MAC DNA was detected on polymerase chain reaction (PCR). Simultaneously MAC growth was observed in BAL cultures. Bacterial and fungal cultures were unremarkable (Unfortunately, I was not able to obtain images for the microscopy).

The patient was started on azithromycin, rifampin, and ethambutol. Within six months of treatment initiation, she reported significant improvement in her symptoms, and repeat sputum studies including culture and AFB stain were negative. On follow-up after completion of one-year treatment, she reported no symptoms of cough or dyspnea anymore. A chest CT after completion of antibiotics course demonstrated improved RML atelectasis, bilateral nodularity and RUL density (**Figure 4**).

3. Discussion

Lady Windermere Syndrome is a lung disease of elderly females who persist in having nodular and cystic bronchiectasis on lung imaging, most commonly involving right upper and middle lobes and lingula. Impaired bronchial clearance is considered the proposed pathophysiological mechanism that leads to retention of mucous and eventual colonization of nontuberculous mycobacteria, including MAC [6]. Classic clinical presentation, as seen in our patient, consists of chronic cough, VCS, dyspnea, and fatigue. Clinically, it may present as an indolent disease, but it progressively worsens on lung imaging performed over time. Most common radiological findings seen on chest CT include scattered centrilobular nodules, tree-in-bud opacities, and fibronodular bronchiectasis; in the absence of primary lung pathology. MAC has been reported as the most common organism in these patients and is responsible for an indolent infectious process [2] [7] [8].

The clinical picture of our patient accounts for all the features of LWS suggested by Reich *et al.* [9]; these include elderly white females with chronic cough suppression, persistent radiological findings including nodular bronchiectasis of RML/RUL and lingula in the absence of predisposing lung disease, and MAC in bronchial secretions [10].

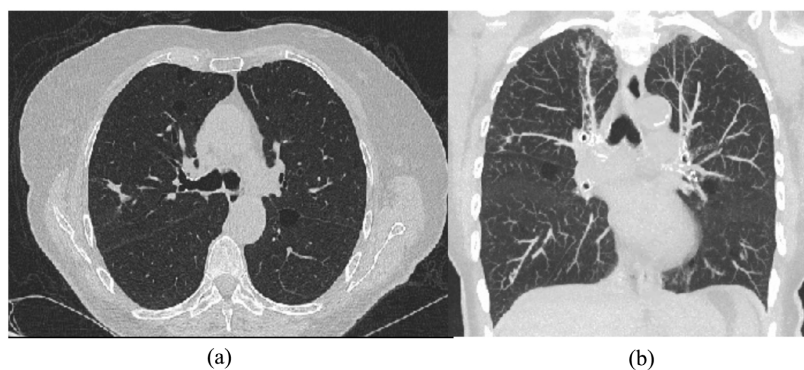


Figure 4. Chest CT after completion of antibiotics course, demonstrates improved nodularity, some residual scarring over RUL area and improved right apical opacities ((a) & (b)). Chronic lung changes and bullae unchanged from previous studies.

The criteria formulated by the American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) state that “there must be at least two positive sputum cultures or one positive culture via bronchoalveolar lavage” to diagnose LWS [11]. In the case of our patient, her initial sputum studies were unremarkable. However, utilization of EBUS was found to be beneficial in both obtaining biopsy of the nodularity and BAL. BAL studies, particularly MAC DNA detection and growth, expedited the diagnosis and treatment initiation.

Recommended treatment regimen consists of a macrolide including clarithromycin or azithromycin, rifampin, and ethambutol three times a week. A once-a-week treatment with macrolides was suggested, but the infection clearance was not as good as the three-times-a-week regimen [7]. Aminoglycosides can also be considered if there is a contraindication to either of these drugs [3]. A gradual initiation of treatment is recommended to avoid drug toxicity or drug resistance [2]. Symptomatic treatment with nebulized hypertonic saline has been shown to help [7]. Coughing is highly encouraged in these patients. Chest physiotherapy, commonly used for stand-alone bronchiectasis, has not been used for symptomatic treatment of LWS but could potentially be utilized if there is no contraindication; this may improve mucous clearance.

In our patient, significant improvement in her symptoms of cough and dyspnea was achieved in about six months, which correlated with negative sputum studies at that time. However, complete resolution of symptoms was noted after completion of the 12-month course.

4. Conclusion

LWS can be considered as an important differential in patients with chronic cough and persistent scattered nodularity, bronchiectasis and tree-in-bud pattern seen on chest CT scan in the absence of predisposing lung disease. In these patients, ultrasound guided endobronchial biopsy and BAL may increase diagnostic yield for mycobacterium avium complex simultaneously ruling out other etiologies. Periodic follow-up and sputum studies may be helpful in assessing response to treatment.

Informed Consent

The case was reviewed by the Institutional Review Board and informed consent was obtained from the patient.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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