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Case report

A tale of two images: From mycobacterium avium complex-lung disease (MAC-LD) to mycobacterium avium complex-pleural disease☆

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ABSTRACT

The typical radiographic presentation for *Mycobacterium avium* complex lung disease (MAC-LD) is either nodular bronchiectasis or cavitary lung disease. The former is seen most commonly in middle-aged or elderly Caucasian females with the characteristic asthenic phenotype, and the latter in middle-aged male smokers with COPD. We present the case of a young, otherwise healthy woman, with no significant risk factors, who was incidentally found to have MAC-LD with associated bronchiectasis. The patient's treatment and clinical course over a period of 5 years was marred by erratic follow up, intermittent treatment and poor adherence to guideline-based antibiotic therapy. Over this period of time, the patient developed significant worsening of her MAC-LD, macrolide resistance and failure to thrive. Upon presentation 5 years after her initial diagnosis, she had developed MAC-Pleural Disease with an empyema and broncho-pleural fistula. This case illustrates the progression of MAC-LD from nodular bronchiectasis to cavitary disease and pleural involvement leading to clinical deterioration. It highlights challenges related to short and long term management of macrolide resistant MAC-LD and the importance and need for surgical intervention and drainage procedures in patient with MAC-Pleural Disease.

1. Introduction

Mycobacterium avium complex lung disease (MAC-LD) usually presents in the form of 2 distinct phenotypical, clinical and radiological features. Upper lobe predominant cavitary disease is commonly encountered in male, smokers with underlying structural lung disease. Nodular bronchiectasis disease, characterized by middle lobe or lingula involvement, tree-in-bud opacities and variable bronchiectasis morphology is usually found in otherwise healthy, Caucasian middle-aged women who are non-smokers. *Mycobacterium avium* complex pleural disease is uncommon, accounting for about 5–15% of all pulmonary NTM infection. Untreated or improperly treated MAC-LD can lead to lung destruction and pleural infection manifesting in the form of pleuritis, pleural effusion, empyema and broncho-pleural fistula. It is hypothesized that the development of pleural disease from MAC lung infection could be either due to contiguous spread of infection from the lungs to the pleura or infiltration of the organism into the pleural space following trauma [1]. We present a case of a young woman with nodular-bronchiectasis MAC-LD whose course was complicated by macrolide resistance and subsequent pleural extension of infection leading to a broncho-pleural fistula.

2. Case report

A 30-year-old, human immunodeficiency (HIV) negative woman with no past medical history presented to the obstetrics clinic in 2014 for an antenatal evaluation. At this time, she was found to have a positive tuberculin skin test and was referred to the tuberculosis clinic for possible treatment. Further workup included a chest radiograph showing right upper and lower zone nodular lung disease necessitating sputum collection for microbial isolation and evaluation (Fig. 1). Induced sputum cultures returned positive for MAC. Given her pregnancy, treatment for latent tuberculosis was deferred and she was subsequently referred to her primary care for follow-up with the instruction that pulmonary follow-up would be necessary post-partum for continued follow up of her MAC infection.

Abbreviations: MAC-LD, *Mycobacterium avium* complex-lung disease; NTM, Non-tuberculous Mycobacteria; GBT, guideline-based therapy; OB, Obstetrics; TB, Tuberculosis; BPF, Broncho-pleural fistula; ALIS, Amikacin liposomal inhaled solution; MIC, minimum inhibitory concentration.

☆ Drs. Lapinel and Ali are members of the Insmed Speakers Bureau and have participated in the ALIS INS-212 (CONVERT) trials.

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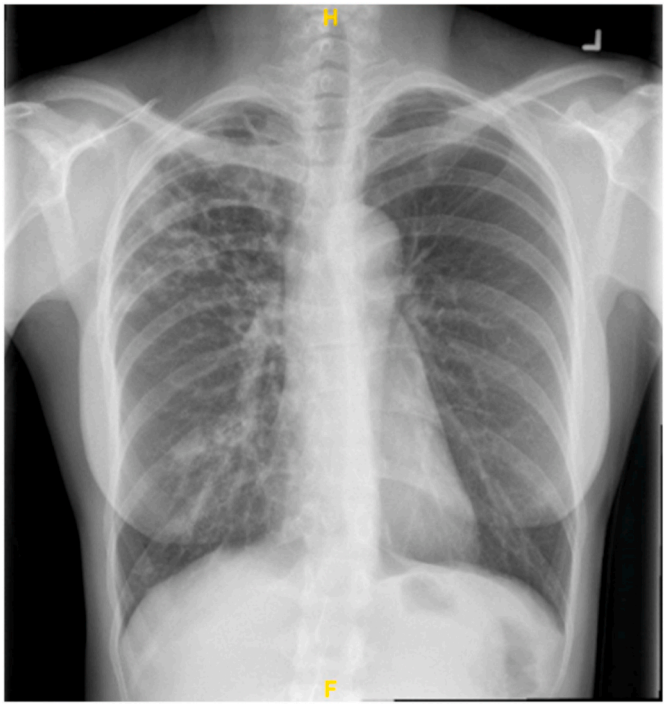

Fig. 1. Showing right upper and lower zone nodular disease. Left lung appears normal.

Her postnatal follow-up was erratic and over subsequent years, she received multiple courses of macrolides for sinus infections, broad spectrum antibiotic treatment for "pneumonia" and at times guideline-based therapy (GBT) for MAC with Rifampin, Ethambutol and Clarithromycin through various clinics and specialists. She remained culture positive for MAC during these clinical encounters and confirmed that she was not adherent to her treatment regimen during this time.

In December 2019, she was hospitalized with fever and cough productive of copious purulent sputum. She appeared malnourished and dyspneic. Vital signs revealed tachycardia, BP 91/45 mm Hg, RR 32/min with 94% oxygen saturation at rest. Lung exam demonstrated decreased breath sounds with transmitted bronchial breathing on the right side. Chest X-ray and CT Scan showed destruction of right lung parenchyma, volume loss, right sided air-fluid level and BPF. A large cavity was also seen in the left lung (Fig. 2A,B,2C).

Pleural fluid analysis revealed WBC count at 1.05 × 106/microliters with 100% lymphocytes and LDH at 1 × 105 U/L, glucose 37 mg/dl and protein 2.8 g/dl. Multiple sputum and pleural fluid cultures showed growth of *Pseudomonas aeruginosa*, macrolide resistance MAC with varying minimal inhibitory concentrations (MIC) to Amikacin. Serologic tests for expanded ANA were negative and Immunoglobulins were within normal range. A1-AT levels were normal. Repeat HIV testing and CFTR screen was negative.

The patient completed a six-week course of parenteral anti-pseudomonas antibiotics and subsequently continued on parenteral Amikacin along with Rifampin, Ethambutol, Clofazimine and Linezolid as long term treatment for macrolide resistant MAC. Chest tube drainage was also concurrently initiated.

CT surgery was planned for long-term surgical drainage with Eloesser flap, but this had to be deferred initially due to patient's poor clinical condition at that time and later due to her reluctance to have this procedure. Meantime, chest tube drainage was continued at home with regular interventional radiology review. On-going multi-drug antibiotic treatment regimen was subsequently supplemented with Amikacin liposomal inhaled solution (ALIS).

3. Discussion

This case highlights 1. MAC-LD Bronchiectasis in a young patient with no risk factors. 2. Impact of erratic treatment with development of macrolide resistance 3. Progression of MAC-LD to cavitary disease and MAC-Pleural disease. Usually, low BMI, cavitary lesions, positive AFB smears at the time of diagnosis and persistent positive cultures are linked to an increased risk of disease progression. The presence of cavitary disease is associated with higher mortality compared to nodular-bronchiectasis MAC [2].

Macrolides are the cornerstone of treatment for MAC-LD. Non-macrolide based regimen have been associated with lower sputum conversion rate and higher mortality. Macrolide monotherapy, macrolide-based regimen without ethambutol and combination of macrolide and fluoroquinolone are risk factors for the development of macrolide resistance [3,4]. Our patient received multiple courses of a macrolide for suspected sinusitis and bronchitis and this highlights unintended consequences of single drug therapy in a patient with possible underlying MAC-LD. Macrolide resistant MAC-LD is associated with low sputum conversion rate of 21% [5]. Mortality rates increase in these cases from 10% at 1-year to 30–50% at 5-years [4–6]. When secondary drugs are needed in macrolide resistant and persistent culture positive cases, Clofazimine has been shown to be equally effective as rifampin. Clofazimine also has fewer side effects compared to bedaquiline and linezolid, which may be used in drug resistant MAC [7–9]. ALIS as supplemental treatment has a higher culture conversion rate in refractory MAC-LD but has not been studied in patients with complicated pleural infections

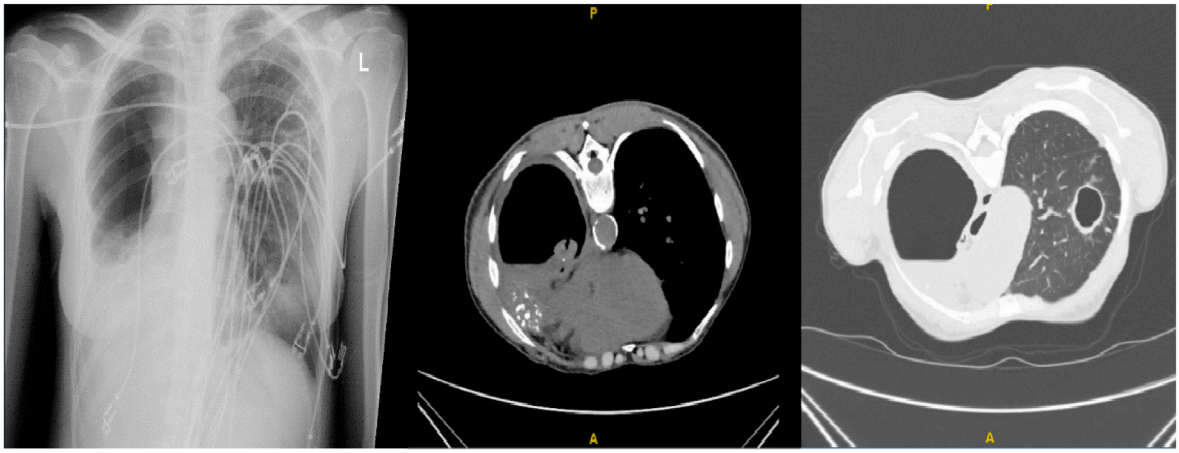

Fig. 2. (A,B,C): Showing destruction of right lung parenchyma, volume loss, right-sided air fluid level and BPF. A large cavity is seen in the left lung.

[10].

Although MAC-Pleural disease has been reported in immunocompetent patients of similar age group, none of them presented with severe form of disease in these case reports [11,12]. Both cases presented with macrolide susceptible MAC-Pleural disease which resolved with medical management alone. In the absence of definite treatment guidelines against macrolide resistant MAC-LD coupled with erratic follow-up, intermittent treatment and poor adherence to therapy in this case, the disease gradually worsened to involve the pleura.

Successful management of MAC-Pleural disease may require a combination of medical and surgical treatment [13–17]. Triple drug macrolide based regimen is less effective in MAC-Pleural disease with a culture conversion rate of 73% compared to 95% in MAC-LD [15]. While the difference in cure rate is not significant, surgical management with Eloesser flap procedure has been able to achieve better treatment outcome and culture conversion [18].

4. Conclusion

Erratic treatment, macrolide monotherapy and disjointed follow up may contribute to refractory drug resistant MAC-LD. The treatment outcomes of MAC-Pleural disease appear to be worse than MAC-LD and clinicians must be aware that a combination of medical treatment and aggressive surgical intervention may be needed to successfully treat patients with MAC-Pleural disease.

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Credit author statement

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Declaration of competing interest

None.

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