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Adjuvant lung resection in the management of nontuberculous mycobacterial lung infection: A retrospective matched cohort study

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ABSTRACT

Background and objectives: Lung resection in patients with nontuberculous mycobacterial pulmonary disease (NTM-PD) is considered when medical therapy alone fails to provide long term control. Data regarding comparative and long-term outcomes are limited. We aimed to review indications and outcomes of adjuvant lung resection for NTM-PD compared with controls.

Methods: We retrospectively studied 27 surgically treated patients, matched 1:1 for age, sex, NTM species, and radiologic pattern of disease, with control patients treated exclusively with antibiotics.

Results: In the surgical group, the median (IQR) age was 55 (49–61) years and 74.1% were female. Eighteen patients had *Mycobacterium avium* complex, and 9 had M. *xenopi*. Operations included 8 pneumonectomies, 20 lobectomies, one segmentectomy and one lobectomy plus segmentectomy. Post-surgical complications occurred in 6 patients (20%), including 2 acute respiratory distress syndrome, 1 bronchopleural fistula, 1 pericardial tamponade, and 2 empyema. Complications were more common among patients operated upon for progressive disease despite medical therapy (OR 10, p = 0.025). Of 24 matched pairs followed for ≥1 year, sustained culture conversion was observed in 21 (87.5%) patients in the surgical group and in 11 (45.8%) patients in the non-surgical group (RR 2.36, 95%CI 1.37–4.03, p = 0.002). Median (IQR) percentage of follow-up time on antibiotics was 14% (0–100%) in the surgical group and 83% (10.8%–100%) in the non-surgical group (p = 0.195) during a median (IQR) follow-up of 16 (2–36) months.

Conclusions: NTM-PD patients who underwent adjuvant lung resection experienced significant morbidity and more frequently achieved sputum culture conversion. Long term antibiotic requirements may have been reduced.

1. Introduction

Nontuberculous mycobacteria (NTM) are widely-distributed environmental organisms that may cause a variety of human infections, most commonly in the lungs. NTM pulmonary disease (NTM-PD) can be severe, causing a chronic illness with lung destruction [1]. Studies from Ontario and the USA have found that NTM-PD is increasing in prevalence [2–4]. NTM-PD is difficult to treat, with standard recommendations for most NTM species including at least three antibiotics continued typically for 16–20 months [1].

Surgical resection of destroyed lung, in addition to antibiotic therapy, is used in some patients with NTM-PD, usually when medical therapy alone fails to provide long-term control of the infection [1]. Several case series have described a high rate of sputum culture conversion following surgical resection for NTM-PD, with acceptable morbidity and mortality rates [5–19]. However, the majority of the

Abbreviations: ATS/IDSA, American Thoracic Society / Infectious Diseases Society of America; NTM, Nontuberculous mycobacteria; NTM-PD, Nontuberculous mycobacterial pulmonary disease; CT, computed tomography; MAC, *Mycobacterium avium* complex

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data are from two centres, with small series from other NTM clinics, all with considerable experience in the surgical management of NTM-PD. It is unclear if patients who undergo surgical resection for NTM-PD in centers with less experience have similarly favourable outcomes. Additionally, long term outcomes of patients with NTM-PD who undergo adjuvant lung resection have not been well described.

The aims of the study were to review indications and outcomes among NTM-PD patients treated at our centre who underwent adjuvant lung resection, and compare their outcomes with patients matched for age, sex, NTM species, and radiologic pattern, who were treated exclusively with antibiotics.

2. Materials and methods

2.1. Study design and patients

This retrospective study was performed in accordance with the Declaration of Helsinki and was approved by the institutional research ethics board, with a waived requirement for informed consent due to the retrospective nature of the analysis. Patients treated in the Toronto Western Hospital NTM clinic between July 2003 and December 2016 who underwent adjuvant surgical lung resection for NTM-PD, excluding lung transplantation, were retrospectively reviewed. Diagnosis of NTM-PD was based on American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines [1]. We compared characteristics of surgical patients with patients who were treated, for ≥1 year, exclusively with medical therapy. Age on the date of surgery, for surgical patients, was compared with age on completing one year of antibiotics, for non-surgical patients. The predominant computed tomography (CT) pattern was classified as nodular bronchiectatic or fibrocavitary in a large majority of patients (Fig. 1), while a few patients had predominantly consolidation, random nodules, or unclassifiable patterns [20]. Details on pre-surgical antibiotic regimen, pre-surgical assessment, surgical technique, and post-surgical care are provided in the supplementary appendix S1.

We attempted to match surgical patients with non-surgical controls (exclusively medical therapy), by age, sex, NTM species, macrolide resistance (for *Mycobacterium avium* complex (MAC) patients), and CT pattern. The baseline CT scan was defined in the surgical patients as the most recent pre-operative scan and in the controls as the scan closest to 12 months after starting antibiotic treatment. CT imaging for surgical patients was reviewed by two thoracic radiologists (Supplementary Appendix 1).

2.2. Outcomes

We compared culture conversion, time on antibiotics, and mortality between the two matched groups. To assess long term outcomes for matched pairs, follow-up duration was determined by the pair member with shorter available follow-up. For follow-up time receiving antibiotics, we considered the starting point as 1 year after surgery for the surgical group, and 18 months after initiation of antibiotics for the non-surgical group. Observations were censored as of December 2016, or at loss to follow-up. Definition of culture conversion is provided in the supplementary appendix 2.

2.3. Statistical analysis

Descriptive statistics are presented as numbers (percentages) and medians (Interquartile ranges, IQR). Unmatched data were compared with chi-square or Fisher's exact tests and t-tests or Mann-Whitney tests, and matched data were compared with the McNemar test and the

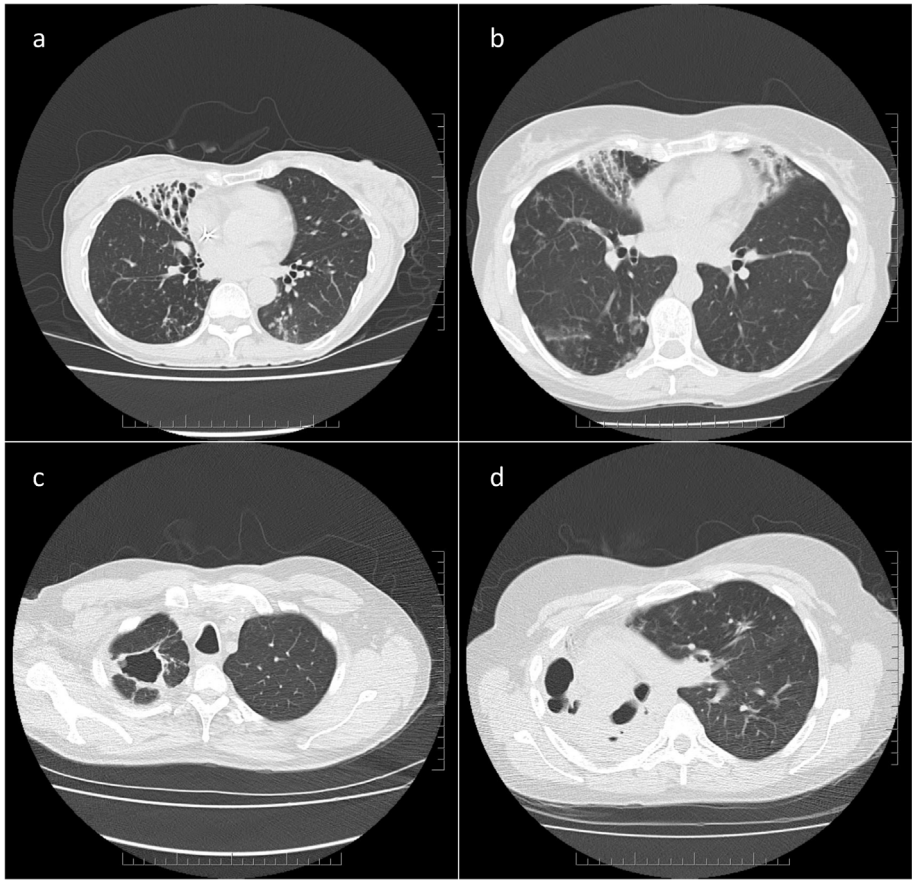

Fig. 1. Most common radiographic patterns on CT scans.
a) Nodular bronchiectasis due to *Mycobacterium avium* in a 59 year old woman with right middle lobe bronchiectasis and bilateral lower lobe nodules with progressive disease despite medical management; Imaged after several years of clarithromycin, ethambutol, rifampin and levofloxacin, and 2 months of added intravenous amikacin and recent sputum conversion; Right middle lobe resection performed 1 month later via VATS.
b) Nodular bronchiectasis due to macrolide resistant *Mycobacterium intracellulare* in a 62 year old woman with right middle lobe and lingular bronchiectasis and bilateral lower lobe nodules; Imaged after 8 months of clarithromycin, ethambutol, rifampin, and two months of clofazimine and intravenous amikacin with recent sputum conversion; right middle lobe resection (via VATS) and lingular resection (VATS converted to thoracotomy) to improve long term control of localized destructive disease performed 4 and 6 months later respectively.
c) Fibrocavitary *Mycobacterium xenopi* disease in a 52 year old ex-smoker with right apical cavitation; Imaged after 8 months of macrolide, rifampin, ethambutol, and 3 months of added moxifloxacin and intravenous amikacin and persistent smear and culture positive sputum; VATS right upper lobectomy to improve long term control of localized destructive disease performed 2 months later.
d) Fibrocavitary *Mycobacterium avium* disease in a 43 year old woman with prior extensive right lung TB with subsequent progressive right lung destruction; Imaged after 8 months of azithromycin, rifampin, ethambutol and moxifloxacin, and 3 months of added intravenous amikacin and persistently positive sputum; Right poneumonectomy to improve long term control of localized destructive disease performed 7 months later.