# Mycobacterial peritonitis: difference between non-tuberculous mycobacteria and *Mycobacterium tuberculosis*

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## Abstract

Unlike tuberculous peritonitis, peritonitis due to non-tuberculous mycobacteria (NTM) has unclear clinical manifestations. This study aimed to clarify the clinical manifestations and laboratory results of NTM peritonitis and compare it to tuberculous peritonitis. This retrospective study was conducted from 2000 to 2008 in a medical centre in Taiwan. Patients with mycobacteria isolated from ascites were identified and compared according to causative pathogens (*Mycobacterium tuberculosis* or NTM). Those with NTM peritonitis were further classified into the 'probable' and 'possible' groups based on diagnostic evidence. Twenty-five patients with NTM peritonitis and 65 with tuberculous peritonitis were reviewed. *Mycobacterium avium* complex was the most common NTM pathogen (52%). There was no obvious difference between the 'probable' and 'possible' NTM peritonitis groups regarding age and laboratory data. Patients with NTM peritonitis and those with tuberculous peritonitis had no differences in age or gender but varied in symptoms and serum laboratory data. NTM peritonitis was 100% associated with underlying co-morbidities and had lower proportions of lymphocytes and albumin level in ascites. Twelve (48%) NTM peritonitis and 21 (32%) tuberculous peritonitis patients died during the 6-month follow-up. Antimycobacterial treatment, but not mycobacterial species, was correlated with better 6-month survival. In Taiwan, NTM is responsible for 28% of mycobacterial peritonitis cases, which have a poor prognosis if untreated. There are some differences in clinical manifestations between NTM and tuberculous peritonitis. NTM peritonitis should be considered in patients with peritonitis but without causative microorganisms identified other than NTM.

**Keywords:** Ascites, lymphocyte predominant, *Mycobacterium tuberculosis*, Non-tuberculous mycobacteria, peritonitis
**Original Submission:** 24 December 2010; **Revised Submission:** 2 April 2011; **Accepted:** 14 April 2011
Editor: M. Drancourt
**Article published online:** 25 April 2011
*Clin Microbiol Infect* 2012; **18:** 246–252
10.1111/j.1469-0691.2011.03547.x

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## Introduction

Diagnosis of extrapulmonary mycobacterial infections is complicated due to variable manifestations and difficulty in collecting clinical samples [1]. One such infection is mycobacterial peritonitis. Though uncommon, mycobacterial peritonitis has a high mortality rate, especially in immunocompromised hosts [1]. Most reported cases are caused by *Mycobacterium tuberculosis*. However, due to ageing, increasing numbers of immunocompromised individuals, and advances in non-tuberculous mycobacteria (NTM) isolation [2–5], the overall incidence of NTM disease has increased in recent years [5–8]. From a clinical standpoint, it is important to know the relative proportions of tuberculosis (TB) and NTM disease in patients with mycobacterial peritonitis.

The clinical characteristics of NTM peritonitis remain unclear. Ding *et al.* reported 11 cases of abdominal NTM infection with a mortality rate of 73% [9]. In their series, 55% had liver cirrhosis and only 18% received anti-NTM treatment. Liver cirrhosis further increases the difficulty of early diagnosis of mycobacterial peritonitis because the transudative ascites may mask the peritoneal inflammation while the bleeding tendency prevents invasive diagnostic procedures such as peritoneal biopsy.

Because anti-NTM treatment can improve survival in NTM lung disease [10], familiarity with the presentations of NTM peritonitis is of practical importance for early diagnosis and prompt treatment. This retrospective study aimed to clarify the clinical manifestations and laboratory results of NTM peritonitis and compare them with TB peritonitis.

## Materials and Methods

This study was conducted in a tertiary referral centre in northern Taiwan and the Institutional Review Board of the Research Ethics Committee approved the study design (No. 201002023R). Medical records and the mycobacterial laboratory registry database were reviewed. In our hospital, mycobacteriological study is routinely performed for the first ascites sample of every patient and for multiple ascites samples of those whose ascites has no definite aetiology, is exudative, or responds poorly to treatment [11]. Mycobacterial culture and identification were performed as previously described [12,13] and quality control assessment of the mycobacterial laboratory was periodically performed by the National Reference Laboratory of the Centres for Disease Control of Taiwan.

All of the patients with ascites samples sent for mycobacterial culture from January 2000 to December 2008 were eligible. In order to know the whole picture of culture-confirmed mycobacterial peritonitis, all of the patients whose samples yielded mycobacteria were recruited and those with concomitant bacterial or cancerous peritonitis were not excluded. The first positive ascites sample was defined as the index sample. The recruited patients were classified into TB and NTM peritonitis groups. Because NTM was ubiquitous in the environment and laboratory contamination was possible, NTM patients were further classified into two groups. Those with additional diagnostic evidences of NTM, including (i) more than one specimen of ascites yielding the same NTM, (ii) having the same NTM species growing in specimens other than ascites or (iii) presence of tissue pathology comparable for mycobacterial infection, were defined as the 'probable group'. Those with single ascites culture positive for NTM were defined as the 'possible group'.

A specially designed reporting form was used to collect data on the clinical characteristics, laboratory findings, treatment course and outcomes. Patients were followed-up for at least 6 months after the index sample or until death or lost to follow-up. The end of follow-up date was defined as the last-visit date for the last group. Mycobacteria-related mortality was considered sepsis complicated by multi-organ failure with no evidence of pathogens other than mycobacteria.

Proper anti-tuberculous and anti-NTM regimens were defined according to the TB treatment guidelines established by the American Thoracic Society [14,15]. Gastrointestinal symptoms included vomiting, haematemesis, tarry stool and haematochezia. The disease was considered disseminated if samples other than ascites yielded the same mycobacteria [15]. The duration from presentation to diagnosis of mycobacterial peritonitis was considered prolonged if it was >6 weeks [16]. Alcoholism was diagnosed when a patient had alcohol abuse or dependence (with history of alcohol withdrawal or tolerance) [17].

Three histological findings from peritoneal tissues were considered typical for mycobacterial infection: (i) granulomatous inflammation, (ii) caseous necrosis or (iii) the presence of acid-fast bacilli [18]. Child–Pugh classification for liver cirrhosis was scored according to a previous report [19]. The estimated glomerular filtration rate was obtained using the Modification of Diet in Renal Disease Study equation [20]. Severe chronic renal disease was defined as an estimated glomerular filtration rate of ≤30 mL/min/1.73 $m^2$.

### Statistical analysis

Inter-group differences were compared using the Student *t*-test or one-way ANOVA for numerical variables, where appropriate, while the chi-square test was used for categorical variables. Six-month survival curves for each variable were generated using the Kaplan–Meier method and compared using the log-rank test. Variables with a significant difference in univariate analysis were entered into the Cox proportional hazard regression analysis. A two-sided $p < 0.05$ was considered statistically significant. All analyses were performed with the SPSS software (version 13.0; SPSS Inc., Chicago, IL, USA).

## Results

During the study period, 10 781 ascites samples from 5298 patients were sent for mycobacterial study, and 65 patients with TB peritonitis and 25 with NTM peritonitis were identified. MAC was the most common NTM species ($n$ = 13), followed by rapidly growing mycobacteria ($n$ = 7). Of the NTM group, 8 (32%) and 17 (68%) patients were classified into the 'probable' and 'possible' groups, respectively (Tables 1 and 2). In the 'probable group', eight had additional culture evidence and three had comparable pathology of mycobacterial infection. Co-bacterial peritonitis with *Salmonella* sp. was noted in one patient with MAC peritonitis and of three patients with TB peritonitis, two patients had *Escherichia coli* and one had *Candida albicans*. Cytology-proven