378. Non-tuberculous mycobacteria pulmonary infections

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Geographic diversity of nontuberculous mycobacteria isolated from pulmonary samples in Croatia

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Background: The incidence of nontuberculous mycobacteria (NTM) as human pathogens is increasing. It has become clear that the NTM species obtained from clinical specimen differ strongly by region.
Aims and objectives: To determine the distribution of NTM species obtained from pulmonary samples of individuals from different geographic regions in Croatia.
Methods: Retrospective analysis on all NTM identified at the National Laboratory for Mycobacteria in 2007-2009. For each isolate the person's birth year, sex, specimen collection date, source and geographic region (costal or inland) were recorded. Microbiological criteria of the ATS/IDSA were used for a laboratory-based definition of pulmonary NTM.
Results: NTM species were isolated from 712 individuals. 56% of isolates came from male (median age 62 y) and 44% from female (median age 64 years) individuals. More than two thirds of all isolates (525) originated from persons from the inland area. Out of those 525 samples, 80 (15.2%) met the pulmonary NTM criteria, compared to 68 (36.4%) out of the 187 samples identified in the costal area ($p<0.0001$). More than 90% of isolated species with insignificant clinical relevance originate from the inland area. Incidence of species with relevant clinical burden was significantly higher in the coastal compared to the inland area.
Conclusions: The majority of all NTM isolates originated from the inland area. However, isolates which met the ATS pulmonary disease criteria were more frequently isolated from persons living in the costal area. There, more than one third of all isolates likely represented true disease. Geographic region plays an important role for colonization or infection with NTMs in Croatia.

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Nontuberculous mycobacteria – Isolation in respiratory specimens and its clinical relevance

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Background: Nontuberculous mycobacteria (NTM) isolation have been increasingly described, particularly in developed countries. Few studies in Portugal characterize and report its clinical relevance.
Aim: Characterize NTM isolated from respiratory samples between 2007-2010 at our center.
Methods: Retrospective analysis of patients followed in our hospital with NTM isolation in at least one respiratory specimen.
Results: NTM were isolated in 108 samples, 68 patients; mean age: 53,5±17,0 years; 60,3% male. Fourteen (20,6%) had HIV, eight with AIDS.
Prior respiratory disease was present in 63,2% of patients, most frequently bronchiectasis (14;32,5%), tuberculosis sequelae (11;25,6%) and COPD (7;16,3%).
Eleven species were isolated, mostly M. avium complex (MAC), including *M. avium* and *M. intracellular* (27; 39,7%) and *M. gordonae* (23,33,8%).
We identified 22 (32,4%) cases of disease; 12 (54,5%) were female; 2 were HIV+. Seventeen (77,3%) had lung disease. One had multiple NTM disease (*M. avium* + *M. genavense*).
The agents related to disease were MAC (16;72,7%); *M. kansasii* (2;9,1%); *M. xenopi* and *M. gordonae* (both 2;9,1%). MAC was associated to disease (p=0.001; OR=3.2). A trend towards significance was observed between HIV infection and NTM disease (p=0.074; OR=2,8).
Discussion: *M. gordonae* was isolated in much higher frequency than that described in literature, possibly a geographical issue. Despite its little clinical significance when compared to MAC, it caused disease in 2 cases. NTM isolation didn't relate to lung disease in 67,6% of cases. We found a statistically significant association between illness and MAC isolation. Further studies are needed to describe NTM and its clinical significance.

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Pulmonary disease caused by non-tuberculous mycobacteria. Descriptive study and comparison with mycobacterium tuberculosis

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Aim: To describe the epidemiological, clinical and radiological data of pulmonary disease (PD) caused by non-tuberculous mycobacteria (NTM) diagnosed in a period of 12 years in an area of Vizcaya, and to compare the incidence with the cases of M. tuberculosis (MT).
Material: We reviewed all cases of PD caused by mycobacteria between 1997-2008 in our center, attending a population of 420,000. The diagnosis of NTM PD was conducted according to criteria of ATS.
Results: We found 1019 cases of PD caused by mycobacterias,788 (77.3%) for MT and 231 (22.7%) NTM: 216 M. kansasii (MK), 11 M. avium complex (MAC), 2 M. abscessus, 1 M.xenopi and 1 M. celatum. NTM PD was more frequent in men (73.2%) and the mean age was 53.9. 2.8% of patients with MK and 9.1% of patients with MAC had extrapulmonary affection. 36 patients (15.6%) had HIV coinfection.Cavitary pulmonary infiltrates were the most common (56.1%), followed by reticulonodular infiltrates (31.9%). The location was unilateral in 54% and affection in upper lobes was observed in 82.6%.The mean age of patients infected by MT was 48.7 and was more frequent in men (60%). 53 patients (6.7%) had HIV coinfection. The annual incidence rate/100.000 of MT infection had the highest peak in 1999 with 22.8 and the lowest in 2008 with 11.9.The highest rate of NTM infection was in 1998 (7.4) and lowest in 2008 (1.2).
Conclusions: 1)The most common NTM specie in our area is M.Kansasii. The rest of NTM causes PD infrequently. 2) PD by NTM has a clinical and radiological presentation similar to tuberculosis. 3) The incidence of PD by NTM and MT had a descendant tendency in the 12 years studied, which is more remarkable since 2005.

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High burden of rapidly growing non-tuberculosis mycobacteria in patients with respiratory disease undergoing elective bronchoscopy

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Background: Pathogenecity of pulmonary non-tuberculous Mycobacteria (NTM) is less well understood than that of M. tuberculosis (MTB) complex. Both will show identical results on acid-fast staining (AFS), but culture characteristics are commonly used for differentiation in the local setting.
Objective: To assess the pattern of mycobacterial culture among patients with respiratory illness and negative sputum for AFS, in a pulmonary tuberculosis (PTB) prevalent environment.
Method: Bronchoalveolar lavage samples from 120 patients were inoculated onto solid media (Lowenstein-Jensen and Middlebrook 7H-10) at 280C and 370C, in both light and dark conditions. All patients were negative for sputum AFS. Indications for bronchoscopy were bronchiectasis, cavitatory lung disease and smear negative PTB.
Results: 67 patients yielded positive colonies within 8 weeks. 37 colonies were positive for AFS, of which 31 were rapidly growing Mycobacteria (RGM; <7 days) and 6 were slowly growing Mycobacteria (>7 days). Rapid colony growth strongly favours towards NTM. PCR based restriction fragment length polymorphism analyses on NTM are in progress. Concomitant sterile water, instrument cleanser fluid and saline samples did not yield culture growth.
Conclusion: We observed a high prevalence (>25%) of RGM in the study population. This raises major concerns on possible over-diagnosis of PTB leading to inappropriate therapy and false categorization of patients, in limited resource settings where sputum AFS results play a central role in managing PTB in clinical practice.

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Ability of IGRAs for diagnosis of tuberculosis infection in adolescents, and role of non-tuberculous mycobacteria in the positivity of tuberculine skin test

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Introduction: A big drawback of tuberculin skin test (TST) is the cross-reaction with bacillus Calmette-Guérin (BCG) vaccine or with non-tuberculous mycobacteria (NTM). In this way, interferon-gamma release assays (IGRAs) are more specific but few data are available for children.
Aims and objectives: To assess the ability of IGRAs to detect *Mycobacterium tuberculosis* infection in healthy adolescents, and to know the influence of previous NTM sensitisation in discordant results as positive TST with negative IGRA.
Methods: TST was performed on 2,346 students aged 12-16 from Valencia city during the 2009-10 academic year. Those with TST ≥5 mm, underwent a checkup, a chest x-ray and QuantiFERON-TB GOLD In-Tube (QFT) test. Those with negative QFT, were tested by T-SPOT.TB (TSPOT) and T cells were stimulated with *Mycobacterium avium* sensitin (MAS).
Results: TST was ≥5 mm in 171 students (4.3%), and QFT was tested in 159. QFT was positive in 33 (21%) and it enabled to diagnose 10 individuals BCG-immunized with latent infection. QFT was negative in the 4 students with radiographic findings of previous tuberculosis (TB), and also in 14 from the 17 diagnosed with active TB. From those with negative QFT (126), TSPOT was tested in 95; it was positive in 5 (2 had been classed as vaccine reactions). Stimulation with MAS was positive in 15 (5 were not vaccinated and TSPOT was negative in all of them).
Conclusions: IGRAs help to detect infection in BCG-immunized, and to rule it out in doubtful cases, avoiding unnecessary treatments. Previous NTM sensitisation may explain some positive TSTs in non-vaccinated.
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Clinical study of mycobacterium avium complex pulmonary disease complicated by interstitial pneumonia

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Background/Aims: We have encountered patients with mycobacterium avium complex (MAC) complicated by interstitial pneumonia (IP) and have had the following questions: 1) Does IP induce MAC as a baseline disease? and, 2) Does steroid therapy for IP cause deterioration of MAC?
Methods: We retrospectively examined the medical records of patients with MAC and/or with IP who consulted at the department of respiratory medicine, Himeji Medical Center, Japan between January 2000 and December 2008, and investigated their clinical course based on chest radiography and CT images.
Results: Of 29,799 patients who consulted at our department in this period, 346 cases were patients with MAC, 1544 cases had IP, and 18 patients had both MAC and IP. There was no significant difference in the prevalence of MAC between IP patients and IP-free patients (0.0115 vs. 0.0116, p=0.797, chi 2 test).
Among 18 patients with both MAC and IP, no difference was seen in the response rate to anti-MAC medication between the steroid-treated group (4/4 cases) and the non-treated group (3/3 cases). Among the patients not receiving anti-MAC medications, little difference was seen in the clinical course of MAC between the steroid-treated group (n=7) and non-treated group (n=4).
Conclusions: IP did not significantly increase the prevalence of MAC. No apparent

difference was seen in the clinical course of MAC whether or not steroid was administered for IP.

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Transitional change of the relationship between clinical efficacy of treatment for pulmonary MAC disease and drug-sensitivity test for MAC isolated

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Objective: We investigated the relaltionship between the clinical efficacy of treamtent for pulmonary MAC disease and drug-sensitivity test for isolated MAC compared 2005-2007 and 2008-2010.
Materials and methods: The subjects consisted of 60 patients who satisfied the diagnostic criteria of ATS and received the combiation therapy using RFP, EB, SM and CAM. We divided into the former period (24 patients) and the latter period (36 patients).
Results: The average administration dose of CAM has been increased from the former period (517mg/day) to the latter period (800mg/day) between both periods. Sputum conversion rate has been increased frm 63% in the former period to 83% in the latter period. Clinical improvement has been increased from 38% in the former period to 53% in the latter period. The causative microorganisms isolated were M.avium in 35 patients and M.intracellulare in 25. There were no significant differences in the sputum conversion rate, clinical improvement, and drug-sensitivity test between M.avium and M.intracellulare in both periods. The isolated MAC strains showed excellent MICs of CAM and RFP in both periods. Regarding the relationship between clinical efficacy and MICs of RFP, EB, CAM, and SM, there was a good relationship only for CAM in both periods.
Conclusions: The good clinical effect has been obtaied with the increase dose of CAM in the latter period. Because there was no significant difference in the result of drug-sensitivity test for isolated MAC in both periods, we speculated that the increase of administration dose of CAM has been influenced the good clinical effect in both periods.