Mycoplasma pneumoniae in pediatric patients: do macrolide-resistance and/or delayed treatment matter?

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Introduction:

Mycoplasma pneumoniae (MP) is a common pathogen for pneumonia in children especially in the post-pneumococcal conjugate vaccination era, up to 30-40%¹. Though self-limited disease was found in the majority of the patients, severe diseases with complication² occurred occasionally and was related to **immune response**. The emergence of **macrolide resistance** was also reported worldwide, up to 90% in some area in Asia. It is important to delineate whether macrolide resistance or delayed treatment affects outcome.

Methods:

We retrospectively collected pediatric patients with clinical suspicion of *Mycoplasma pneumoniae* infection and confirmed by positive PCR from respiratory tract specimen subsequently in a tertiary medical center in Taiwan from 1st Jan. 2010 to 30th Jun. 2017. Patients with incomplete or loss of medical record, immunocompromised condition or malignancies were excluded.

Resistant rate and strain

Patients' history, demographics, clinical manifestations, laboratory parameters, radiographic findings, MP bacterial load, co-infection pathogens and treatment for MP were reviewed from medical charts and performed statistical analysis. Polymerase chain reaction assay were performed when clinically suspicion twice weekly, the segment of 4596–4725 nucleotides of cytoadhesin P1 gene was targeted for MP detection. Resistant gene was examined by nested PCR which detecting reported sites in 2758–2769 (A2063G/C, A2064G/C, C2617G/A).

Macrolid resistant or not

(in days)	MRMP	MSMP
febrile duration*	9.7	6.9
hospitalization*	6.2	4.9
time to active abx*	10.3	5.2

CXR findings

Results:

Among 471 children with positive MP PCR in 2327 tested, the mean age is 6.6 years and 51% are male. 95% were diagnosed with pneumonia, 2.5% had severe disease (respiratory failure needs ventilator support, SJS, encephalitis), 15% had pleural effusion (50% effusion were PCR positive), 17% had extrapulmonary complications (43 with skin rash, 42 with impaired liver function, and 5 with CNS involvement).

The mean rate of macrolide resistance was 24% (19-30%) and macrolide resistance was related to longer febrile duration, longer hospital stay, lung consolidation and impaired liver function tests. Mean resistant rate among patients age < 2 were 14%. The medium bacterial load of all cases was 1.5x10⁵ copies/ml (2.6x10² to 1x10⁸ copies/ml). No significant difference between high and low load except patients with load lower than medium had extrapulmonary manifestations and viral coinfection. Overall viral co-infection rate was 7.1% and bacterial co-infection rate was 4.6%.

Effect of delayed treatment

Delayed active treatment (longer than medium, 5.6 days), which related to MRMP, was also associated with severe disease, prolonged fever after MP-active treatment, extrapulmonary manifestations and higher CRP. In patients presented with pleural effusion in the clinical course, extrapulmonary manifestation and severe diseases were more often. Second-line antibiotics includes doxycycline and quinolones were prescribed more often, however, pleural effusion it is not associated MRMP.

Conclusions:

Macrolide resistance was fairly common and might lead to delayed appropriate antibiotic treatment in Taiwan. Delayed appropriate antimicrobial treatment, no matter macrolide resistance or not, was associated with more severe and/or prolonged diseases among pediatric patients with *Mycoplasma pneumoniae* infection. Early diagnosis of *Mycoplasma pneumoniae* as well as the awareness of macrolide resistance makes early effective antibiotic treatment possible and may improve clinical outcomes.

With or without pleural effusion

1. Chen, C.J., P.Y. Lin, M.H. Tsai, et al., Etiology of community-acquired pneumonia in hospitalized children in northern Taiwan. *Pediatr Infect Dis J*, 2012. **31**(11): p. e196-201.

2. Marc, E., M. Chaussain, F. Moulin, et al., Reduced lung diffusion capacity after *Mycoplasma pneumoniae* pneumonia. *Pediatr Infect Dis J*, 2000. **19**(8): p. 706-10.