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ORIGINAL ARTICLE

Impact of bacterial and viral coinfection on mycoplasmal pneumonia in childhood community-acquired pneumonia

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Background/Purpose: Coinfection of *Mycoplasma pneumoniae* is not uncommon in children with respiratory syndromes. The purpose of this study was to investigate the impact of bacterial and viral coinfection on mycoplasmal pneumonia in hospitalized children with community-acquired pneumonia (CAP).
Methods: Children coinfected with *M. pneumoniae* in a prospective study of the etiology of CAP at a tertiary pediatric facility Children's Hospital were enrolled and retrospectively reviewed. The data of clinical characteristics, complications, and outcomes of these children were collected and analyzed.
Results: A total of 59 children were enrolled and stratified into three groups: *M. pneumoniae* infection alone ($n = 31$), *M. pneumoniae* with *Streptococcus pneumoniae* coinfection ($n = 9$), and *M. pneumoniae* with virus coinfection ($n = 19$). As compared with children infected with *M. pneumoniae* alone, coinfection of children with *S. pneumoniae* was more likely to occur under the age of 5 years with a longer duration of fever and hospital stay. Furthermore, total leukocyte count and serum C-reactive protein level were also significantly higher in these children ($p < 0.01$). However, no significant difference in clinical characteristics, complications, and outcomes was observed between the patients infected with either *M. pneumoniae* alone or with virus coinfection.

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Conclusion: In children with CAP, the influence on the clinical outcomes of *M. pneumoniae* infection may be heavily dependent on the coinfected pathogen. A potential coexistence of *M. pneumoniae* infection should be considered in children with features suggesting typical bacterial pneumonia.

Introduction

Mycoplasma pneumoniae is recognized as an important and frequent cause of community-acquired respiratory illness in children.[1,2] *M. pneumoniae* causes up to 40% of community-acquired pneumonia (CAP) in children and as many as 18% of cases require hospitalization.[3] Recent studies showed that 7—30% of the hospitalized children with CAP had evidence of mixed viral—bacterial infections.[1,4—8] Coinfection of *M. pneumoniae* is not uncommon in children with respiratory syndromes. In Taiwan, a prospective study on the etiology of hospitalized children with CAP demonstrated a high incidence (41%) of mixed infections and 37% with *M. pneumoniae* infection.[9] Furthermore, concurrent viral—bacterial infection was identified in approximately 60% of children with *M. pneumoniae* infection. Although most *M. pneumoniae* respiratory infections are mild and self-limited, the clinical features of coinfection of *M. pneumoniae* are not well described. The aim of this study was to investigate the impact of bacterial and viral coinfection on mycoplasmal pneumonia in hospitalized children with CAP. The manifestations and clinical outcomes in such instances are also defined and discussed.

Materials and methods

Study population and design

This study was approved by the Institutional Review Board of Chang Gung Memorial Hospital (No. 102-0401B). Between August 1, 2001 and July 31, 2002 children coinfected with *M. pneumoniae* in a prospective study of the etiology of CAP at a tertiary pediatric facility Children's Hospital were enrolled and retrospectively reviewed. Pneumonia was defined as the combination of acute respiratory symptoms and infiltrates on chest radiographic images, which were interpreted by attending physicians and radiologists. Children with *M. pneumoniae* pneumonia were stratified into three groups: *M. pneumoniae* alone, *M. pneumoniae* coinfected with *Streptococcus pneumoniae*, and *M. pneumoniae* coinfected with virus. The clinical, laboratory, and radiographic data on admission, as well as complications and outcomes of these patients, were collected, analyzed, and compared.

Microbiological diagnostic method

For *M. pneumoniae*, both acute and convalescent serum were obtained and measured for antibody response (IgM and IgG) to *M. pneumoniae* by enzyme-linked immunosorbent assay methods (Savyon, Ashdod, Israel).[10] Criteria for acute mycoplasmal infection were either a single serum showing positive *M. pneumoniae*-specific IgM or a seroconversion of IgG.[11] *S. pneumoniae* infection was defined by a positive result in blood or pleural fluid culture or the detection of antigens in the pleural fluid by latex agglutination testing. Acute pneumococcal infection was also included for patients who had necrotic lung parenchyma with a positive urine test for *S. pneumoniae* (Binax, Portland, ME, USA).

For viral etiology, viral direct immunofluorescent assay and cultures were performed using sputum or oropharyngeal swabs. A positive result for respiratory syncytial virus (RSV), adenovirus, parainfluenza 1, 2, and 3, and influenza A and B was considered significant. Serum specimens were also examined for these seven respiratory viruses by the complement fixation method (BioWhittaker, Walkersville, MD, USA). A $\geq$4-fold rise in titer, a titer of at least 1:16, or a single titer of at least 1:64 (initial titer 1:2) was considered positive and indicative of acute infection.

Statistical analysis

Statistical analysis was performed using SPSS 10.0 for Windows (SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant. Parametric data were compared using analysis of variance (ANOVA) followed by Bonferroni's multiple comparison test. When the data were not normally distributed, or were nonparametric data, the Kruskal—Wallis test was used as appropriate. Categorical data were analyzed using contingency table analysis and the Chi-square or Fisher's exact test.

Results

Patients and microbiological diagnosis

Seventy-seven children had evidence of acute *M. pneumoniae* infection (Table 1). In children with paired serum samples for *M. pneumoniae* infection, specific IgM was positive for both occasions in 31 patients and for one occasion in 25 patients. Another 20 patients were positive for specific IgM with a single serum sample obtained at the acute stage. Seroconversion to specific IgG was identified in only one patient who was negative for IgM. For *S. pneumoniae* infection, two of these 77 patients were positive for *S. pneumonia* by blood culture. Of the cases with complicated pleural effusion available for study, eight cases were positive for *S. pneumoniae* by latex agglutination test and eight cases were diagnosed with *S. pneumoniae* infection