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Original article

The utility of biomarkers in differentiating bacterial from non-bacterial lower respiratory tract infection in hospitalized children: Difference of the diagnostic performance between acute pneumonia and bronchitis

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ABSTRACT

The aim of this study is to investigate the utility of several biomarkers in differentiating bacterial community-acquired lower respiratory tract infection (CA-LRTI) from non-bacterial CA-LRTI in children and the difference of their diagnostic performance between pneumonia and bronchitis. A retrospective cohort study composed of 108 pediatric patients hospitalized for CA-LRTI was performed during 2010–2013. Based on the findings of chest X-ray and sputum samples, patients were divided into 4 categories, group of bacterial pneumonia or bronchitis, and non-bacterial (viral or etiology-unknown) pneumonia or bronchitis. Peripheral white blood cell and neutrophil counts, and serum C-reactive protein (CRP) and procalcitonin (PCT) levels were compared among the 4 groups. Finally, 54 patients were the subject of this study. In the patients with pneumonia, serum CRP and PCT levels were significantly elevated in the group of bacterial pneumonia (CRP: $p = 0.02$, PCT: $p = 0.0008$). The area under the receiver operating characteristic curve for PCT for distinguishing between bacterial and non-bacterial pneumonia was the largest, and sensitivity, specificity, positive predictive value and negative predictive value of PCT were best among 4 markers. On the other hand, in the patients with bronchitis, neutrophil count was significantly decreased in non-bacterial bronchitis whereas no significant differences of WBC count, CRP level or PCT level were seen. In conclusion, PCT was the most useful marker to differentiate bacterial pneumonia whereas neutrophil count contributed most to the discrimination of bacterial bronchitis. The diagnostic performance of biomarkers may be different between pneumonia and bronchitis.

1. Introduction

Community-acquired lower respiratory tract infection (CA-LRTI) is one of the most common diseases in children. Causative pathogens of CA-LRTI are mainly bacteria and virus, and frequent occurrence of bacterial infection is confirmed in children hospitalized for pneumonia [1,2]. Appropriate antimicrobial therapy following early differentiation of bacterial infection has been recommended in the patients diagnosed as pneumonia [1,3]. Many biomarkers are used for the discrimination of bacterial infection and the therapy evaluation in pediatric patients with pneumonia, in which the utilities of serum C-reactive protein and procalcitonin, widely prevalent in clinical practice, have been reported [4–6]. In addition to these markers, peripheral white blood cell (WBC) and neutrophil counts are also traditional markers to distinguish bacterial pneumonia [7,8].

In contrast to pneumonia, the administration of antimicrobial agents in the early phase of acute bronchitis is not recommended because most causative pathogens are viruses [9,10]. However, patients with the abnormality of respiratory system are more likely to develop bacterial CA-LRTI, in whom early differentiation of bacterial bronchitis may be important to avoid progression to

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severe condition [11]. The utilities of serum CRP and PCT for distinguishing bacterial from viral etiology in LRTI such as acute exacerbations of chronic obstructive pulmonary disease (COPD) and bronchitis are controversial [12–14]. In addition, there had been few reports evaluating the utility of biomarkers for the differentiation between bacterial and viral bronchitis in pediatric patients.

In the present study, we assessed the utilities of peripheral WBC and neutrophil counts, and serum CRP and PCT levels, which are widely utilized in clinical practice, for differentiation of bacterial infection in the pediatric patients with CA-LRTI. Furthermore, we also examined the difference of their diagnostic performance between pneumonia and bronchitis.

2. Material and methods

2.1. Study population

We performed a retrospective cohort study on 108 consecutive patients less than 15 years old who were admitted to the Department of Pediatrics at Kyushu University Hospital from January 1, 2011 to December 31, 2013 for CA-LRTI. The diagnosis of CA-LRTI was based on both clinical history such as fever, cough and dyspnea, and ausculatory findings of abnormal breath sounds, wheezes or crackles [15]. In addition, the patients with consolidation on the chest X-ray were diagnosed as having pneumonia and the patients without the evidence of pneumonia were diagnosed as having bronchitis. Clinical information on each patient was collected using a standardized case report form. The laboratory data on admission included peripheral white blood cell (WBC) and neutrophil counts, serum C-reactive protein (CRP) and procalcitonin (PCT) levels, the findings of chest X-ray, the bacteriological findings of sputum samples, and the virological findings of sputum, nasopharyngeal aspirate samples or throat swab. The presence or absence of consolidation on the chest X-ray was assessed by 4 of the authors (T.H., E.N., S.K. and H.N.).

2.2. Sputum collection, bacteriological examination, and its evaluation

Sputum samples were obtained for the confirmation of bacterial infection. The sputum collection and the judgment of their qualities using Geckler's classification were performed as previously described [16]. Smears, classified as Geckler's group 4 or 5, were judged to be suitable for bacterial examination. Only sputum samples suctioned through the tracheostomy orifice were judged to be suitable, even when they were classified as Geckler's group 6. When phagocytized bacterial cells were seen on the Gram stain smear of the sputum sample and corresponding bacterium was isolated later, it was identified as causative agent of bacterial infection.

2.3. Confirmation of viral, chlamydial and mycoplasmal infection

Rapid antigen detection tests for adenovirus (SA Scientific, San Antonio, TX, USA) using throat swab, and for influenza virus (FUJIREBIO, Tokyo, Japan) and respiratory syncytial virus (RSV) (SA Scientific) using sputum or nasopharyngeal aspirate, and serologic tests for *Chlamydophila pneumoniae* (enzyme immunoassay for IgM antibody, Mitsubishi Chemical Medicine, Tokyo, Japan, positive cut off index > 2.0) and *Mycoplasma pneumoniae* (particle agglutination antibody, FUJIREBIO, Tokyo, Japan, positive: four-fold or more rise of antibody titer in paired sera) were carried out when clinically indicated.

2.4. Statistical analysis

Comparisons of the quantitative values were analyzed by Mann–Whitney *U*-test. The Fisher's exact test was applied for the qualitative analysis. The diagnostic performance of each marker in identifying bacterial pneumonia or bronchitis was assessed as area under a receiver operating characteristic (ROC) curve, and optimal sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated based on the cut-off values determined by the ROC curves. *p*-values less than 0.05 were considered to be statistically significant. SPSS statistics (version 21; SPSS Inc., Chicago, IL, USA, and IBM, Armonk, NY, USA) was used for analysis.

3. Results

The profile for the patients enrolled in the present study was shown in Fig. 1. Of 108 patients with LRTI, 2 patients were excluded because of having severe complication (cardiac failure due to

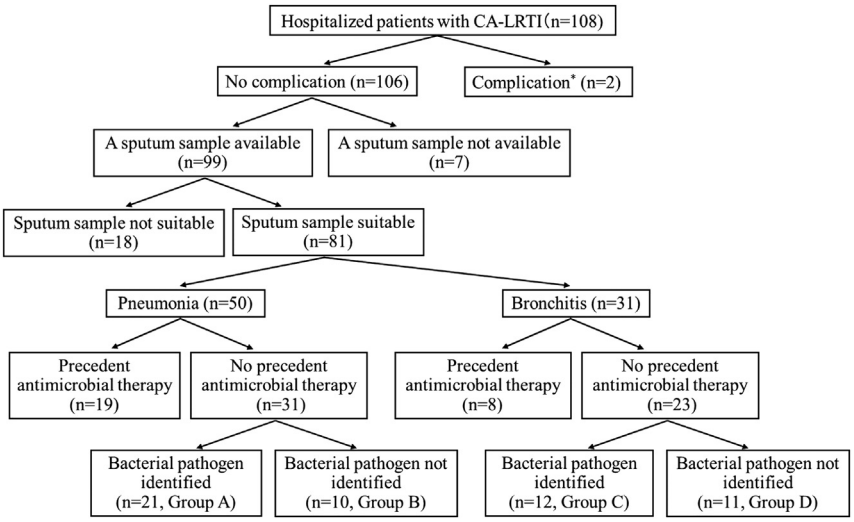

Fig. 1. Patient profile. * One patient was complicated by cardiac failure due to dilated cardiomyopathy, and another patients was complicated by rhabdomyolysis.