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ORIGINAL ARTICLE

Risk factors for slowly resolving pneumonia in the intensive care unit

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Background: Slowly resolving pneumonia (SRP) poses early challenges for identification and medical expense for clinicians in intensive care units (ICUs); to date, the literature has been very limited in this regard.
Methods: This was a retrospective and cohort-based study in the ICU of a university-affiliated hospital in Shanghai. Medical records of pneumonia patients in the ICU between April 2008 and February 2011were reviewed retrospectively to evaluate the risk factors for SRP.
Results: In all, 106 pneumonia patients in the ICU were identified as immune-competent with a diagnosis of bacterial pneumonia. There were 62 (58.49%) patients who showed SRP and their radiographic infiltrations were completely resolved between 5 weeks and 8 weeks. Multivariate logistic regression analysis demonstrated that initial treatment with an inappropriate antibiotic, multilobar infiltration, and a high CURB-65 score were independent risk factors for SRP, with odds ratio (OR) values of 8.338 [95% confidence interval (CI) 2.117–32.848], 11.184 (95% CI 2.526–49.514), and 2.329 (95% CI 1.172–4.626), respectively. The length of the ICU stay in the SRP group was twice as long as that of the normally resolving pneumonia (NRP) group (62.27 ± 73.73 vs. 32.25 ± 23, $p = 0.002$). The 28-day and 60-day mortality rates in the SRP group were 17.74% and 25.81%, respectively. In addition, the 60-day mortality rate was significantly higher in the SRP group than the NRP group (25.81% vs. 6.82%, respectively; $p = 0.012$). Moreover, SRP was an independent risk factor for 60-day mortality (OR 5.687, 95% CI 1.334–24.240).

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Conclusion: Treatment with an inappropriate antibiotic, multilobar infiltration, and a high CURB-65 score were independent risk factors for SRP.

Introduction

The unapparent resolution of pulmonary infiltrates in both nonresolving and slowly resolving pneumonia (SRP) poses diagnostic and treatment challenges for clinicians as a common consultation problem.[1,2] Nonresolving pneumonia often represents a noninfectious process that mimics an infectious process.[3,4] SRP is usually associated with host- or treatment-related factors.[5,6] Advances in procedures used to diagnose pneumonia have led to a declining incidence of nonresolving pneumonia, while the incidence of SRP is definitely rising with multiple supporting methods.[7,8] Kirtland and Winterbauer[9] first proposed a definition of SRP that referred to immune-competent patients who exhibited improved clinical symptoms with antibiotic therapy and chest radiographs with less than 50% clearing by 2 weeks or less than complete clearing at 4 weeks.[10] To date, the literature concerning the evaluation and treatment of SRP has been limited. Although the precise incidence of SRP is not well established, early studies reported that 25—67% of the pulmonary infiltration of pneumonia patients showed delayed resolution along with high mortality,[11] prolonged hospital stays, and high treatment costs.[8] Some studies on critically ill patients found that as many as 47% of pneumonia cases showed delayed resolution.[12] Due to its high incidence and poor outcome, the recognition and resolution of SRP in intensive care units (ICUs) deserve more attention from clinicians.

The objective of this study was to investigate the incidence, length of ICU stay, outcome, and risk factors associated with SRP in critically ill patients to promote the identification of high-risk patients.

Methods

Ethical statement

The extent of our involvement with participants was limited to the evaluation of radiographic resolution and analysis of the participants' clinical features. We promised to hold all the information of participants in a confidential manner. The study protocol and consent procedure with waiver of written consent was approved by the Shanghai Jiao Tong University School of Medicine and affiliated to the Ruijin Hospital Ethics Committee.

Study population

The study group was sampled from patients who were admitted to the ICU of a 1300-bed university-affiliated hospital with a diagnosis of pneumonia between April 2008 and February 2011. {Pneumonia was defined as a new or progressive infiltrate as seen on a chest radiograph or computed tomography (CT) scan along with a high clinical suspicion of pneumonia, defined by at least one of the following: fever ($>38^{\circ}C$); leucopenia [$<$ 4000 white blood cells (WBC)/mm^3] or leukocytosis ($>$ 12,000 WBC/mm^3); altered mental status with no other recognized cause (for adults older than 70 years); and at least two of the following: (a) new onset of purulent sputum, change in characteristics of sputum, increased respiratory secretions, or increased suctioning requirements, (b) new onset or worsening cough, dyspnea, or increased ventilation demand.}

The inclusion criteria included pneumonia patients who reached clinical stability due to treatment in the ICU with a complete resolution or resolution of infiltrate differentiated from chronic changes. [Clinical stability was defined as a temperature $\leq 37.8^{\circ}C$, a heart rate $\leq$ 100 beats/min, a respiratory rate $\leq$ 24 breaths/min, systolic blood pressure $\geq$ 90 mmHg, arterial oxygen saturation $\geq$ 90% or $PaO_2 \geq$ 60 mmHg in room air, the ability to maintain oral intake, and a normal mental status.[10]]

The exclusion criteria included patients with immunodepression, interstitial pneumonia, pulmonary tumor, pulmonary tuberculosis, influenza A virus subtype H1N1 or another respiratory tract virus, legionnaires pneumonia, mycoplasma pneumonia, chlamydia pneumonia, and acute respiratory distress syndrome. [Immunodepression was defined as a recent history of neutropenia ($< 0.5 \times 10^9$ neutrophils/L for 110 days); the receipt of an allogeneic stem cell transplant; the prolonged use of corticosteroids (a mean minimum dose of 0.3 mg of prednisone equivalent/kg/day for 13 weeks); treatment with another recognized T cell suppressant such as cyclosporine, tumor necrosis factor-alpha (TNF-α) blockers, specific monoclonal antibodies, or nucleoside analogs during the past 90 days; or inherited severe immunodeficiency (such as chronic granulomatous disease or severe combined immunodeficiency).[13]]

Study methodology

Every eligible patient had pre-pneumonia radiography as basic radiographic data and a CT scan performed to identify pulmonary destruction and multilobar infiltration. Each pneumonia patient was evaluated once a week in the ICU by bedside X-ray examination or CT scan if possible until the pulmonary infiltrates were completely resolved or their radiological signs normalized to previous levels. Two specialized radiography colleagues who were blinded to clinical status evaluated the radiographic infiltrates. The patients with SRP reached clinical stability but exhibited either persistent pulmonary infiltrates 4 weeks after an initial pneumonia-like syndrome or demonstrated less than 50% clearing on chest radiographs taken 2 weeks after starting antibiotic therapy. The normally resolving