

Commentary

Can we predict septic shock in patients with hospital-acquired pneumonia?

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See related research by von Dossow *et al.* in this issue [<http://ccforum.com/content/9/6/R662>]

Abstract

Hospital-acquired pneumonia is a serious and potentially life-threatening complication, with reported pneumonia-attributable mortality rates as high as 50%. Rapid diagnosis and immediate institution of adequate empirical antimicrobial treatment are of paramount importance in patient management. Nevertheless, some patients deteriorate and develop respiratory insufficiency, septic shock and a multiorgan dysfunction syndrome. Early recognition of these patients might help in reducing morbidity and mortality. Elevated systemic levels of proinflammatory cytokines (IL-1 β , IL-6, IL-8 and IL-10) at the time of diagnosis of hospital-acquired pneumonia appear to be indicative of subsequent progression to septic shock. Should this now become a part of patient management?

In the present issue of *Critical Care*, van Dossow and coworkers [1] report their findings in predicting progression from hospital-acquired pneumonia (HAP) to septic shock based on systemic levels of proinflammatory cytokines at the time of HAP diagnosis. They evaluated 76 patients with a clinical diagnosis of HAP, of whom 29 (38%) progressed to septic shock. Systemic levels of IL-1 β , IL-6, IL-8 and IL-10 at the time of diagnosis were higher in patients who subsequently progressed to septic shock. Moreover, these systemic levels predicted disease progression better than do currently used parameters such as C-reactive protein and leucocyte counts in peripheral blood. Before we modify our daily practice in accordance with these interesting findings, we must consider whether the data were rigorously obtained, are generalizable and are likely to improve the standard of care.

The spectrum of pneumonia has been divided into three areas, with similar sounding acronyms. HAP is defined as

pneumonia diagnosed 48 hours or more after hospital admission, without clinical signs of pneumonia at the time of admission. If such signs are present and pneumonia is diagnosed within 48 hours after admission, then it is termed community-acquired pneumonia. If a patient has already been receiving mechanical ventilatory support for more than 48 hours at the time of diagnosis, then it is termed ventilator-associated pneumonia (VAP). To make matters even more confusing, VAP has been divided into early-onset VAP (occurring within the first 4 days of ventilation or hospitalization) and late-onset VAP (occurring thereafter). Early-onset VAP is more likely to be caused by antibiotic-sensitive bacteria and is considered to carry a better prognosis than late-onset VAP, which is frequently caused by multidrug resistant pathogens [2]. HAP occurs at a rate of 5–10 cases per 1000 hospital admissions, with the incidence increasing as much as 6-fold to 20-fold in mechanically ventilated patients [3]. So what types of pneumonia were evaluated in the study conducted by van Dossow and coworkers? All patients underwent surgery, and the average time between hospital admission and the diagnosis of pneumonia was 42 and 33 hours for patients developing and not developing septic shock, respectively. In addition, all patients were mechanically ventilated at some point, although it remains unclear whether patients needed ventilatory support because of pneumonia or were still receiving mechanical ventilation after surgery at the time of diagnosis. Assuming that patients were hospitalized because of surgical procedures, and not because of community-acquired pneumonia, a considerable proportion of the patients should probably be categorized as very early-onset VAP. Microbial aetiology and appropriateness of empirical

antibiotic therapy are important prognostic variables in nosocomial pneumonia. Unfortunately, the microbiological data provided are rather nonspecific. Gram-positive bacteria more frequently caused pneumonia that did not progress to septic shock (86% of cases with 100% survival), whereas 47% of patients developing septic shock were infected with Gram-negative bacteria (survival 55%). Moreover, 12 patients (16%; five without and seven with subsequent shock) did not initially receive appropriate therapy, which was changed when cultures became available. However, no differences in outcome or inflammatory parameters could be discerned between these patients.

Did all patients truly have pneumonia? Diagnosing nosocomial pneumonia is difficult and is usually based on the presence of a new or progressive radiographic infiltrate along with clinical findings suggesting infection, such as fever, purulent sputum, leucocytosis and decline in oxygenation. The combination of these criteria has a high sensitivity, but specificity is rather low. More specific diagnostic approaches are needed, especially in mechanically ventilated patients, in whom abnormalities on chest radiography may also result from noninfectious causes (such as atelectasis, congestive heart failure, pulmonary embolism with infarction, lung contusion [in trauma patients] and chemical pneumonitis after aspiration). For such patients the best evaluated approach is use of invasive diagnostic techniques (in order to avoid sampling of the colonized upper respiratory tract) with quantitative microbiological cultures (in order to distinguish true infection from procedure-related contamination). In the only prospective randomized trial evaluating both approaches [4], the clinical suspicion of VAP was not confirmed by quantitative cultures in approximately 50% of patients and antibiotics were withheld in most of them. However, despite withholding of antibiotics in a considerable fraction of patients, survival was better among patients randomly assigned to the invasive diagnostic strategy. Importantly, in the study conducted by van Dossow and coworkers [1], pneumonia was diagnosed based on a combination of radiographic and clinical criteria (as mentioned above) and some patients might have been misclassified as having pneumonia. Although patients with cardiac problems and acute lung injury were excluded, the diagnostic strategy used does not rule out alternative infections or noninfectious foci. Therefore, one could ask whether clinical deterioration truly resulted from pneumonia in all patients.

So, can we predict deterioration of HAP to septic shock using biochemical means? Taking into account all of the considerations mentioned above, in their study van Dossow and coworkers [1] were able to distinguish between patients who developed and those who did not develop septic shock based on systemic levels of proinflammatory cytokines, while currently used variables (such as C-reactive protein) could not. However, bedside determination of interleukins using enzyme-linked immunosorbent assay is still far from common

clinical practice. Even if this were possible, what potential clinical consequences could be identified based on elevated cytokine levels if the diagnosis of pneumonia has been firmly established with other sources of infections excluded, if the causative pathogens have been isolated and if appropriate antimicrobial therapy has been instituted? There is no current evidence that immunomodulation (e.g. with corticosteroids) or sepsis treatment (e.g. with activated protein C) would prevent disease progression in such patients. However, reliable tools with which to predict disease progression would be the first step in establishing a new field of infectious disease management in critically ill patients.

Competing interests

The author(s) declare that they have no competing interests.

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