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Community-acquired pneumonia: challenges of the situation in Brazil

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Community-acquired pneumonia (CAP) is the leading cause of morbidity, hospitalization, and mortality worldwide and represents a diagnostic and treatment challenge.[1] In Brazil, CAP constitutes the leading cause of hospitalization (excluding causes related to pregnancy, childbirth, and puerperium) via the Brazilian Unified Health Care System. In 2017, there were 598,668 CAP-related hospitalizations and 52,776 CAP-related deaths in our country.[2] Although CAP is one of the most common infections, there have been few clinical or epidemiological studies of CAP in Brazil.

In the current issue of the JBP, Bahlis et al.[3] publish a single-center cohort study of CAP conducted in the interior of Brazil and involving all patients hospitalized for CAP over a one-year period. Despite some limitations, the study has the great virtue of reinforcing some of our conceptions about CAP and alerting to the need for implementing measures to improve the management of CAP in our country. Chief among these conceptions are initial misdiagnosis of pneumonia, difficulty in identifying the pathogen, the advantages of using severity scores in the initial assessment of patients, and the importance of implementing measures to improve in-hospital management of cases.

We see in daily clinical practice that there is a lot of misdiagnosis when it comes to CAP. Clinical and laboratory signs that are characteristic of severe infection, such as tachycardia, fever, and altered leukocyte counts, are nonspecific and are frequently present in other acute conditions. Biomarkers, such as C-reactive protein and procalcitonin, are also nonspecific and have more value in ruling out a diagnosis of infection than in establishing a definitive diagnosis. It has long been known that errors in radiological interpretation made by non-pulmonary specialists working at emergency rooms occur relatively frequently.[4] As a result of these difficulties in the initial clinical assessment, an accurate diagnosis of CAP can often be a challenge. It is of note in the study by Bahlis et al.[3] that practically one third of the patients hospitalized for respiratory infection did not meet the diagnostic criteria for CAP and were excluded from the analysis. This may raise a debate as to whether the data for a large number of hospitalizations for CAP in Brazil are correct. Would our statistics for CAP be inflated by inclusion of other respiratory infections misdiagnosed as CAP?

After diagnosis, major guidelines recommend that CAP severity should be assessed against criteria to determine the place of treatment and antibiotic therapy. The implementation of guidelines into care protocols has always been a major challenge, because, in daily practice, severity scores are not used by all emergency department attending physicians. However, despite assessment errors that are attributable to these scores, their implementation reduces mortality.[5] Silveira et al.[6] reported that admission and treatment criteria were guideline-concordant in most of a sample of Brazilian patients (in 73.2% and 58.9%, respectively), and that guideline-concordant treatment was associated with lower 30-day mortality. In addition, Bahlis et al.[3] found that major severity scores showed good ability to predict in-hospital mortality, with no statistical differences between the **C**onfusion, **U**rea, **R**espiratory rate, **B**lood pressure, and age > **65** years (CURB-65) score and the Pneumonia Severity Index (PSI). Therefore, especially with regard to using severity scores in the initial assessment of patients, we might apply the old saying "bad with them, worse without them."

Difficulty in identifying the pathogen causing the infection increases the challenge in CAP management. Certain microorganisms are particularly difficult to cultivate, requiring specific culture media or a particular environment. Although it is well established that *Streptococcus pneumoniae* is the pathogen most commonly associated with CAP, the fact is that studies of the etiology of CAP fail to identify the pathogen in most patients.[7] The currently published study[3] is not different in this respect and identified the pathogen in only 17% of the cases, with the most commonly isolated agent being *Streptococcus pneumoniae* (in 36%).

Knowing the potential etiologic agents in CAP, which ones are increasing in incidence, their degree of resistance, and their lethality rate is critical to an effective therapy. Bahlis et al.[3] observed a high rate of change in antibiotic regimen during hospitalization (63%). In most cases, the initial treatment regimen consisted of amoxicillin + clavulanate, and the most common change was the addition of azithromycin to the regimen, on the basis of clinical assessment by the attending physician. The mean length of hospital

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stay was 7.2 days (median, 5 days), and, over the patients' course, 29% required ICU treatment and 15.5% died in hospital.

If early identification of the etiologic agent were possible, a likely consequence would be a more rational use of antibiotics, with a reduction in complications and mortality from CAP. However, the current standard for diagnosis is blood culture, which usually takes at least 48-72 h to obtain a result, and cultures often remain negative even when bacterial or fungal infections are strongly suspected. This results in patients being initially treated empirically and often with broader spectrum antibiotics to increase the likelihood that a pathogenic organism will be adequately covered. This approach, despite being currently valid, has negative aspects, which include the potential for toxicity from use of multiple antibiotics, the high associated costs, and the development of resistance to antimicrobials.

Results after the recent development of rapid and highly sensitive molecular assays have produced surprising information about the causes of CAP. For the first time, multiple agents that had not been observed in older studies were detected. These methods increasingly identify respiratory viruses, including rhinovirus and influenza virus, in patients with CAP.[8] Pathogens were identified in the bloodstream of infected patients within 6 h, with high sensitivity and with a three times higher likelihood of identification than that of standard culture. These findings could potentially have resulted in a change in antibiotic treatment in up to 57% of the patients studied.[9]

Knowledge about CAP has undergone phases in which the presence of the so-called atypical pathogens was highly valued, and today we are going through a phase in which viruses are being strongly considered. The true importance of finding viruses in the respiratory secretions of patients with CAP has yet to be established, as it remains unknown whether viruses are effective pathogens or copathogens in pneumonias. We also need to develop skills to handle molecular tests; they bring the prospect of rapidly defining the cause of CAP and changing the initial approach. This may allow targeted antibiotic therapy rather than empirical antibiotic therapy, which is what we currently use.

Another important challenge when it comes to treatment of CAP is the time from diagnosis to initiation of antibiotic therapy. Studies have established that a delay in initiation of antibiotic therapy of more than 4 h increases the potential risk of complications and death.[10] Current guidelines on sepsis recommend that antibiotic therapy ideally be initiated within the first hour, given that any delay in therapy can result in decreased survival.[11] The study published in the current issue of the JBP[3] also raises this issue when it reports the long elapsed time to initiation of antibiotic therapy (mean, 10 h), with few patients receiving antibiotics within the first 4 h: only 19%. Because the vast majority of patients received the first dose of antibiotics after quite a long time, the authors could not correlate this delay with the high in-hospital mortality rate and the great need for ICU admission in the study population. These data alert to the need for hospitals to implement measures to expedite administration of the first dose of antibiotics in cases of CAP in the emergency room, with the suggestion that this be done even for those as outpatients.

CAP constitutes a serious public health problem in Brazil. At a time when we are reviewing and updating the Brazilian guidelines for the management of CAP, studies that lay bare the situation in the country and alert to the need for measures to improve the diagnosis and therapeutic management of CAP are essential. Promoting the adoption of care protocols in health facilities, with measures tailored to the situation in our country, can reduce excessive hospitalizations and the rate of mortality from pneumonia in Brazil.

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