

## Pulmonary infiltrates in critically ill patients: the importance of lung biopsy

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Acute respiratory insufficiency resulting from diffuse diseases in the pulmonary parenchyma is a severe condition that presents high mortality rates and, consequently, requires early appropriate treatment. In recent decades, there have been advances in measures for ventilatory, hemodynamic, and nutritional support, as well as for substitution of renal function and infection control, all of which have, overall, been improving survival in intensive care units. However, despite the efficacy of all of these support measures, patient recovery depends on the specific treatment of the disease, which must therefore be identified. At this point, cases of diffuse pulmonary infiltrate in critical patients pose a great challenge, since there are a number of diagnostic hypotheses, and because the results of clinical tests and less invasive complementary examinations do not always provide sufficient data to differentiate among these hypotheses. Lung biopsy may be the only means of making a definitive diagnosis, although it is an invasive procedure that should only be performed in patients with severe forms of disease.

Infectious diseases are generally the first to come to mind in cases of acute respiratory insufficiency with diffuse pulmonary infiltrate. This is relevant because they constitute the most common etiologies in this situation. However, there are numerous infectious etiologic agents (bacteria, fungi and viruses) that can be implicated in isolation or in combination. Such agents include *Pneumocystis carinii/jiroveci*, *Mycobacterium tuberculosis*, other mycobacteria and *Nocardia*.<sup>(1-2)</sup> In the absence of an etiological diagnosis, broad-spectrum antimicrobial treatment regimens tend to be used and are frequently extended over the course of the treatment if a satisfactory response is not obtained. These treatments expose the patients to side effects from a great number of antibiotics, increase the risk of nosocomial infection, facilitate the emergence of resistant strains, and are costly. In addition,

considering the possible diversity of agents, it is likely that the antimicrobial treatment is not appropriate.

Noninfectious causes are also common in patients with acute respiratory insufficiency caused by diffuse disease of the pulmonary parenchyma. Examples include edema, neoplasia, embolism, drug toxicity, alveolar hemorrhage, bronchiolitis obliterans with organizing pneumonia, acute interstitial pneumonia, and actinic pneumonitis.<sup>(1-2)</sup> In this case also, although some clinical and laboratory data can provide diagnostic clues, a definitive diagnosis can only be made through histopathological analysis. Since the treatments for each of these different conditions are specific, occasionally involving deleterious immunosuppressant drugs, making a definitive diagnosis in cases of infection is therefore quite important.

In this issue of the *Brazilian Journal of Pulmonology*, Barbas et al. present an interesting study on the role of open-lung biopsy in critical patients with diffuse pulmonary infiltrates.<sup>(3)</sup> From among the biopsies performed in their institutions between 1997 and 2002, the authors selected and reviewed those obtained from critically ill patients who were under mechanical ventilation. Out of a total of 500 biopsies, they found only 12 cases meeting their criteria, demonstrating that, despite the importance of making a definitive diagnosis in such cases, the surgical procedure is still rarely ordered. In all cases, a specific cause for the respiratory insufficiency was identified, and in 11 of them the result led to a change in the previously determined treatment regimen. Many such changes probably would not have occurred if the biopsy had not been performed, although the nature of the study does not allow us to conclude this categorically. Among the infectious causes found, the viral etiologies stand out, since they are rarely treated using the established empirical treatments. In some cases, specific treatments, such as treatment with corticosteroids and heparin, were established,

whereas in others the drugs were discontinued, either for being the cause of the pulmonary injury or for being unnecessary.

Despite having been obtained from a small sample of patients, their results illustrate the importance of open-lung biopsy in critically ill patients with diffuse pulmonary infiltrates. At the same time, the authors showed that the rate of complications is low, and there were no deaths related to the procedure. Postoperative air leakage is the most feared complication. Its presence can preclude the use of mechanical ventilation, causing leakage of part of the tidal volume delivered. However, mechanical ventilation itself can cause air leakage, above all when high pressures, which are often inevitable, are maintained in the respiratory system. This complication requires a thoracic drain, which is a risk factor for another complication, namely empyema. In this series, only 2 patients presented air leakage. One presented a more severe form and required adjustments in the mechanical ventilation.

In a study published in the Brazilian Journal of Pulmonology in 2005, Monteiro et al. found similar results.<sup>(4)</sup> In 24 patients with diffuse pulmonary infiltrate, submitted to mechanical ventilation, and not having been diagnosed by less invasive techniques, open-lung biopsy provided the diagnosis in 100% of the cases. The diagnosis resulted in a change in the treatment in 18 patients (72%), either adding drugs such as antibiotics or immunosuppressants or removing others. In that study, there were also no deaths resulting from the procedure. Complications occurred in 5 patients (20%) - one case of empyema and four cases of bronchopleural fistula - the latter corresponding to the most feared adverse effect of this procedure.

Despite the high diagnostic yield of the procedure in determining the cause of respiratory insufficiency and the implications of treatment, these studies were unable to evaluate the impact that this procedure has on prognosis. The mortality rates observed in the two studies were comparable (50% in the Barbas et al. study and 46% in Monteiro et al. study) and were similar to those reported in the literature. However, in order to know if the open-lung biopsy contributed to these results, a control group (composed of patient not submitted to biopsy) would be needed. That would allow the comparison of the results obtained for the two groups, above all those related to survival. For ethical reasons,

studies of this nature are not performed. Therefore, decisions on whether or not to perform invasive diagnostic procedures must be made on a case-by-case basis.

When making such a decision, we should take into consideration not only the condition of the patient but also the diagnostic possibilities and whether the clinical condition of the patient allows us to perform the procedure. We should also take into consideration the technical skills of the team involved in performing the surgical procedure as well as of that involved in providing the intensive care. In addition, the analysis of the material obtained must be optimized in terms of the techniques employed and the time frame in which the results are delivered. In the Barbas et al. study, for instance, the microbiological analysis included (in addition to the direct testing for etiologic agents) culture for aerobic bacteria, anaerobic bacteria, mycobacteria, fungi, *Nocardia*, *Chlamydia*, and viruses. The histopathological studies were performed in an institution with considerable experience in pulmonary pathology. We can not simply extrapolate these results, for they will not necessarily be reproduced in all locations. An unfavorable relationship between the risks of the procedure and the benefits of the diagnostic investigation can even impede the execution of open-lung biopsy. One means of improving this relationship is to send the material to referral centers for the diagnosis of lung diseases, which is now an option in Brazil.

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