EDITORIAL

Life after death: Lessons in lung injury physiopathology with necropsies on H1N1 infected patients

Vida después de la muerte: lecciones de fisiopatología de la lesión pulmonar con necropsias de pacientes con infección por H1N1

I. López-Alonso\(^a\), G.M. Albaiceta\(^ab,c,\)

\(^a\) Departamento de Biología Funcional, IUOPA, Universidad de Oviedo, Oviedo, Spain
\(^b\) Servicio de Medicina Intensiva, Hospital Universitario Central de Asturias, Oviedo, Spain
\(^c\) CIBER-Enfermedades Respiratorias, Instituto de Salud Carlos III, Spain

The threat posed by the influenza A (H1N1) respiratory infections epidemic has triggered a worldwide response that has been felt in practically all aspects of respiratory medicine.\(^1\) The study of antiinflammatory treatments in lung injuries\(^2\) or of extracorporeal gas exchange techniques,\(^3\) tested during the epidemic, extends beyond the viral infection itself, with an impact upon the entire spectrum of acute lung injuries (ALIs). The knowledge generated is moreover common to multiple aspects of lung injury, not only to that referred to H1N1 virus infection.\(^4\)

The present number of Medicina Intensiva publishes the special article of the SEMICYUC, offering an update on the management protocol for patients with severe H1N1 infection,\(^5\) and the January issue contains the study of Nin et al.,\(^6\) documenting both the presence of viral antigens and the activity of different pathogenic mechanisms in lung tissue samples from patients who have died of H1N1 infection. The findings of this work illustrate not only different aspects of the viral infection, but also of acute lung injury.

Regarding the contributions of the work of Nin et al. to our knowledge of influenza A (H1N1) infection, mention should be made of the capacity of the virus to infect different types of cells in the lung tissues. On the other hand, the virus shows a persistent presence in lung tissue samples for up to 36 days—a circumstance that suggests the advisability of reconsidering the duration of antiviral therapy.

However, many of the findings of the present article may be common to multiple forms of lung injury, independently of the triggering cause. Thus, the observation of an increase in oxidative and nitrosylative stress, already reported in other forms of acute lung injury,\(^7\) reinforces the importance of these processes in the pathogenesis of respiratory distress. The use of antioxidants is one of the eternal treatment promises that has failed to show significant benefits at clinical level, though the supporting experimental evidence is strong.\(^8,9\) The increased relevance of oxidative stress in murine models versus humans\(^10\) could help explain the discrepancies between the laboratory and clinical findings.

On the other hand, mention must be made of the presence of tissue repair mechanisms acting from the very early phases of injury. Four of the 6 patients studied present granulation tissue in the samples, and one of them shows signs of lung fibrosis. Possibly, the existence of an adequate inflammatory response, with granulation tissue favoring tissue remodeling, constitutes a critical step in limiting the posterior appearance of fibrosis. In other words, the coordinated intervention of inflammation, granulation and posterior collagen lysis must be preserved in order for good functional recovery to occur.\(^11\) This need for an adequate inflammatory response in turn would justify the poorer results obtained in patients treated with corticosteroids.\(^2\)

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\(^\star\) Corresponding author.

E-mail address: Guillermo.muniz@serspa.princaet.es (G.M. Albaiceta).

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The study also shares the positive aspects and the limitations of studies made with patient samples. Access to lung tissue in patients with acute lung injury is often very limited. The availability of samples for conducting studies of this kind is essential for the furthering of knowledge, and the valuable information generated therefore must be analyzed and shared down to the last details. On the other hand, necropsy studies may involve bias associated to the analysis of material only from deceased patients. Nevertheless, the presence of findings in common with those of experimental studies reduces the likelihood of such bias.

All the contributed information, together with its correspondences and discrepancies with previous results, clearly illustrates the inter-dependency between laboratory studies and clinical findings, whereby the former demonstrate the relevant pathogenic mechanisms, which in turn must be confirmed in patients. In the same way, the circuit receives feedback, and the discrepancies, or novel clinical findings, must stimulate our knowledge of the underlying molecular mechanisms. Over the short or long term, all this will contribute to improvements in patient treatment. May this represent translational research?

References