Accused and prosecutor: The importance of a trial

Andrea Montisci, MD,^a and Antonio Miceli, MD, PhD^{a,b}

From the ^aCardiothoracic Center, Sant' Ambrogio Clinical Institute, Gruppo Ospedaliero San Donato, University and Research Hospitals, Milan, Italy; and the ^bDepartment of Clinical Science at South Bristol, University of Bristol, Bristol, United Kingdom.

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Address for reprints: Antonio Miceli, MD, PhD, Cardiothoracic Center, Istituto Clinico Sant' Ambrogio, Gruppo Ospedaliero San Donato, Via Giuseppe Faravelli, 16 20149 Milan, Italy (E-mail: antoniomiceli79@alice.it).

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Leukemoid reaction, commonly defined as a rise in white blood cell count beyond 30,000 cells/ μ L,¹ is a rare finding after cardiac surgery, with only sparse reports.^{2,3} In unselected populations, leukemoid reactions are associated with a high morbidity rate and a high mortality,¹ and systemic infections and myeloproliferative disorders are often identified as causative factors. In this issue of the *Journal*, Ellison and colleagues⁴ highlight the importance of recognizing a leukemoid reaction after cardiac surgery to reduce the potential risks associated with unnecessary prolonged treatments. Even though leukemoid reaction is a rare event in cardiac surgery, this case report has the merit of bringing to our attention the pivotal question of inflammation in cardiac surgery. Surgical trauma, cardiopulmonary bypass, cardiac ischemia, active endocarditis, and chronic heart failure are all conditions well known to be able to trigger systemic inflammation,^{5,6} potentially associated with increased morbidity and mortality.⁷ When faced with these clinical issues, we have to be aware that our diagnostic power is poor and the therapies are limited. In the last years, much epidemiologic and clinical attention has been addressed to systemic inflammatory response syndrome. As recently questioned, however, the definition of systemic inflammatory response syndrome lacks specificity,^{8,9} and it is no longer used to define sepsis.¹⁰

Many cardiac surgical patients who satisfy diagnostic criteria for systemic inflammatory response syndrome often undergo an uneventful postoperative course.¹¹ This is even more true when we rely on common clinical markers, as white blood cell count or C-reactive protein level, to determine the degree of inflammation. The low specificity of these definitions might lead to misdiagnosis and overtreatment, with the known detrimental consequences of antibiotic misuse. Nevertheless, in clinical situations such as chronic heart failure,¹² in which a self-perpetuating and dysregulated inflammatory process takes place, our therapeutic panel is narrow and limited. Effective therapies specifically addressing the inflammatory process are lacking

Andrea Montisci, MD (left), and Antonio Miceli, MD, PhD (right)

Central Message

Although well characterized from a pathophysiologic point of view, systemic inflammation still lacks specific diagnostic criteria and effective therapies.

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because of multiple failures in randomized, controlled trials. Statins have been proposed as a potential treatment option to mitigate dysregulated inflammatory states, but their utility has not been confirmed in clinical trials.¹³ Moreover, 2 recent large, randomized, controlled trials heavily questioned the usefulness of corticosteroids during cardiopulmonary bypass.^{14,15} Among new therapies, cytokine absorption seems to be the most promising option, whether used intraoperatively or postoperatively in selected cases.¹⁶⁻¹⁸ The evidence is growing, and the expectations are high: we know the accused (inflammation), but we are still trying to put it on trial!

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