

Systemic inflammatory response of COVID-19 and its morphological expression, multiple organ damage

Respuesta inflamatoria sistémica de la COVID-19 y su expresión morfológica, el daño
múltiple de órganos

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Editor;

The COVID-19 pandemic has been the greatest health, social and economic disaster suffered by humanity since the Second World War, which has been the reason for numerous scientific works, interested in finding a solution to the multiple problems it causes. Among these studies are those related to the reaction produced in the body and especially the systemic inflammatory response (SIR) that it triggers.

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In Cuba, for several decades, SIR⁽¹⁾ and its morphological expression, identified through autopsy studies, have been studied as multiple organ damage (MOD).^(2,3) Thanks to the high number of cases studied and their results, introduced and processed by the Automated System for the Registration and Control of Pathological Anatomy (SARCAP), developed in the country since the 1980s.⁽⁴⁾ RIS is common to numerous causal factors, leading to vital damage to the organism (Fig. 1).

This response of the body, by itself or by appropriate therapy, can be controlled and its stability restored; otherwise, it produces an exaggerated response, which manifests itself, at first, in an immunological hyperreactivity and gives rise to a storm of mediators (a term that, due to its breadth, the authors prefer, to that of Cytokine Storm). This, in turn, causes damage to the entire body and especially to various organs, including the main ones: lung, kidney, brain, blood and blood vessels (vascular endothelium), liver, digestive tract and heart.

The clinical expression of these damages is manifested in multiple organ dysfunction the syndrome (MODS) and morphologically, in MOD. The latter is diagnosed when 3 or more of the indicated organs are involved with the morphological alterations, which correspond to the triggered response. Under ideal conditions, a scoring system of greater diagnostic accuracy is applied. Therefore, there are three stages: SIR, MODS and MOD. In the current literature related to COVID-19, SIR is referred to as a syndrome, that is, they do not differentiate SIR from MODS.^(5,6)

In previous studies, supported by autopsies, burn disease was a very suitable model for MOD; later it was the autopsies performed on patients with acquired immunodeficiency syndrome (AIDS). Currently, COVID-19 is a causal factor that has proven to be an exemplary model. Once the SIR is uncontrolled, the damage produced by SARS-CoV-2 in the mentioned organs is more intense than what has been observed until now by other causal factors.

In April 2020, the Temporary Group of Pathological Anatomy was formed, made up of professors of the specialty, authors of this work, to study the autopsies of those who died from COVID-19 in Cuba.⁽⁷⁾ Until the month August 2021, they have studied, using the same methodology, more than 300 autopsies and the above has been verified. The autopsies were performed by pathologists and technicians from various hospitals, the largest numbers at the Central Military Hospital Dr. Luis Díaz Soto and Salvador Allende Teaching Surgical Clinic Hospital, Havana, Dr. Mario Muñoz Monroy, from Matanzas, Comandante

Manuel Fajardo Rivero Military Hospital, from Santa Clara and Amalia Simoni Surgical Clinical Hospital, from Camagüey.

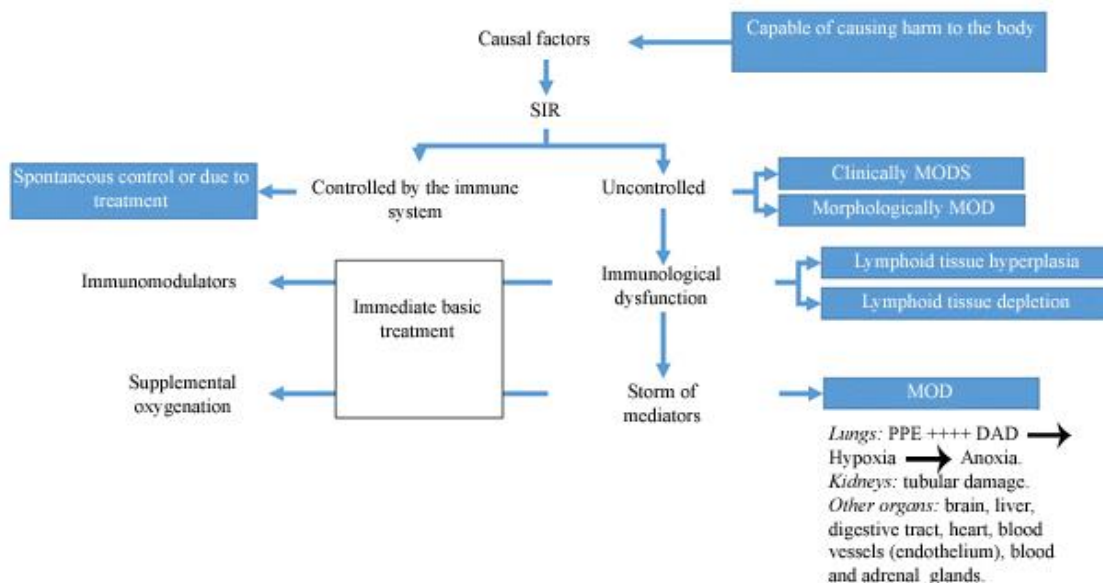
The main results have been:

- Autopsies with COVID-19 as the basic cause of death (BCD): 63.5% (195 of 307). In the 65 autopsies in 2020, the result was 47.7% and in 2021; 68%.
- In these cases, the most frequent direct causes of death have been lung damage. It begins with a permeability pulmonary edema (PPE) that is accompanied, according to severity, by other lesions: hyaline membranes, cellular hyperplasia with desquamation, metaplasia, and atypical changes. This initial PPE, due to the accompanying lesions noted, when they occur, is generally diagnosed as diffuse alveolar damage. It was present in 92.8% of the cases.
- The kidney, with acute tubular damage, has been present in practically all cases. Other lesions, generally associated with the two most frequent comorbidities, clinically diagnosed hypertension or the most frequent, its fundamental morphological expression, hypertensive heart disease and diabetes mellitus, are very frequent.
- MOD, in COVID-19 cases such as BCD, was present with a high frequency: 70.3%.

As can be seen in Fig. 1, when the RIS gets out of control, an immune dysfunction occurs and the consequent storm of mediators; produces PPE and its immediate effect, a hypoxia that affects all organs.⁽³⁾

For this reason, proven and collected in the doctoral theses of two authors⁽⁴⁾ of this work, the use of immunomodulators and supplemental oxygenation of the ozone type has been proposed as basic and immediate therapy.

In conclusion, COVID-19 is the typical and more intense example of what has been proposed. It is recommended to deepen the studies of the SIR, especially at the moment when it is out of control, and to use at that moment, the therapy already indicated. In the book *Autopsia. Garantía de Calidad en Medicina*,⁽⁴⁾ the main criteria indicated here are collected in various chapters.



DAD: diffuse alveolar damage.

++++: lesions that are added to PPE, such as hyaline membranes, cellular hyperplasia, thrombosis and others that allow the diagnosis of diffuse alveolar damage.

Fig. 1 - Vital damage to the organism, as a result of SIR.

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Conflicts of interest

The authors state that they have no conflicts of interest in relation to this work.