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Pseudosepsis in Acute Inflammation of the Lung

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Letter to Editor

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Abbreviations: WHO: World Health Organization; CAP: Community-Acquired Pneumonia.

Letter to Editor

Sepsis has become one of the global problems in the healthcare system in recent decades. According to the World Health Organization (WHO), 49 million people suffer from sepsis every year, treatment of which leads to death in 11 million cases [1]. These figures of unfavorable treatment results are many times higher than similar statistics of the last SARS-CoV-2 pandemic [2], however, if the invasion of the coronavirus was accompanied by general shock and anxiety when changing the usual rhythms of public life, then the problem of sepsis, being constantly present, continues its gradual growth, attracting mainly the interest and attention of specialists. At the same time, on the one hand, the nature and features of septic complications belong to the category of extreme situations that are concentrated in emergency departments, but, on the other hand, the diagnosis of sepsis does not occur suddenly and such a patient's condition is usually preceded by long-term monitoring and treatment of the underlying primary disease.

There is no point in proving the obvious truth that the possibility of avoiding the disease, and even more so its complications, surpasses in its effectiveness and results any of the most modern and maximum possible therapeutic measures. In this regard, understanding the origins and causes of any medical problem is crucial, as it helps to create a system of measures both to prevent the development of new cases of the disease and to prevent complications. Returning to the comparison of sepsis with the coronavirus pandemic, it should be noted that in the latter case, the main focus in the fight against coronavirus was on vaccination as a preventive measure, while practical medicine did not succeed at all in treating the most severe patients with COVID-19 pneumonia. Against this background, solving the problem of sepsis in the light of modern ideas looks extremely difficult, since its main cause remains the pathogen, but an endless list of such potential non-specific representatives of the microbiological fauna puts the very concept of vaccination in this case as unpromising.

The current widespread understanding of sepsis is based on the concept of a universal autonomous syndrome, which is attributed to broad prerequisites for its development [3]. This presentation presents various, sometimes incomparable nosologies as the main cause of sepsis. This diversity of its prerequisites directs and concentrates practical efforts on early diagnosis of the pathogen and its suppression. The question of possible features of septic conditions depending on the underlying disease remains outside the scope of discussion and special studies, and the description of the observed shifts and the principles of their correction is the same for all patients, regardless of the initial pathogenetic mechanism of the process. A reflection of this approach to the interpretation of sepsis is the fact that in most publications on this topic there is no information about the underlying disease, which served as a source of septic complications.

Nevertheless, in a number of published works on sepsis, it is possible to find figures for the distribution of patients depending on the underlying disease. In such publications, attention is drawn to the fact that not only the main, but also the predominant group of patients with generalized infection are cases in which the disease began with acute inflammation of the lung tissue. Some studies report that community-acquired pneumonia (CAP) is the most common cause of sepsis and septic shock [4,5], while others published over the past couple of decades consider this disease to be

the main cause of septic complications in 40-50% of cases [6,7] and even exceeds half of the analyzed material, reaching 61-68% [8-11]. An indicative feature of the statistics on the origin of sepsis is the fact that among the available materials, only CAP appears as the leading cause of sepsis and there was not a single mention of the leading role of any other inflammatory process. This distribution of patients among the possible causes of septic complications, in my opinion, has a very real scientific explanation that allows us to look beyond the boundaries of established conceptual dogmas.

Previously, for the diagnosis of sepsis, along with clinical symptoms, confirmation of bacteremia was important, although not decisive. However, some clinicians, analyzing the results of treatment of patients with sepsis, noticed that the lowest rates of positive blood cultures among all the root causes of this complication, which amounted to only a few percent, were observed among patients with CAP [12-15]. However, if earlier we were talking about bacterial forms of inflammation, where a blood test could give a result, then in recent years the number of viral pneumonia has increased significantly, in which there are no reliable tests that can prove the mass penetration and influence of viruses on the circulatory system. Since diagnostic methods that do not include mandatory microbiological examination of blood have become widespread in recent years, the parameters of viral sepsis were determined only on the basis of analogies with bacterial ones. It should be added that viral forms of inflammation, which can acquire signs of septic complications, are mainly caused by damage to the lungs, rather than other organs and tissues, and viral sepsis in patients with CAP has reached 61% in recent years [10].

The principles of early determination of the etiology of AP and the choice of the most effective means of suppressing the pathogen, which practical medicine has tried to use throughout the entire period of the antibiotic era and active attempts to introduce which continue to the present, were initially a unilateral decision. In the first decades of antibiotic use, while their administration still brought the necessary result, although it required constant development of new, more effective drugs, misconceptions about the priority role of this therapy remained unnoticed, and cases of AP in which aggressive development of the process required additional assistance were quite rare. However, as the side effects of antimicrobials increased (an increase in resistant strains, a decrease in the activity of drugs, a constant change in the pathogens of AP, a significant increase in the number of viral forms of the disease), the number of cases when additional and intensive therapy was required increased. In this situation, the choice of additional drugs and treatment methods was determined based on the concept of the leading role of the pathogen, which was formed under the influence of antibiotics, while the classical and fundamental provisions on the inflammatory process ceased to attract due attention.

Modern interpretations of the features and nuances of the clinical picture of the disease continue to be explained by the type and virulence of the pathogen. At the same time, it is well known that, for example, pneumonia, meningitis or otitis media can be caused by pneumococcus, but hardly any of the specialists will take the liberty to claim that these different diseases will have an identical clinic, since they have the same pathogen, right? In addition, the long-term experience of attempts to differentiate AP depending on the characteristics of the pathogen was not successful, and the continuation of these efforts in bacterial forms of inflammation began to be recognized as hopeless [13,16]. In recent years, the search for differential diagnostic criteria between bacterial and viral pneumonia has proved equally fruitless [17,18]. All these results strongly suggest that the observed changes in the condition of patients with AP do not significantly depend on its etiology, but the continuation of research in this direction reflects the persistence of these deep misconceptions that influence the choice of treatment strategy.

The existing long-term misconception becomes quite obvious if we pay attention to the nature of functional disorders depending on the localization of the inflammatory process and the specifics of the lesion of anatomical structures. In this case, we are talking about the fact that AP is the only nosology from the category of inflammatory processes with localization in the small circle of blood circulation. In this situation, the problem concerns inconsistencies between the mechanism and nature of the emerging primary disorders in the body of patients with AP and the principles of diagnosis and interpretation of the results obtained.

As is known, the main purpose of the respiratory function is gas exchange at the level of tissues and cells of the body. The full realization of this function is impossible without a circulatory system. At the same time, the unique and irreplaceable role of pulmonary vessels in the general circulatory system and their functional antagonism with vessels of the large circle are known, the vital proportions between which are automatically maintained by the autonomous system of regulation of the small circle [19,20]. In addition to these basic concepts of the circulatory system in the body, basic medical information is well known that the cause of inflammatory tissue transformation is always the inevitable involvement of blood vessels in this process. Knowing about these prerequisites, there should be no doubt that the chain of shifts in the general blood flow system in AP, unlike other localizations of inflammation, begins with damage to the pulmonary vessels and will have a different, directly opposite mechanism of development, right?.

The appearance of a focus of inflammation in the lung tissue is a powerful irritant to local receptors, and the classic sign of any inflammation is pain. However, as is known, lung tissue does not have pain receptors, and pain in AP occurs only during the period of involvement of pleural leaflets in the process [21]. In the latter case, nature has provided a more important mechanism for the body than just a pain signal about the appearance of a problem. Pulmonary vessels are abundantly equipped with baroreceptors, which immediately respond to the slightest increase in blood pressure in them. This reflex, first described almost a hundred years ago and now known as the unloading reflex, has a regulating effect, aligning the proportions between the two circulatory circles and maintaining balance in the work of the two halves of the heart [22]. All this restructuring takes place automatically and autonomously, without our volitional efforts, which plays an invaluable role in extreme situations. The root cause of the changes is obstruction of blood flow and increased pressure in the pulmonary vessels as a result of the inflammatory process, and the response and adaptive reaction are changes in blood circulation in a large circle, which is expressed by a tendency to hypotension and deposition of circulating blood.

The rate of restructuring of the general circulation in patients with AP directly depends on the speed and aggressiveness of the development of the inflammatory process in the lung tissue. Consequently, the slow development of inflammatory transformation can occur without any external manifestations. At the same time, the rapid development of the disease is accompanied by reflex generalized vasospasm of the small circle, which manifests itself as a rapid change in systemic blood flow with changes in skin color and temperature, as well as pressure shifts in the arterial and central venous sectors. The presence of generalized pulmonary vascular spasm in the aggressive onset of AP was proved by us more than 30 years ago using the results of comparative tests [23]. Currently, when studying tomograms in patients with COVID-19 pneumonia, additional evidence of such a reaction has been obtained and a sharp decrease in blood volume in vessels of a small circle with a diameter of less than 2 mm [24-27] has been established.

With an aggressive course of AP, signs of such disorders appear already at the very beginning of the disease. Currently, such signs are usually considered as precursors of septic complications and their correction begins with intravenous infusions. It is easy to understand that early administration of parenteral solutions in AP will increase venous return and stimulate circulatory disorders in the pulmonary vessels. Therefore, some authors frankly report that sepsis and septic shock in many patients occur after hospitalization against the background of ongoing treatment, continuing to consider this phenomenon to be the result of virulence of the pathogen and a lack of etiotropic agents [3,28]. The above circumstances may explain the significant differences in statistical indicators that are given in the literature. Thus, PT Reid, et al. [29] note that the overall mortality rate among hospitalized patients with CAP is 5-10%, but with an aggressive course of the disease it increases to 50%. In this regard, it is necessary to note an increase in the intensity of infusions, which in the most severe situations are prescribed in the form of boluses [7,11,15]. Intravenous infusions, regardless of the primary diagnosis preceding sepsis, also increase the risk of possible cardiac overload during this procedure, which, according to these mechanisms, may be more typical for patients with AP. Optimal infusion volumes in sepsis patients have been discussed for a long time, but clear informed decisions on this issue remain an open vacancy [15,30-32].

In previous years, for many years, the author's work has observed a situation reminiscent of the organization of specialized departments for patients with COVID-19 pneumonia during the pandemic. Due to circumstances, the most severe patients from the nearby region with bacterial forms of AP were sent to our department. The rapid development of complications and high mortality in the initial period of this work was then completely eliminated among newly hospitalized patients. When under your supervision there are not individual patients with a severe course of the disease, but about ten or even more, and in all cases the intensive therapy initiated brings the result directly opposite to what is expected, then completely different ideas arise about the causes of this phenomenon, and not only about the action of virulent microflora. The success of the work was achieved due to a radical revision of the concept of the disease and the principles of its treatment, which initially had the same interpretation that has been preserved in modern approaches. Pathogenetically sound principles of treatment made it possible to avoid so-called septic complications, which actually have a mechanism of pulmonogenic shock due to the influence of the focus of inflammation, and not its causative agent [23].

Thus, if we summarize all the above data, the conclusions become quite obvious. Hyperbolized ideas about the leading role of the pathogen in the development of AP continue to dominate the professional worldview, supporting the prevailing misconceptions about the causes and mechanisms of the development of complications of the disease. The most problematic group of these patients are cases of aggressive development of the disease, which require intensive therapy already in the initial period. In principle, it is from this category of patients that the results of treatment and mortality rates depend. Long-term education of reverence for the pathogen, developed under the influence of antibiotics,

has formed false ideas about the high frequency of so-called septic complications in patients with AP, the mechanism of which actually corresponds to the pathogenesis of the unique process, and not its etiology. Modern therapeutic measures carried out in sepsis and septic shock in patients with peripheral localization of inflammation have the opposite effect in the case of inflammatory lesions of the lung tissue. All these statements are based not on theoretical assumptions, but on the fundamental materials of medical science, supplemented by the author's own research and, most importantly, the indicative results of practical testing [23]. Therefore, we can speak with such confidence about the need for a radical revision of the concept of the disease and the principles of its treatment.

If we consider the principles of diagnosing the condition of patients with AP from the positions presented above, then potential prerequisites for the development of pulmonogenic shock exist in every patient with this disease. Indications for hospitalization of a patient with AP indicate that in this case, signs of vascular disorders have already appeared, which, at least, can be considered as precursors of shock, and in more severe situations - as a state of shock. But, unlike other localizations of inflammatory processes, the observed disorders in the work of the pulmonary-cardiac apparatus in patients with AP are due to the unique pathogenesis of pulmonogenic shock, and not the result of septic complications. Such a revision of views on this problem will significantly reduce the number of patients with sepsis and septic shock, most of whom currently incorrectly account for cases of AP. But the main goal that can be achieved after adjusting the doctrine of the disease is not to bring statistics to a new denominator, but to change the final results of treatment. An incorrect interpretation of the mechanisms of AP development is the reason for inadequate care for this category of patients, which explains the insufficient success of practical medicine in this section. Therefore, this step should be considered as a real opportunity to reverse the negative trend in this segment of the healthcare system and change the fate of millions of patients with AP and sepsis, whom we lose every year.

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