

The Role of Five Classical Signs of Inflammation in the Pathogenesis and Clinical Picture of Acute Pneumonia

Igor Klepikov*

Professor, Retired Renton, WA, USA.

*Corresponding Author: Igor Klepikov

Email: igor.klepikov@yahoo.com

Short commentary

The modern understanding of the acute inflammatory process of the lungs is based on the characteristics of pathogens, the aggressive properties of which modern medicine has been trying for many years to explain the severity and nuances of clinical manifestations, and their effective neutralization is presented as the main and in fact the only way to achieve a therapeutic effect. This concept of solving the problem arose after receiving the first results of the use of antibiotics and, despite a significant change in primary conditions and the loss of antimicrobial drugs of their effectiveness and even their previous purpose, has established itself as an absolutely dominant professional point of view. A number of important factors that become more and more convincing over time, contradict existing views and reflect the further futility of attempts at an applied solution, are mentioned in the literature only as a statement of reality, but remain without practical conclusions and changes in strategy.

Firstly, as the effectiveness of antibiotics decreased, great efforts were made to early identify the causative agent of pneumonia and prescribe targeted therapy. Long-term efforts to restore the previous success of this therapeutic method thus did not bring the expected results, and the proportion of unidentified etiology of this disease continued to grow and in recent years reached 40-60 percent or more [1-4].

Secondly, having failed to succeed in diagnosing the causative agent of pneumonia, practical medicine began to use its classification depending on the conditions of the disease, which suggested a difference in its etiology. The latest innovation also did not improve the effect of etiotropic therapy, but it was still about one nosological form, which for a long time was designated as Acute Pneumonia (AP).

Thirdly, attempts to find differential diagnostic criteria for pneumonia, depending on their etiology, did not and do not give the desired results [5-7], which is one of the evidences of

the absence of dependence of the AP picture on its causative agent.

Fourth, over the past decades, there have been numerous changes in the leading pathogens of this disease, which differ in their microbiological qualities, but the overall clinical picture of the disease has not undergone drastic changes as a result of such changes [8].

Finally, the steady increase in the number of viral pneumonia has actually begun to deprive this category of patients of conventional etiotropic treatment. The experience of the last SARS-CoV-2 pandemic is very indicative in this regard, when patients with severe lung lesions with coronavirus received only symptomatic and supportive therapy, but this did not increase the overall mortality rate [9,10]. At the same time, despite the fear of coronavirus, as is known, up to 80% of those infected did not need additional help, and at least a quarter of those infected suffered such contact asymptotically [9].

Inflammation as a manifestation of pathological damage to body tissues has been known to medicine for many centuries, forming one of the fundamental sections of medical science. The process of inflammation began to be studied incomparably earlier than microbiology was born. The classic signs of inflammation described by Celsus and Galen about two thousand years ago have passed a long practical test of time and constitute the golden fund of our knowledge in this section. It remains only to express surprise and bewilderment at the inattention to these signs and even their ignoring in attempts to find a solution to the whole problem.

Of the five classic signs of inflammation (*heat, pain, redness, swelling, and loss of function*), the first four differ mainly in local manifestations, which in patients with AP have their own specifics. For example, an increase in local temperature (heat), which is observed with external forms of inflammatory processes, in patients with AP loses its significance as a result of deep internal localization of the focus. An increase in tissue temperature

in the area of inflammation is not as important as other signs. This phenomenon is caused by excessive blood flow to the inflammatory zone and increased metabolic processes in it, but with damage to the lung tissue, this sign remains inaccessible for its assessment.

Pain: Which is a signal to the body about the sudden occurrence of a problem and serves as an incentive to limit the activity of this area of the body and an incentive to protect it, does not occur in patients with AP in the initial period of the disease due to the absence of pain receptors in the lung tissue [11]. This seemingly paradoxical fact has quite reasonable explanations. Pain, depending on its intensity and individual sensitivity, can cause a shock reaction, which is accompanied by changes in respiratory and circulatory parameters [12]. However, patients with AP usually experience shortness of breath and tachycardia at the very beginning of the disease. The appearance of pain syndrome against this background cannot bring a positive result to the body, but can only enhance shifts in vital functions. Therefore, nature, taking care to prevent sudden critical conditions in case of damage to such an important organ as the lungs, has replaced pain receptors with baroreceptors of pulmonary vessels, which automatically coordinate and adapt circulatory disorders, saving our body from a sudden catastrophe [13]. Pain in AP occurs only when the inflammatory process reaches the pleural leaflets with pain receptors [11].

If we consider the cumulative clinical significance of pain in patients with inflammation, then this syndrome has a greater effect on the function of the affected organ than it represents a simple signaling reaction. In this regard, a kind of natural transformation of the reflex reaction in case of inflammation of the lung tissue is quite naturally combined with an important life-supporting function of the affected organ. Only such a feature of the reflex reaction to the development of inflammation in the lung, instead of a typical pain syndrome, is able to respond in a timely manner and support the necessary adaptation of vital functions.

The redness: Characteristic of external inflammatory processes is caused by increased blood supply in this area and at the same time is the cause of an increase in local temperature (heat). With AP, this external sign remains hidden from our view, however, the underlying local changes in blood flow lead to a slowdown in blood flow and an increase in blood pressure in this area. These factors are the trigger for baroreceptors in the vessel wall, which send signals about changes in circulatory conditions in the vessels of the small circle.

The swelling: Is the result of swelling and infiltration of tissues in the area of inflammation. This feature is also inaccessible to our naked eye. However, it is precisely this phenomenon of tissue transformation in combination with increased blood filling in the perifocal zone that makes it possible to obtain objective confirmation of inflammatory changes against the background of surrounding air tissues when performing radiation diagnostics methods. In this regard, it should be noted that such a term as radionegative pneumonia is widely used in medical practice. This term has been used for many years, and the main purpose of such a diagnosis, in my opinion, was determined by the need to justify the appointment of antibiotics in cases where the patient was not under constant supervision. Such situations were mainly observed in outpatient practice [14,15]. On the one hand, the uncertainty in the diagnosis created prerequisites for the use of antimicrobials as the main therapeutic agent, but, on the other hand, it was necessary to adhere to the

recommendations in order to exclude their unjustified use.

Usually, for the primary diagnosis of AP in an outpatient setting, a chest X-ray is performed in a direct projection. It has long been known that with such an angle of transmission of the lungs in one projection, small foci in the basal segments can be layered on the shadow of the diaphragm and heart, remaining unrecognized. Therefore, in the old rules of X-ray diagnostics of AP, it was recommended to make an additional image in a lateral projection from the side of the alleged focus. In recent years, there have been reports that with negative X-ray results, subsequent Computed Tomography (CT) often reveals foci of AP mainly in the basal sections and more often on the left [16,17]. At the same time, clinicians note that such foci of inflammation of the lung tissue have a milder clinical course and less intensive infiltration [17]. However, the myth of the existence of radio-negative pneumonia continues to exist in outpatient practice, since not every patient with the discussed situation is referred for computed tomography after lung radiography during primary diagnosis. At the same time, the prescription of antibiotics requires a diagnostic justification, which, despite the growth of viral forms of inflammation, retain their priority among therapeutic agents.

The noted signs of pulmonary edema and infiltration are very important for the diagnosis of the disease, but these signs are less important compared to their pathogenetic role. The abundant blood flow to the area of inflammation and a sharp increase in the permeability of the vascular walls create conditions for the rapid movement of the contents of the vessels into the surrounding space. The more intensively this process develops, the speed of which depends on the individual reaction of the body to damaging factors, the faster the volume and back pressure of tissues on the vessels increases. This mechanism is capable of completely squeezing the lumen of not only small, but also sufficiently large vessels, which in the most aggressive cases deprives this area of blood supply [18]. In addition to possible variants of impaired blood flow in the area of inflammation, tissue infiltration is accompanied by compression of small bronchial branches, which disrupts their drainage and cleansing function and prevents the subsequent restoration of airiness.

The most important feature that determines the specifics of the clinical picture of each of the known diseases is the loss of function. It is due to this feature of inflammatory processes that it is impossible to confuse clinical manifestations, for example, tonsillitis, otitis media, paronychia or meningitis with AP, even if all these diseases are caused by a single pathogen. Consequently, long-term attempts to determine the features of the clinical manifestations of AP, depending on its etiology, are doomed to failure in advance. It is only surprising and perplexing that, despite the lack of desired and expected results, the AP clinic continues to be analyzed from the point of view of its etiology.

The speed and severity of our body's response to emerging triggers in its structures are its unique individual feature, regardless of the pathogen. A striking example and a valuable lesson for modern medicine was the SARS-CoV-2 pandemic, when countless response options were observed in conditions of infection with a single pathogen - from asymptomatic cases to the development of severe and complicated cases of COVID-19 pneumonia [9]. A number of researchers have drawn attention to the last feature of the body's reaction when encountering a pathogen and to the important role of this reaction for the severity and progression of the disease during a pandemic [19-21]. Last year, at an international conference held under

the auspices of the American Thoracic Society [22], program reports and subsequent discussions were devoted to the topic of heterogeneity of body reactions to an equivalent pathogen [23,24]. At the moment, we can only say that this important section of the AP problem has finally been brought to the attention of specialists, however, the necessary prerequisites for comprehensive conclusions and practical application of pathogenetic agents are not yet visible.

Along with the obvious misconception noted above in interpreting the causes and mechanisms of AP development, the idea of functional disorders is frankly selective. Currently, all attention is focused on lung ventilation disorders in this contingent of patients, and emergency care is focused on various options for their most effective oxygen supply. At the same time, the discussion of the existing problem does not extend to the entire chain of gas exchange in the body. Considering ways to correct ventilation disorders, the search for solutions practically does not affect the next inextricably linked link of gas exchange - blood circulation in a small circle. But it's no secret that the inflammatory process always begins with a vascular reaction and primarily causes changes in the circulatory system of the organ, isn't it? The unique parameters of blood flow in the vessels of the small circle of circulation and their preservation in the necessary proportion during artificial ventilation of the lungs is one of the most important functions of the lung tissue. At the same time, in order to consider and separately evaluate the functions of ventilation and blood flow in them, in reality, their joint analysis is required, since they are closely interrelated.

If we take into account the above-mentioned feature of the lung tissue about the replacement of pain elements in it with baroreceptors, we can predict in advance the possible reaction of the vascular system to the sudden appearance of a trigger. However, nothing needs to be predicted. It is only necessary to take into account in this process those changes that inevitably occur and which have already been studied and described. About a century ago, H. Schwegk [25] described the reflex he studied when irritating the walls of the pulmonary arteries. In response to this irritation, reactions were observed, among which special attention was drawn to a decrease in the tone of the vessels of the large circle with a delay in the periphery of the circulating blood and a decrease in venous return. This mechanism reflected the ability of the body in case of unforeseen circumstances along the course of the pulmonary vessels to instantly reduce blood flow to them, which was accompanied by their unloading.

Unfortunately, these important materials on the adaptive mechanisms of lung tissue attracted the attention of specialists only in pulmonary embolism [26,27] and pathophysiologists in experimental studies [28-30], and in recent decades the trend of studying the mechanisms of the disease at the molecular and cellular levels has completely eliminated interest in integrative and reflex phenomena. Inflammatory processes of the lungs surprisingly avoided the analysis of their pathogenesis, taking into account the inevitability of the action of this reflex, which is more often called the discharge reflex. Nevertheless, in our clinical practice, using cervical novocaine vagosympathetic blockade (CVSB) for differential diagnosis between abdominal AP syndrome and intra-abdominal causes of acute pain, we were able to obtain objective evidence of the reflex effect of lung inflammation on the occurrence of vascular and respiratory disorders in patients with AP [31]. The further use of other treatment methods, the effect of which, according to objective

tests, was identical to the effect of CVSB, allowed to radically change the results of treatment [32].

Conclusion

In this context, we are not talking about the final total results of treatment of patients with AP. The purpose of this presentation is the need to pay attention to an infinite number of variants of the development of this disease, the clinical picture of which is determined by the classic signs of inflammation and the rate of development of an individual reaction of the body. As the inflammatory response accelerates, the severity of clinical manifestations and the degree of functional disorders increase. Consequently, the more aggressively AP develops, the more important the timeliness and pathogenetic orientation of first aid becomes. In order to obtain a positive therapeutic effect from such assistance, it is necessary to radically change the views on the causes and mechanisms of the development and course of the disease. Without such a correction of professional ideas, one should abandon hopes for success in this field.

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