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Early clinical signs and laboratory abnormalities indicating risk for the development of sepsis in community-acquired pneumonia.

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Abstract

Between 2012 and 2019, 192 patients were diagnosed with sepsis based on characteristic clinical symptoms and laboratory abnormalities. In all septic patients, community-acquired pneumonia (CAP) led to the manifestation of sepsis. In all patients, the diagnosis of CAP was based on the findings from bidirectional chest X-ray, in some cases chest CT, and detailed laboratory tests. After confirming the diagnosis of CAP, the severity of the process was determined as well. In the days before the development of sepsis, patients were continuously monitored. The authors examined in the course of CAP presenting with clinically clear characteristics whether there were any clinical or laboratory abnormalities that could predict the risk of the development of sepsis days before the actual onset of sepsis. Their studies have identified several characteristic clinical and laboratory abnormalities that, when properly evaluated, may draw clinicians' attention to the risk of imminent development of sepsis.

Keywords: Community-acquired pneumonia, sepsis, early alarming clinical and laboratory abnormalities.

Introduction

In our article published in 2019, the relationship between CAP (community-acquired pneumonia) **[1]** and the resulting sepsis was analysed in detail. of the 1654 patients with pneumonia, 160 developed sepsis. In addition to the clinical examination of the patient, the analysis of the radiological acquisition, laboratory abnormalities and chest CT examinations are of great importance in the diagnosis of pneumonia. In the case of pneumonia, adequately determining the severity of the process (pneumonia severity index = PSI) is essential, because based on this, taking into account the presence of comorbidities, the process of developing sepsis is predictable in many cases. Sepsis is the cumulation of a complex interaction developing between an infectious microorganism and the body's immune, inflammatory, and coagulation systems, resulting indirectly and indirect microvascular damage in vital organs. **[1,2,3]** The interaction of the complex responses of the pathogen and the body may result in the development of multiorgan dysfunction syndrome (MODS) **[1,2]**. As a result, tachycardia, tachypnoea, hypotension, arterial hypoxemia, and decreased consciousness develop. Arterial hypoxemia, impaired renal function, metabolic acidosis, mental disorder, hyperglycaemia, jaundice indicate the manifestation of multiorgan dysfunction syndrome. In our CAP cases (n=160), supplemented by an additional 30 patients treated over the past 2 years (n=192), we examined that in the course of CAP presenting with clinically clear characteristics whether there was any warning, alarming clinical and laboratory abnormalities that may predict the risk of the imminent development of sepsis days /48-72 hours/ before the onset of "classical" sepsis. Our detailed examinations and observations showed several clinical and laboratory characteristics that may draw the clinician's attention to the risk of the development of sepsis, thus providing the physician with the opportunity to closely monitor the patient's clinical condition and start targeted therapy as soon as possible.

Patients and methods

In our publication, between 2012 and 2019, community-acquired pneumonia (CAP) was diagnosed in 192 cases. The clinical diagnosis was based on the characteristic clinical symptoms, bidirectional chest X-ray images, detailed laboratory tests, and in some cases chest CT scans. The mean age of the patients was 65 years, and 101 male and 91 female patients were studied. Among the clinical symptoms, high fever, chest pain, cough, and purulent sputum were the most common. Based on the chest X-ray images and chest CT scans, unilateral pulmonary infiltration was detected in a smaller proportion of patients, while bilateral lobar lesions were detected in the majority of the patients. Cardiovascular diseases, COPD, malignant diseases in the past medical history, and neurological disorders were the most common comorbidities. Pleural effusion (n=12) and pulmonary infiltration with cavitation (n=4) were observed in only a few cases in patients with CAP. Pneumonia severity index (PSI) was determined

in each patient. One-third of our patients were in the more favourable stages (stage II-III), the other patients were classified into stage IV-V. We continuously monitored the clinical status of our patients with CAP: in addition to continuous monitoring of oxygen saturation, heart rate, heart function, blood pressure, and respiratory rate, detailed laboratory tests (blood glucose and serum electrolyte values, complete blood count, detailed liver and kidney function, CRP and procalcitonin, D-dimer), blood gas testing, and urinalysis was performed daily, and the exact amount of diuresis was measured as well. In cases of changes in the clinical status (recurrent pain in the chest and/or in the back, fever, chills, changes in the amount and/or quality of sputum), a repeated chest X-ray was performed.

During the continuous monitoring of our patients, we examined whether there were any warnings, alarming clinical and laboratory abnormalities in the days before the development of sepsis that could predict the risk of imminent manifestation of sepsis. The results of our investigations and observations are summarized in **Tables 1 and 2.**

Table 1: Early clinical characteristics (n=192)

Symptoms	**Number of patients (n)**	**%**
Very severe physical weakness - muscle pain - malaise	180	94
Altered level of consciousness: - increased awareness - tension, - irritability	82	43
Orthostatic hypotension	94	49
Lability in heart rate (Effort tachycardia)	128	67
Spontaneous changes in oxygen saturation (SpO2) values	106	55
Decreased amount of diuresis	148	77
Dyspnoea without tachypnoea	167	87

Table 2: Early laboratory characteristics (n=192)

Symptoms	**Number of patients (n)**	**%**
Leukocytosis: WBC=14.0-18.0x10^9 Left shift in the blood count, with toxic granulation of granulocytes	178	93
Moderately increased CRP: 20-40 mg/ml	192	100
Normal procalcitonin value	192	100
Increased platelet count: 300-600 x10^9/l	116	60
Moderately increased blood urea nitrogen level: 16-20 µmol/l serum creatinine level increased to 150-200 µmol/l	132	69
Development of proteinuria	86	45

Discussion

In the study of 192 patients with CAP, the most common symptom was the presence of significant physical weakness (nearly 100 %). The second most common clinical sign was the onset of dyspnoea in patients (87 %). Dyspnoea without tachypnoea was developed (87 %), and in these cases oxygen saturation levels were normal and the blood gas valuesdid not confirm the decrease in the partial pressure of oxygen or metabolic acidosis either. 148 patients (77 %) showed a 30-40 % reduction in the 24-hour volume of diuresis. Lability in heart rate (so-called effort tachycardia) was observed in 128 patients (67 %), this symptom occurred with minimal physical exertion as well, and typically the high heart rate returned to baseline very slowly (in over 10 minutes). Spontaneous changes in oxygen saturation levels (90-96 %) were observed in 106 patients (65 %), however, in no case did this value falls below 90 %. Orthostatic hypertension was common

in our patients **(49 %)**, when the systolic and diastolic BP values measured in standing position decreased by 30 mmHg and 20 mmHg, respectively, compared to the supine position. A very remarkable phenomenon was observed regarding the changes in the level of consciousness of the patients: in almost 50 % of our cases, increased awareness, often repetitive, with tension and irritability were observed. However, the progression of the patients' level of consciousness (somnolence, soporous state) was not detected in any of the cases.

Among the laboratory abnormalities observed in the early stage, leukocytosis was the most common (93 %), with marked left shit in the blood count and toxic granulation of the granulocytes. An increase in platelet count (300-600x 10^9/l) was observed in 60 % of our patients, but no thrombocytopenia was observed in this phase of the disease. Moderate increases in CRP (in almost all cases) and levels of procalcitonin within the normal range are considered to be typical. In the majority of our patients (69 %), a moderate increase in blood urea nitrogen levels and elevated serum creatinine levels can be highlighted. Proteinuria was detected in 45 % of our patients **(Table 2).**

All of these clinical and laboratory abnormalities are most likely due to the microvascular damage of the organs. From a pathogenetic point of view, the infectious microorganism and the inflammatory and proinflammatory cytokine release activated by the pathogen play a fundamental role. (1-3-4) Abnormal changes in microcirculation are mainly indicated by early renal symptoms, and hematopoietic abnormalities are closely associated with inflammation induced by the pathogenic microorganism.

In patients with CAP, it may be of great importance that, prior to the development and complete manifestation of sepsis, there are certain clinical symptoms and laboratory abnormalities which can be demonstrated by methods that are relatively easy to use, and these symptoms and abnormalities draw the clinician's attention to the risk of developing sepsis. A weighted assessment of these warnings, alarming clinical symptoms may direct attention to the development of sepsis, and on the other hand, there may be an opportunity to start "goal-directed therapy" as early as possible, thereby significantly increasing the chances of recovery.

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