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Haematological abnormalities in patients with severe community acquired pneumonia who did not require mechanical ventilation and in patients with severe pulmonary tuberculosis

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Abstract

During the 10-year follow-up period (2008-2019) authors analyzed the different hematological changes in 1280 hospitalized patients with sever community acquired pneumonia (CAP) who did not require mechanical ventilation. The severity of illness was identified by the „pneumonia serverity index" and by the „CURB" (confusion, urea nitrogen, respiratory rate, blood pressure) severity scores. Normochromic-normocytic type of aneamia was diagnosed in 12% of patients: hypocromic microcytic type of anemia was observed on 8% of patients: immune-mediated-hemolytic anemia occurred in 6 patients. Usual degree of leucocytosis with left shifted periferial blood smear was detected in 32% of patients: extreme degree of leucocytosis was observed in 20%, leucopenia (granulocytopaenia) occured in 16% of patients. Elevated plateled count was defined in 18% while thrombocytopaenia was found in 6% of patients.

Authors prospectively followed 380 patients with pulmnary tuberculosis according to the characteristics of chest radiograph and sputum Ziehl-Neelsen's stain positivity, and a result of quantiferon test. In 380 patients with severe pulmonary tuberculosis anemia was present in 52% of patients: leukocytosis occured in 20% leucopenia, granulocytopedia and lymphopenia was observed in 16% of patients. Elevated platelet count occured in 26% which was compicated with deep vein leg thrombosis in 18 patients. Dysmyelopoietic bone marrow alteration with peripheal pancytopenia was diagnosed in one case as the result of mycobacterial sespsis. This survey has revealed that the various haematological abnormalities are common in cases of community acquired pneumonia, and in patients with severe pulmonary tuberculosis. The other clinical consequence is that the special haematological alterations, such as extreme leucocytosis, leucopenia, granulocytopenia and severe degree of anemia are useful indicators of the severity of lower respiratory tract infection.

Introduction

Community acquired pneumonia (CAP) is an important health-care concern, and is the most common cause of death associated with infectious disease and the sixth most comon cause of death [1-3]. The annual incidence rate in the USA 6/1000 in the 18-39 age group, and 34/1000 in people aged 75 [3]. Admission to the hospital in patients with CAP is needed in 20-40% and about 5-10% of these patients are admitted to intnsive care unit (ICU) [3,4]. The mortality rate of CAP in outpatients setting is in the range of <1-5%, but among patients who require hospitalization, the rate averages 12% [1,3].

Severe CAP (sepsis syndrome and septic shock syndrome) has been separeted from cases of less severe pneumonia requiring hopsitalization, because of the high mortality rate (up to 50%) Although there is no uniformly accepted definition of sever CAP, the original ATS guidelines, and in one more recent study nine criteria was identified for severe illness, and the presence of any one was used to define severe CAP [1-7]. The nine criteria for severe CAP were divided into five „minor" criteria that could be present on admission and four „major" criteria [3,7]. The minor criteria included respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major criteria included a need for mechanical ventilation, an increase in the size of infiltrates by >50%, septic shock or the need for pressors and acute renal failure. During the 10 year follow-up period (2008-2018) we have analyzed prospectively the different hematological changes in 1280 hospitalized patients with severe CAP, who didn't required mechanical ventilation. In the other part of this survey we retrospectively followed 380 patients with pulmonary tuberculosis according to the characteristics of chest radiograph and Ziehl-Neelsen stain positivity, and quantiferon test in association with haematological changes.

Patient and methods

During the 10 yeras follow-up period (2008-2018) we identified a severe community-acquired pneumoia in 1280 patients. For all patients with severe CAP, diagnostic testing should include a chest radiograph, routine laboratory tests (complete blood counts, serum sugar and electrolytes, hepatic enzymes and test of renal function). All admitted patients have oxygen saturation assessed by oxymetry. Artrial blood gas has been obtained in each patient with severe CAP. For he identification of the pathogen microorganism the diagnostic test has included a sputum Gram stain and culture. Two sets of blood

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cultures have been drawn before initiation of antibiotic therapy, and may help to identify presence of bacteriemia and of resistant pathogen. When Legionella airways infection was suspected in patients with severe CAP, we measured of urinary antigen. Table 1 displays disease state characteristics at baseline for all patients with severe CAP. The identification of pathogen microorganism by sputum Gram's stain and culture, blood culture, urine test, and serologic testing have been established in only small proportion of patients: Streptococcus pneumoninae 24% staphylococcus 12% haemophylus influanze 10% atypical pathogens (M. pneumoniae, Legionella species) 10% Klebsiella species 6%. Patients were stratified into pneumonia severity index risk classes (I-V) and CURB-65 (0-5) risk strata.

During the same time (2008-2019) we 380 patients with severe pulmonary tuberculosis according to the clinical signs and symptoms, to the characteristics of chest radiograph, and to the positive sputum Ziehl-Neelsen's stain/and quantiferon test (Table 2). We analyzed the extent and severity of haemotological abnormalities in all patients with severe CAP and with severe pulmonary tuberculosis (Table 2). We assessed the haemoglobin conentration, hematocrit value, the serum iron level, saturation index a free iron-brinding capacity, complete blood count (white blood cells, platelet counts)and different other special laboratory test were done (serum LDH concentratio, direct and indirect Coombs-test, serum haptoglobin value, urinary sedimentation and hemoglobin analysis, measurement of liver enzymes) for the detection of autoimmune-hemolytic anemia. In only one patient a bone marrow aspiration and crista trephine biopsy was made because of a pancytopaenia in a patient with mycobactrial sepsis.

Results

During the 10 year follow up period we identified severe community acquired pneumonia in 1280 patients. Severe lower respiratory tract infection definide the presence of acute radiographic infiltrates: multilobar, bilateral infiltrates of the lung and coexistent clinical symptoms and signs were detected in most of the pateints (Table 1). Severe from of pneumonia was classified in all of the patients according to the clinical symptoms (high temperature, tachypnea, tachycardia, altered mental status, low systolic and diastolic blood pressure), and laboratory findings (low oxgen saturation, leucocytois, left shifted blood smear, increased blood sugar and urea nitrogen level). Patients were stratified into pneumonia severity index risk classes I-V and CURB-65 4 strata. During the same period and quantiferon test positivity (Table 3) (2008-2019). We diagnosed pulmonary tuberculosis according to the characteristics of radiographic pulmonary infiltrates, and the positive result of the sputum Ziehl-Neelsen's stain (Table 3). The severity of pulmonary tuberculosis was detrmined by clinical symptoms (high temperature, weight loss, tachypnea, dyspnoe, tachycardia), laboratory findings (increased C-reactive protein, anemia, low oxygen saturation), positive results of sputum Ziehl-Neelsen's stain and characteristics of radiographic infiltrates.

Hematological changes

Anemia occurred in 20% of the patients identified with community acquired pneumonia, usual degree of leucocytosis with left shifted blood smear was detected in 32% of patients with CAP. Extreme degree of leucocytosis (WBC>20x10/1) was diagnosed in 20% in the preferial blood smear some myelocytes, metamyelocystes and promyelocytes can be seen. Leucopenia-granylocytopenia occurred in 16% while increased platelet count was observed in 18% of patients with CAP. In this group we obseved autoimmune-hemolytic anemia in 6 patients, while in the other group there was no immune-mediated hemolytic

Table 1. Baseline characteristics of patients with severe CAP

Characteristics	Numbers	Percent%
Demographic factors		
Age		
>50 years	720	-
≥65 years	560	-
Physical examination findings		
Temperature ≥39	878	68
Pulse≥125/min	1136	88
Systolic blood pressure <90 mm Hg	962	75
Diastolic blood pressure ≤60 mm Hg	841	66
Respiratory rate ≥30/min	1090	85
Altered mental status	128	10
Laboratory and radiograph finding		
Blood urea nitrogen>20 mg	296	23
Glucose≥250 mg/dl	314	24
Hematocrit<30%	256	20
Sodium<130 mmol/l	316	25
Oxygen saturation<90%	1190	93
PaO2<60 mmHg	983	77
One lobular infiltrates	178	14
Multilobular infiltrates	691	54
Bilateral multilobular infiltrates	503	39
Pleural effusion	329	26

Table 2. Haemtological changes in patients with severe CAP, and in patients with severe pulmonary tuberculosis

Haematological characteristics	CAP-group n=1280		Tuberculosis-group n=380	
	Number	%	Number	%
Anemia				
Normochromic-normocytic: hgb<8 mmol/l	153	12	159	42
Anemia				
Hypocromic-microcytic:hgb<8 mmol/l	102	8	38	10
Autoimmun-hemolytic anemia	6	0,4	-	-
Leucoytosis (usual degree):WBC 12-20x10/1	410	32	76	20
Extreme degree of leucocytosis:WBC>20x10/1	256	20	-	-
Leucopenia:WBC<4x10/1	205	16	68	18
Granulocytopenia: granulocytes<0,8x10/1	205	16	68	18
Thrombocytosis:platelet≥200x10/1	230	18	99	26
Thrombocytopenia:platelet <100x10/1	205	6	8	2

anemia diagnosed. The most common hematological alteration in the 380 patients with pulmonary tuberculosis was anemia (52%) and thrombocytosis (26%). Leukocytosis occured in 20 percent in patients without an extreme degree of leucocytosis. Leucopenia and granulocytopaenia were defined in 18% of patients with pulmonary tuberculosis. There was only one patient with pancytopaenia in the group of pulmonary tuberculosis: the bone marrow aspiration and biopsie revealed dysmelopeietic changes (Table 3).

Discussion

During the 10 year follow-up period authors retrospectively analyzed the different haematological changes patients with severe community acquired pneumonia, and in patients with pulmonary tuberculosis. This study surveys the extent and severity of hematological abnormalities and a correlation between the hematological changes

Table 3. Baseline characteristics of patients with severe pulmonary tuberculosis, n=380

Characteristic	Numbers	Percent (%)
Demographic factors		
Age	231	-
>40 years	149	-
>60 years		
Physical examination findings		
Temperature >38°C	344	90
Weight loss >10 kg	329	60
Chest pain	340	89
Shortness of breath	328	86
Haemoptoe	132	35
Systolic blood pressure <90 mmHg	172	45
Diastolic blood pressure <60 mmHg	168	44
Microbiological and radiograph findings		
Sputum Ziehl-Neelsen stain pozitivity	380	100
Quantiferon test	286	80
Bilateral multilobular patchy infiltrates	100	26
Bilateral micronodular infiltrates	87	23
Bilateral multilobular infiltrates with cavitation	286	80

and the severity of pulmonary infectious illness. Community acquired pneumonia remains a common and serious illness, despite the availability of potent new antimicrobials. In the United States, pneumonia is the 6 leading cause of death and the number one cause of death from infectious diseases [3]. All patients with community acquired pneumonia should have established an early correct diagnosis, the presence of complications and the severity of the illness by clincal laboratory and radiographic findings. The major variables that influence the specturm of etiological agent and the initial approach to therapy are the severity of illness at initial presentation, the presence of coexisting illness, and the presence of identified clinical risk factors for drug-resistant and unusual pathogens [3]. The recognition and analysis of the hematological abnormalities in associations with lower rspiratory tract infection and pulmonary tuberculosis can give some new valuable information to define the prognostic score of the patient's diseases, and the severity of the infectious illness [2]. Normocytic and microcytic type of anemia is one of the most frequent blood disorders in patients with severe community acquired pneumonia and most often in patients with pulmonary tuberculosis [8]. Immune- mediated hemolytic anemia is a very rare hematological disorder in patients with CAP: the incidence of this blood disorder can occur in patients with CAP who can have mixed infection involving both bacterial and „atypical" pathogens [3]. Leucocytosis with left-shifted blood smear is a very common and usual additional hematological change in both infectious groups. The presence of extreme degree of leucocytosis with myeloid precursors in the peripheral blood pulmonary infections. Pancytopaenia is a rare, but severe blood disorder in association with respiratory tract infection due to the myelosupression of bacteriemia. Fort he diferentiation between pulmonary infection and primary hematological diseases (dysmyelopoietic syndrome, acute hemoblastosis, involvment of bone marrow by lymphoma or other solid malignant disease) crista Jamshidi's biopsy is indicated. An extreme high platelet count accompanied with leucopenia and with severe anemia represents a very sensitive predictive (risk) factor of the severity of the illness in patients with pulmonary tuberculosis [10-12].

Our study demonstrates that a potential advantage can be obtained by the immediate recognition of blood disorders in patients with severe acute respiratory tract infection and in patients with pulmonary tuberculosis for prediction of the severity of the pulmonary infection.

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