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 (2008-2018) authors analyzed the different hematological changes in 1280 hospitalized patients with severe community acquired pneumonia (CAP) who did not require mechanical ventilation. The severity of illness was identified by the „pneumonia severity index“ and by the „CURB“ (confusion, urea nitrogen, respiratory rate, blood pressure) severity scores. Normochromic-normocytic type of anemia was diagnosed in 12% of patients: hypochromic microcytic type of anemia was observed on 8% of patients: immune-mediated-hemolytic anemia occurred in 6 patients. The major criteria included respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The major 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 respiratory rate ≥30/min, Pao2/Fio2<250, bilateral or multilobar pneumonia, systolic BP ≤90 Hgmm, and diastolic BP ≤60 Hgmm. The majority of 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 year follow-up period (2008-2018) we identified a severe community-acquired pneumonia 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 the identification of the pathogen microorganism the diagnostic test has included a sputum Gram stain and culture. Two sets of blood
cultures have been drawn before initiation of antibiotic therapy, and may help to identify presence of bacteremia 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 pneumoniae 24% staphylococcus 12% haemophilus influenzae 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, 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 haematological abnormalities in all patients with severe CAP and with severe pulmonary tuberculosis (Table 2). We assessed the haemoglobin concentration, hematocrit value, the serum iron level, saturation index a free iron-brining capacity, complete blood count (white blood cells, platelet counts) and different other special laboratory test were done (serum LDH concentranato, 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 pancytopenia in a patient with mycobacterial sepsis.

Results

During the 10 year follow up period we identified severe community acquired pneumonia in 1280 patients. Severe lower respiratory tract infection define the presence of acute radiographic infiltrates: multilobar, bilateral infiltrates of the lung and coexistent clinical symptoms and signs were detected in most of the patients (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 oxygen saturation, leucocytosis, 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 determined 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, metamyelocytes and promyelocytes can be seen. Leucopenia-granulocytopenia occurred in 16% while increased platelet count was observed in 18% of patients with CAP. In this group we observed autoimmune-hemolytic anemia in 6 patients, while in the other group there was no immune-mediated hemolytic anemia diagnosed. The most common hematological alteration in the 380 patients with pulmonary tuberculosis was anemia (52%) and thrombocytosis (26%). Leukocytosis occurred in 20 percent in patients without an extreme degree of leucocytosis. Leucopenia and granulocytopenia were defined in 18% of patients with pulmonary tuberculosis. There was only one patient with pancytopenia in the group of pulmonary tuberculosis: the bone marrow aspiration and biopsy revealed dysmelopoietic 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 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 radiographic 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. Haematological 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<9 mmol/l            | 153         | 12       | 159 | 42  |
| Anemia                                           |             |          |
| Hypochromic-microcytic: hgb<8 mmol/l            | 102         | 8        | 38  | 10  |
| Autoimmune-hemolytic anemia                     | 6           | 0,4      | -   | -   |
| Leucocytosis (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  |
| Thrombocytopenia: platelet≤200x10/1             | 230         | 18       | 99  | 26  |
| Granulocytopenia: platelet <100x10/1            | 205         | 6        | 8   | 2   |
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 clinical laboratory and radiographic findings. The major variables that influence the spectrum 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 respiratory 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. Pancytopenia is a rare, but severe blood disorder in association with respiratory tract infection due to the myelosupression of bacteriemia. Fort he differentiation between pulmonary infection and primary hematological diseases (dysmyelopoietic syndrome, acute hemoblastosis, involvement 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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### 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 positivity | 380     | 100         |
| Quantiferon test                      | 286     | 80          |
| Bilateral multilobular patchy infiltrates | 100   | 26          |
| Bilateral micronodular infiltrates    | 87      | 23          |
| Bilateral multilobular infiltrates with cavitation | 286   | 80          |