A LETHAL CASE OF VIRAL-BACTERIAL PNEUMONIA WITH RELATIVE LYMPHOPENIA: RETROSPECTIVE EVALUATION

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Abstract

The author presents a clinical case of a fatal course of community acquired viral-bacterial pneumonia in a patient without underlying risk factors but with atypical course. Lymphopenia and neutropenia development is considered a prognostic factor for severe course and the probability of a fatal outcome. Morphology demonstrated impairment of vascular endothelial cells, hypoplasia of the lymphoid follicles in the spleen, massive necrosis of the liver parenchyma with hemorrhages. At present such case should be differentiated with pneumonia caused by mycoplasmas, legionella, rickettsias, chlamydia, pneumocystis, as well as, in the presence of epidemiological data, with influenza A (H1N1) California 2009, influenza H5N1, coronaviral infection (MERS-CoV), that is infections complicated with acute respiratory distress syndrome (ARDS). The mechanisms of neutropenia and lymphopenia development in viral lesions of the respiratory system require further inverstigation.

Keywords: *viral-bacterial community acquired pneumonia, parainfluenza, S. aureus, lymphopenia, morphology.*

Introduction

Due to the evolution of viruses in the respiratory group, a change in the clinical presentation of viral and viral-bacterial pneumonia is possible [1, 2]. In addition, there are some similarities in the mechanisms of lung damage in viral respiratory infections(H5N1 Flu, A (H1N1) California 2009 influenza, MERS-CoV), which may cause relatively high mortality rates [3–9]. Neutropenia, lymphopenia in viral and viral-bacterial lesions of the respiratory system are associated with a severe course and the possibility of death [10, 11]. The bacterial process caused by viral infection of the respiratory system and St. Aureus, may be fatal even in young people without major risk factors. [12, 13]

Case

A 38-year-old female patient was brought to the hospital by ambulance on the third day of the disease in severe condition and was immediately admitted to the intensive care unit with pronounced general weakness, blackening of the eyes, sore throat when swallowing, breathing, talking, and similar pains along the trachea, as well as aphonia. The disease started 3 days before with sore throat, hoarseness, runny nose, fever up to 39–40 °C. Antipyretic drugs did not relieve the condition, she lost consciousness twice. Her blood pressure measured at home was 60/40 mm. Hg. The ambulance doctor administered dexamethasone 1.0, strophanthin 1.0, glucose 200.0 4%, intravenous drip, cordiamine 2.0 intramuscularly after which the patient was hospitalized.

Life history. She had vegetative vascular disorders in the past. At the age of 2 she was operated on for volvulus. There was no history of allergy. She also had furunculosis, long-time diet, took nutritional supplements. She denied ever the use of illicit drugs.

Epidemiological history. The patient denied any contact with infectious patients. Seven days before the onset of the disease she came back from China.

On examination. The patient presented on day 3 of the disease. The general condition was

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severe. The patient was sluggish but conscious. On examination, the skin was pale, there was diffuse hyperemia of the soft palate, submandibular lymph nodes were slightly enlarged. There was aphonia. Auscultation of the lungs to the right downward from the angle of the scapula demonstrated shortened percussion sound, there was no wheezing, and breathing was weakened. Her body temperature was 37.6°, blood pressure was 70/40 mm Hg and her heart rate was 128 per minute. The heart sounds were muffled, rhythmic. The respiratory rate was 32 per 1 min. Liver +1.5 cm. Urination was not changed, meningeal signs were absent. Chest X-ray showed inhomogeneous infiltration of the lung tissue in the form of large-focal shadows, in places of confluence, mainly in basal regions on the right, excluding the apex. On day 5 the infiltration of lung tissue on the right became homogeneous, the dome of the diaphragm on the right was not differentiated, which indicated the presence of effusion in the right pleural cavity. Homogeneous intensive left infiltration appeared (Segment 6). The damage to lungs progresses rapidly. By the decision of the case cinference, the antibacterial therapy was changed.

Laboratory and instrumental studies. On admission elevated leukocyte count (10.2×10^9/L) was revealed. There is well known fact that the percentage of various types of leukocytes sometimes does not reflect their absolute number, therefore an assessment of their relative and absolute values (in μL) is required (*Table*).

Lymphopenia, as a rule, is associated with severe infectious [14, 15]. Due to severe leukopenia and the appearance of solitary blast cells in two blood tests, a hematologist consultant was invited to rule out blood disease. His conclusion was leukemoid reaction. Thrombocytopenia was observed on day 5 of the disease (170,000 in 1 μl). Prothrombin index was 65% on admission, and 65% on the day of death. On day 5 urea (12.5 mmol/l) and creatinine (0.14 mmol/l) content elevated. Total bilirubin was 47 mcm/l, Alanine aminotransferase (ALT) – 0.42 mmol/l.h, on the day of death ALT was 3.8 mmol/l.h. Immunofluorescent test of a smear from the nasopharynx revealed antigens of parainfluenza virus. On day 6, Candida, Staphylococcus aureus (sensitive to oxacillin, rifampicin, cyfran, cephalexin) were revealed. ELISA HIV test was negative. Bacteriological examination of the blood for sterility was negative. Ultrasound examination on day 11 showed that the liver was enlarged by 2.5 cm, echo parenchyma increased, spleen measured 11×4.7 cm, echo was slightly elevated. A conclusion of parenchymal reaction of the liver and spleen was drawn. Urinalysis showed density 1024, protein 0.16 g/l, 5–6 white blood cells in the field of vision, 2–3 hyaline cylinders, red blood cells 30–40 unchanged in the field of vision, 15–20 in the field of vision, small amount of mucus. Feces test demonstrated liquid consistency, 30–40 leukocytes in the field of vision, 2–3 red blood cells the field of vision, small amount of mucus.

Reaction of nondirect agglutination with antigens of Sh. Sonnei, Sh. Flexneri (1–5 serotype) was negative, with antigen of salmonella group D (1, 9, 12 serotype) was also negative. Her blood group was A (II), Rh negative. Bacterioscopy of thick drop of blood did not identify any bacteria. On admission T helpers level was 27% (reference range (RR) 35–69). T suppressors made 15% (RR 5–20). Total complement amounted 0.956 units (normal 1.0–1.1). The patient was twice consulted by a phthisiologist, tuberculosis was excluded. Three times she was examined by a cardiologist, a neuropathologist.

The patient was administered ampioks 1 gram IV 6 times a day, arbidol 0.2g 4 times a day orally, lincomycin 0.6g 3 times a day. From day 3 she received contrical 10,000 U, indomethacin, levofloxacin 500 mg 1 time a day IV from day 8 to day 11 of illness, rovamycin IV 1.5 million

Hematology laboratory data in the dynamics

Parameter	Date of examination							
	03-Mar	4-Mar	05-Mar	06-Mar	8-Mar	09-Mar	10-Mar	11-Mar
White cells (10^9/l)	10.2	1.5	16.8	13.8	42.5	27.8	113.0•	75.0•
Neutrophils (%)	29	41	59	41	27	19	8	9
Lymphocytes (%)	48	18*	2*	4*	10*	4*	5*	5*
Lymphocytes absolute amount (ref. 1200–3000) in mcl	4896	270*	336*	552*	4250	1112*	5650	3750

Note. * – Lymphopenia • – Leukemoid blood reaction.

3 times a day, ceftriaxone 2 g 2 times a day IV from day 4 to day 11 of the disease. On day 4h artificial ventilation was administered; intubation was applied from day 8 of the disease to the death. Normal human immunoglobulin was administered IM 4 doses (6 ml) on day 4 of the disease. She constantly received high doses of 600 ml dopamine for 6 hours, 1200 ml for 6 hours of detoxification, dextrans, glucocorticosteroid (prednisone 90 mg per day). ECG showed sinus tachycardia, violation of repolarization, acute myocardiopathy.

Differential diagnosis. The rapid progression of the clinical signs required an early clinical differential diagnosis. It was necessary to exclude SARS, legionellosis, lung lesions in anthrax and plague. At present it is necessary to differentiate such clinical situations and avian influenza A (H5N1), A (H1N1) and Middle East respiratory syndrome (MERS – CoV). [16–18]. In the patient were forced to differentiate primarily SARS clinically, but with the help of an immunofluorescent test, parainfluenza was diagnosed and *S. aureus*, MSSA was isolated from sputum.

Auscultation did not reveal moist rales or crepitation, X-ray confirmed extensive pneumonia with an atypical character. The patient was admitted on day 3 of the disease and died on day 11. Another reason for differentiation is community-acquired pneumonia caused by methicillin-resistant staphylococcal strain and Panton-Valentine leukocidin (PVL) – producing *Staphylococcus aureus*. Necrotizing pneumonia due to PVL-positive *S. aureus* [19].

On admission the diagnosis of influenza, severe course, tracheobronchitis, bilateral pneumonia, septic shock was made.

Clinical diagnosis. Acute respiratory viral infection (tracheobronchitis, laryngitis), acute focal bilateral pneumonia right total left subtotal (from sputum bacteriologically was isolated *S. aureus*), severe course, grade 3 toxic shock, infection-toxic cardiomyopathy, pulmonary edema, grade 3 respiratory failure, swelling of the brain, secondary hypochromic anemia, DIC syndrome were diagnosed in the hospital.

Pathomorphologycal data. At autopsy, the mucous membrane of the larynx, bronchi, trachea were bluish, dull with greyish-yellowish overlays. The lungs were voluminous, dense throughout the lung tissue, the pleura was dull, greyish with dirty filamentous overlays. The tissue was motley, dark-red, with grayish pattern and brown sites. The spleen was enlarged, reddish on incision with moderate pulp scraping. Mediastinal lymph nodes were grayish on incision, mesenteric ones are enlarged and grayish. On microscopy, the alveoli contained serous exudate, solitary macrophages, desquamated cells of the alveolar epithelium, erythrocytes, solitary neutrophils, interalveolar septa were thickened due to proliferation of septal cells and infiltration with lymphoid cells. Liver hepatocytes were in a state of granular dystrophy, interstitial edema, a sharp plethora of capillaries of the sinuses, in places with hemorrhages per diapedesum. The brain had pronounced perivascular and pericellular swelling, plethora and paretic dilatation of blood vessels. Spleen microscopically is shown in Figure 6. There was hypoplasia (atrophy) of lymphoid follicles in the spleen, desolation of follicles. Thus, severe toxic damage of the vessels is noticeable: endothelial cells with picnotic nucleus, sometimes desquamation. The lungs have different size infiltration with neutrophils and apoptosis.

The presence of focal infiltration in the lung parenchyma with the destruction of lung tissue, presence of neutrophils and apoptotic bodies is determined. The beginning of formation of granulomatous tissue on its periphery.

Pathoanatomical diagnosis of bilateral serous-hemorrhagic pneumonia was made. On day 4 immunofluorescent test identified antigen of parainfluenza virus. There was swelling of the brain, trunk dislocation, incision, pronounced plethora of paretic vascular dilation, hemorrhages in the internal organs. Proteinaceous and fatty degeneration of parenchymal organs was recognized. The cause of death was intoxication.

Discussion. Today respiratory viruses threat to global health and cause epidemics and pandemics with significant morbidity and mortality [20]. Presumably, it was a variant of atypical viral-bacterial pneumonia [21, 22], but testing for atypical pathogens in our patient was not conducted. For parainfluenza the temperature does not rise to 39 degrees on the first day of illness. Auscultation did not reveal moist rales or crepitation, X-ray confirmed extensive pneumonia with an atypical character. Lymphopenia was not pronounced, including in absolute values, leukopenia, colitis syndrome, hypoplasia of the lymphoid follicles of the spleen were not characteristic for community acquired pneumonia due to parainfluenza virus and *Staphylococcus aureus*. The decrease in the number of T-lymphocytes indicates a deficiency of cellular immunity, namely insufficiency of cellular immunity. Despite the long-term study

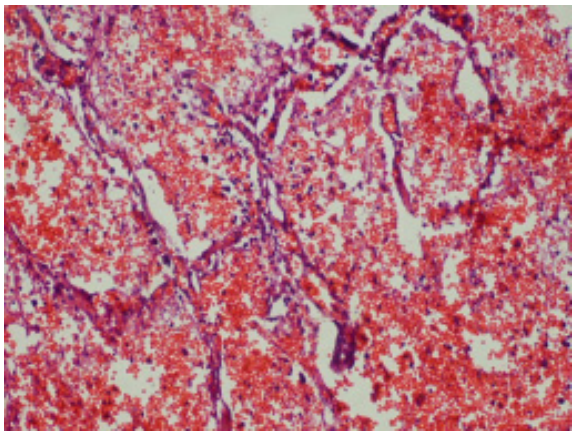

Fig. 1. Photomicrographs of lung tissue. ×400. Hematoxylin and eosin. The alveoli contain exudates with hemorrhagic component and a small number amount of macrophages, lymphocytes

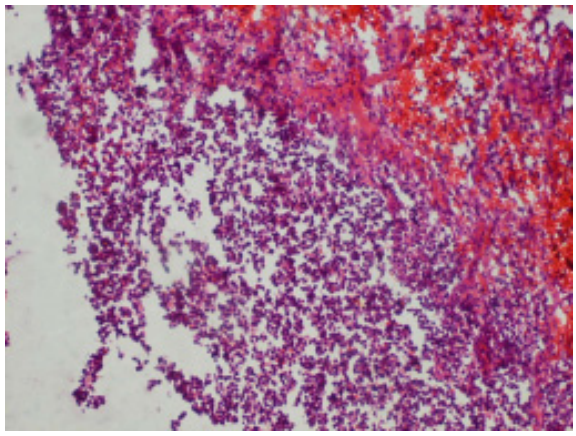

Fig. 2. Photomicrographs of lung tissue.×400. Hematoxylin and eosin

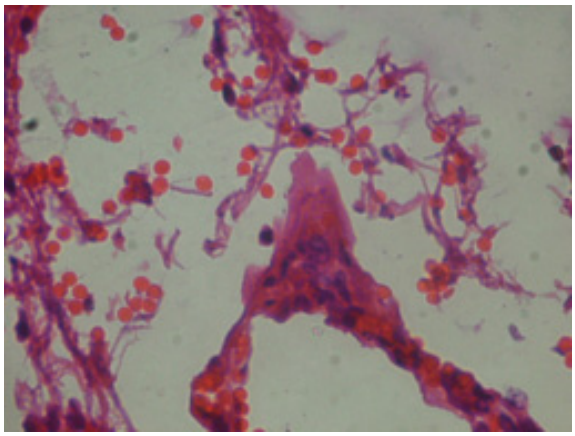

Fig. 3. Photomicrographs of lung tissue. ×400. Hematoxylin and eosin Plethora of capillaries of alveolar septa, red blood cells and sticks up to 20 microns long (Candida?) in the lumen of the alveoli

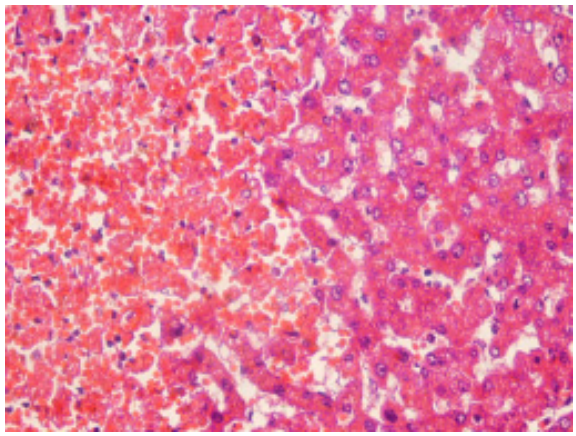

Fig. 4. Photomicrographs of liver tissue. ×400. Hematoxylin-eosin. Massive liver necrosis with hemorrhages

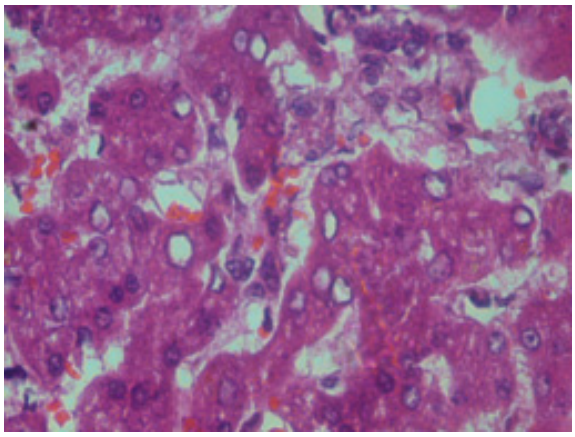

Fig. 5. Photomicrographs of liver tissue. ×400. Hematoxylin-eosin. Toxic damage to the liver. Polyploidy. Many hepatocytes have a nucleus with chromatin marginalization (apoptosis stage)

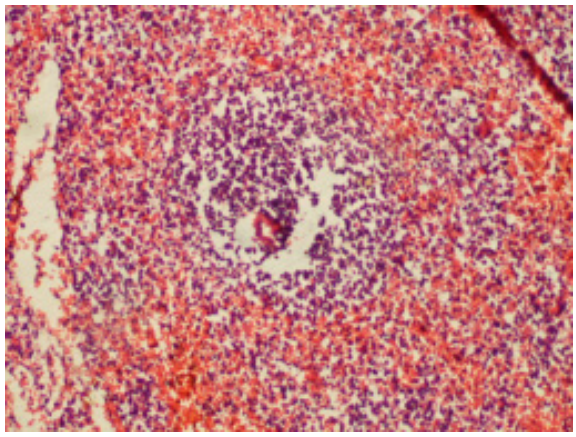

Fig. 6. Photomicrographs of spleen tissue. ×400. Hematoxylin and eosin-. Hypoplasia (atrophy) of lymphoid follicles in the spleen, desolation of follicles

of the pathogenesis of viral infections, its causes remain insufficiently studied. [23]. Cases of viral infection with the development of severe respiratory failure in the absence of a typical clinical picture of pneumonia may be associated with the threat of bioterrorism. It is also known that SARS pandemic was accompanied by high mortality. Atypical pneumonia can occur against a background of secondary immunodeficiency states. The mechanisms of neutropenia, lymphopenia are not clear enough. Perhaps their development is associated with the mechanisms of nonspecific immunosuppression. A feature of the pathogenesis of MERS-CoV, in which the virus infects the cells of the respiratory epithelium, causes changes in the regulation of cellular genes. It has been established that 207 genes in lung cells under the action of the virus are deregulated [24].

We are forced to make a retrospective assessment of fatal clinical cases of viral-bacterial pneumonia due to the emergence of new features of pathogens, which leads to changes in certain parts of the pathogenesis and clinical presentation of pneumonia.

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