Clinic morphological features of Goodpasture’s syndrome manifested with respiratory disorders

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Goodpasture’s syndrome is one of rare pathological conditions. It stipulates problem of timely diagnostics and prescription of early pathogenic therapy for cessation of progressive autoimmune inflammation and safe of patient’s life. Presented clinical case demonstrates difficulties of recognizing Goodpasture’s syndrome in case of its debut with dominating symptoms and signs of bacterial affection of the lungs and severe respiratory failure.

Case presentation. We described case of Goodpasture’s syndrome in the middle-aged woman (54 years old) which began from symptoms of community-acquired pneumonia, hemoptysis and finished tragically with developing severe respiratory and renal failures.

Conclusions. Management of community-acquired pneumonia patient, who has recurrent hemoptysis, minimal changes of the urinary system, who does not give adequate answer to the antibiotic treatment, must include additional investigation for revealing immunological systemic genesis of pulmonary tissue injury. It improves prognosis by virtue of early use adequate pathogenic therapy.

Клинико-морфологічні особливості перебігу синдрому Гудпасчера, що маніфестував респіраторними розладами

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Синдром Гудпасчера є одним із рідкісних патологічних станів, що зумовлює проблему його вчасної діагностики та призначення ранньої патогенетичної терапії, яка здатна зупинити прогресування автімунного захалення та зберегти життя пацієнта. Наведений клінічний випадок демонструє складності розпізнавання синдрому Гудпасчера у разі його дебюту з домінуванням ознак бактеріального ураження легень і важкої легеневої недостатності.

Представлення випадку. Описали випадок синдрому Гудпасчера у жінки середнього віку (54 роки), який починався із симптомів негоспітальної пневмонії, кровохаркань та трагічно завершився розвитком важкої легеневої та ниркової недостатності.

Висновки. Курація пацієнта з негоспітальною пневмонією, який має рецидивуюче кровохаркань, мінімальні зміни сечовидільної системи та не дає адекватної відповіді на антибактеріальну терапію, має включати додаткове дослідження, що дадуть змогу виявити імунологічний системний генез ураження легеневої паренхими. Це поліпшить прогноз завдяки ранньому призначенню адекватної патогенетичної терапії.

Клинико-морфологические особенности течения синдрома Гудпасчера, манифестировавшего респираторными расстройствами

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Синдром Гудпасчера – одно из редких патологических состояний, что обусловливает проблему его своевременной диагностики и назначения ранней патогенетической терапии, способной остановить прогрессирование автімунного васпаления и сохранить жизнь пациента. Представленный клинический случай демонстрирует сложности распознавания синдрома Гудпасчера в случае его дебюта с преобладанием признаков бактериального поражения легких и тяжелой легочной недостаточности.

Представление случая. Описан случай синдрома Гудпасчера у женщины среднего возраста (54 года), который начинался симптомами внебольничной пневмонии, кровохарканьем и трагически завершился развитием тяжелой легочной и почечной недостаточности.

Выводы. Курация пациента с внебольничной пневмонией, который имеет рецидивирующее кровохарканье, минимальные изменения мочевыводительной системы и не дает адекватного ответа на антибактериальную терапию, должна включать дополнительные исследования, позволяющие установить иммунологический системный генез поражения легочной паренхимы. Это улучшит прогноз благодаря раннему назначению адекватной патогенетической терапии.
Diagnosis of autoimmune diseases of lung parenchyma remains one of the most difficult problems of modern pulmonology, due to their rare prevalence and the absence of specific clinical signs. One of these diseases that arises due to the production of antibodies to the basement membranes of the renal glomeruli and the pulmonary alveoli, is the Goodpasture’s syndrome. It occurs in less than 1 case per million population per year [1] and usually develops in young people (20–30 years) or in elderly people (60–70 years), more often in men [2].

For the first time, this syndrome was described by Harvard pathologist E. Goodpasture during the management of a young man who had a bilateral infiltrative lung injury accompanied with hemoptysis and anemia after influenza. The patient died 6 weeks after the onset of the disease. Alveolar bleeding, diffuse necrosis of the alveoli and proliferative nephritis have been detected during the autopsy. Later, such cases were described by M. Stanton and J. Tange (1958). They proposed the term «Goodpasture’s syndrome» [3]. In Ukraine, one of the brightest descriptions of the case of Goodpasture’s syndrome was made by Y. M. Mostovoy et al. in 1984 [4].

Clinically Goodpasture’s syndrome is manifested with symptoms of simultaneous lung and kidney damage (60–80 % of cases). Kidney damage preceded changes in the lungs in 20–40 % of patients, and in less than 10 % of cases, hemorrhagic vasculitis of the alveolar tissue is advanced, often without clinical signs of lesions of the glomerular apparatus [2,5,6].

The causes of this syndrome are unknown. Its connection with smoking, virus infection (influenza A virus), use of cocaine, inhalation of metal dust, sepsis, treatment with monoclonal antibodies has been revealed [7]. A number of convincing data regarding the genetically determined nature of this disease have been obtained. Patients with HLA-DR15 and DR4 mutations have an increased risk of Goodpasture’s syndrome compared to DR1 and DR7 carriers. A specific molecular analysis of the DRβ chains revealed a special sequence of six amino acids common for DRw15 and DR4, which may increase the risk of developing Goodpasture’s syndrome. The indicated sequence is absent in the carriers of HLA-DRB1 [8–10].

The basis of the pathogenesis of Goodpasture’s syndrome is the formation of anti-glomerular basement membrane (GBM) antibody to the capillaries of the kidneys and alveoli. These antibodies belong to the IgG class, they are directed against the non-collagen (NC-1) domain of the alpha-3 chain of the type IV collagen, which at the highest concentration is presented in the basement membranes of the pulmonary and renal capillaries [1]. Smoking, viral infections of the respiratory system, inhalation of hydrocarbanates activates the presentation of antigens of alveolar capillaries for circulating antibodies in people with hereditary predisposition. Circulating anti-GBM antibodies bind to basement membranes, fix the complement and cause the immune-inflammatory process in the renal glomeruli (glomerulonephritis) and alveoli (alveolitis). The main participating cells in immune inflammation are T-lymphocytes, monocytes, endothelial cells, polymorphonuclear leukocytes, and alveolar macrophages. Interaction between them is provided by molecular mediators, cytokines. Important role in the development of immune inflammation is played by metabolites of arachidonic acid, free oxygen radicals, proteolytic enzymes, adhesion molecules [1,7,11,12].

The activation of alveolar macrophages, which produce about 40 cytokines, is extremely important in the development of alveolitis. Group I cytokines (chemo-taxins, leukotrienes, interleukin-8) increase the migration of polymorphonuclear leukocytes in the lungs. Cytokines of II group (growth factors of platelet and macrophage) contribute to the transfer of fibroblasts in the lungs, which leads to the rapid development of proliferative-sclerotic processes. Alveolar macrophages also produce active forms of oxygen, proteases that destroy the tissue, causing alveolar hemorrhage [1,7].

The immuno-inflammatory process has a rapid progressive development and often presented with a nonspecific clinical symptoms and signs. Considering the rareness of the Goodpasture’s syndrome, it raises the problem of early diagnosis. The timely recognition of anti-GBM antibody disease, when the function of the kidneys and lungs is still preserved, is the key to the effectiveness of modern pathogenetic treatment, which allows recovery in the vast majority of patients. Otherwise, the fulminant development of respiratory and renal failure leads to a lethal outcome [7,11,12].

We present ourselves a clinical case of the Goodpasture’s syndrome with dominating rapidly progressing respiratory symptoms, which made it difficult to diagnose.

Case presentation

Patient A., 54 years-old female, was admitted to the pulmonology department with complaints of cough with mucous-purulent sputum, hemoptysis, fever with body temperature up to 38.7 °C, shortness of breath during mild activity, decreased appetite, weight loss. The disease began acutely 18 days before hospitalization. Suddenly body temperature increased, dry cough arose. She received paracetamol for treatment. When hemoptysis appeared, the patient called “ambulance” and was taken to a hospital.

From the anamnesis it is known, the patient suffered from anemia during the last 17 years and its cause was not established. Treatment for anemia has not been received.

During an objective examination, the patient’s condition was severe. Skin and mucous membranes were pale. Tachypnea was 32 per minute. Percussion determined the areas of small dull sound in the lower part of the both lungs. During auscultation rough vesicular breathing, fine moist rales were heard over the entire surface of the lungs. Pulse was 102 per minute, rhythm, weak filling. Arterial pressure was 90/60 mm Hg. The heart sounds were rhythmic, weakened. Oxygen saturation was 90 %. Palpation of the stomach revealed painfulness in the right hypochondrium, the liver was 3 cm below the edge of the rib arc. The Pastematsky’s symptom was negative, peripheral edema was absent.

According to laboratory tests and instrumental investigations it was determined:

- Anemia (hemoglobin 76 g/l, erythrocytes 2.1 × 10¹²/l, hematocrit 23 %).
- Urinalysis revealed a small proteinuria (protein – 0.066 g/l), erythrocytes 0–4 in field of view, single hyaline cylinders.
Chest X-ray: there were parenchymal nodules and consolidation, more pronounced in the basal segments. The right hilum was not differentiated due to infiltration. The left hilum was non-structural. Heart was not changed. Conclusion: bilateral polysegmental pneumonia.

Chest CT scan: Lymphadenopathy of the mediastinum (enlargement of intrathoracic lymph nodes up to 20 × 11 mm), diffused decrease in the pneumatization of both lungs due to multiple infiltration of round and irregular shape, up to 25 mm in size. Uneven thickening of the intercellular membranes and fibrous changes with the formation of hollow structures up to 15 mm. Peripheral parts of the lungs were clear (Fig. 1).

In the sputum analysis – erythrocytes in large quantities, leukocytes 20–25 in the filed of view, cocci.

Biochemical tests did not reveal pathological changes. ECG data, echocardiography were within the norm. Ultrasound examination of the abdominal cavity revealed signs of chronic pyelonephritis, and renal calculi.

Based on the obtained data, the diagnosis was established: Community-acquired pneumonia of the upper, middle and lower lobes of the right lung, upper and lower lobes of the left lung, severe course, IV group. Respiratory failure of III degree. Hemoptysis.

Taking into account severity of the patient’s condition for the treatment of community-acquired pneumonia, she was given a combined antibiotic therapy: intravenous infusion of levofloxacin 500 mg once daily, ceftriaxone/sulbactomix 1.0 g twice daily, amikacin 1.0 g once a day. For symptomatic treatment of hemoptysis hemostatic drugs were prescribed (aminocaproic acid 5 %, 100 ml intravenously once a day, dicinone 2 ml intramuscularly once a day), for the correction of anemic syndrome – drugs that influence the synthesis of hemoglobin (vitamin B12 up to 500 units once a day intramuscularly, folic acid – 1 tablet, 3 times a day, inside), transfusion of erythrocyte mass (100 ml intravenously, once a week), oxygen therapy.

During a week, the patient’s condition improved: body temperature was normalized, cough, shortness of breath, hemoptysis, sputum excretion decreased. According to the full blood test, anemia was stable. Control chest X-ray revealed a decrease in infiltrative changes of the lungs.

Taking into account the presence of hemoptysis in the patient and the peculiarities of lung infiltration during the hospital stay, a differential diagnostic search for a possible cause of hemoptysis was conducted.

To confirm or exclude lung cancer, tuberculosis, a cytological and bacteriological sputum examinations were performed. They did not detect malignant cells, mycobact-
terium tuberculosis and other morphological features of the tuberculosis process.

Biopsy of the pulmonary parenchyma would confirm bronchoalveolar cancer or interstitial lung disease (sarcoidosis, idiopathic pulmonary fibrosis), or rare lung syndromes (Goodpasture’s syndrome, hemorrhagic vasculitis). The patient refused from transthoracic pulmonary biopsy.

However, two weeks after the onset of treatment, the patient’s condition worsened again: body temperature increased to 38 °C, shortness of breath, weakness, cough increased. There was discomfort in the lumbar region. There was an episode of loss of consciousness, after which signs of respiratory failure increased – severe dyspnea, cyanosis, the oxygen saturation decreased to 77 %. In the full blood test signs of progression of anemia were found. In the urinalysis – macrohematuria (50–60 red blood cells in the field of view), leukocyturia, proteinuria of 0.15 g/l, which was evaluated as signs of chronic pyelonephritis exacerbation. According to ultrasound examination of the abdominal cavity, signs of splenomegal, echocardiography – exudative pericarditis have been revealed.

It was assumed that a possible deterioration in the patient’s condition was associated with the ineffectiveness of antibiotic therapy because the disease was caused either by resistant pathogens or non-bacterial infection. As a result, the antibacterial treatment of the patient was replaced. She was prescribed meropenem intravenously 1.0 g every 8 hours, linzolid 600 mg twice daily, fluconazole 150 mg once daily, monoxifloxxacin 400 mg once daily.

Progression of anemia, an episode of loss of consciousness, accompanied by a deterioration of respiratory failure, gave reason to think about a possible occult pulmonary haemorrhage. Signs of the progressive inflammatory process against the background of antibiotic therapy have made it possible to assume the immunological or neoplastic pathogenesis of the disease.

Considering confirmation of these pathological changes in the pulmonary tissue can only be obtained by morphological study the patient was offered a transthoracic lung biopsy, but she refused the procedure.

On the other hand, an immunological study was performed to detect lung injury as a component of systemic connective tissue disease (vasculitis, systemic lupus erythematosus, Goodpasture’s syndrome, etc.). It revealed an increase in IgG anti-GBM-antibodies (7.7 times) which was the confirmation of a rare systemic disease with combined lung and kidney damage – Goodpasture’s syndrome or anti-GBM-antibodies disease.

The current treatment of this syndrome includes the immunosuppressive therapy using pulse therapy with systemic corticosteroids and cyclophosphamide in combination with plasmapheresis [10–12].

After diagnosis conformation, the patient received methylprednisolone in pulse therapy. Due to progression of respiratory failure, she was given artificial ventilation of the lungs with the help of the “Fabius” apparatus in the BiPAP mode. For the correction of anemic syndrome, an erythrocyte mass (100 ml) was re-administered. Parenteral nutrition was carried out using glucose and amino acids.

In spite of the treatment the patient’s condition progressively deteriorated: signs of kidney damage increased – hematuria, proteinuria, cylindrury, renal failure. Despite the adequate artificial ventilation of the lungs,
the respiratory failure progressed and acute heart failure arose. The patient died on the 23rd day of hospitalization.

According to the results of the autopsy, the diagnosis of Goodpasture’s syndrome was confirmed. Morphological signs of edema, hemorrhagic pulmonary syndrome and diffuse proliferative-productive glomerulonephritis were revealed (Fig. 2, 3).

In the lungs, alveolitis with a massive hemorrhagic exudate, eosinophilic deposits, the formation of hyaline membranes in the lumen of the alveoli, and hemosiderosis were observed. In the interstitial membranous there were signs of capillaritis with the phenomena of proliferation, hyalnosis, pneumofibrosis (Fig. 2).

In the kidney examination, extracapillary, focal, segmental, and necrotizing glomerulonephritides were determined with eosinophilic deposits on the basement membranes of the Shumlyansky–Bowman capsule, in places with total sclerosis of the glomeruli (Fig. 3).

The cause of the patient’s death was progressive respiratory failure.

Discussion

The presented clinical case of Goodpasture’s syndrome in a middle-aged female demonstrates the complexity of diagnosing rare systemic diseases affecting the alveolar parenchyma. During hospitalization of the patient signs of bacterial infection and respiratory failure were dominated on the background of chronic anemia of unknown origin.

The infiltrative changes in the lungs were interpreted as signs of severe community-acquired pneumonia and the patient received appropriate treatment. The absence of convincing signs of kidney damage in the present case caused the delay in diagnosing this syndrome.

During the stay in a hospital, the patient’s condition changed wavelikely. After a primary antibiotic therapy, a short-term improvement was noted. However, subsequently, signs of respiratory failure increased again, hyperthermia persisted, pulmonary bleeding developed, anemic syndrome, renal insufficiency increased. The immunological examination with the detection of high IgG liters of the anti-GBM-antibodies was decisive test for the correct diagnosis – the Goodpasture’s syndrome. Despite the prescribed pathogenetic treatment, it was not possible to stop the development of the fatal outcome.

According to the data of different studies, the use of pathogenetic treatment in the absence of signs of respiratory and renal failure leads to the survival of 86.9 % of patients within one year; otherwise, the vast majority of patients die within several weeks or months after diagnosis [12,13]. Patient survival rates improved significantly after 2007, which are associated with the timely use of immunosuppressive therapy and plasmapheresis, however, dependence on hemodialysis, a decrease in the number of normal functioning nephrons and widened infiltrating changes in interstitial tissue considerably worsen the prognosis of patients [14]. There are few references to the effective use of rituximab, which is able to radically affect the key mechanisms of immunopathogenesis – to remove activated B-cells that produce anti-GBM-antibodies. The drug contributed to the positive change of the course of the disease, which was complicated by severe respiratory and renal failure, resulting in a complete reversion of lung injury, saving the patient’s life, but the function of the kidneys did not resume [15].

Conclusions

Management of the patient with acute onset of disease, recurrent hemoptysis, minimal urinary tract changes, progressive respiratory failure, and fever, who does not provide an adequate response to antibiotic therapy, should include additional investigations and tests to detect the immunological systemic genesis of lung parenchyma injury. This will positively affects the outcome due to the early prescription of adequate pathogenetic therapy.

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