ОГЛЯД ЛІТЕРАТУРИ

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THE MODERN VIEW OF PULMONARY-RENAL SYNDROM

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Summary. In the review of the literature pulmonary-renal syndrom describes the occurrence of renal failure in association with respiratory failure, characterised by autoimmune-mediated rapidly progressive glomerulonephritis and diffuse alveolar haemorrhage, respectively. Pulmonary-renal syndrome is associated with significant morbidity and mortality, and prompt diagnosis significantly improve outcomes. Prompt diagnosis of pulmonary-renal syndrome requires a high index of suspicion, as clinical features are non-specific, and immunological testing aids the diagnosis in many cases. The commonest causes of pulmonary renal syndrome include antineutrophil cytoplasm antibody-associated vasculitis and antiglomerular basement membrane disease.

Key words: pulmonary-renal syndrome, diffuse alveolar haemorrhage, rapidly progressive glomerulonephritis, ANCA-associated vasculitis, antiglomerular basement membrane disease.

A significant number of patients have concomitant dysfunction of the lungs and kidneys [1]. But the primary combined lesion of these organs − pulmonary-renal syndrome (PRS) − is associated with significant morbidity and mortality, and its clinical features are non-specific [4].

In 1919, during massive influenza epidemic William Goodpasture tried to cure 18-year-old boy. A month after undergone influenza in this patient developed pulmonary lesions accompanied by type of hemorrhagic alveolitis with severe respiratory failure and rapidly progressing glomerulonephritis. Soon after that patient has died. In

1958, M. Stanton and J. Tange reported about nine cases of combined lung and kidney, which were characterized by recurrent pulmonary hemorrhage, pulmonary hemosiderosis and glomerulonephritis, with a fatal outcome within a few months of onset [27]. They first described this syndrome and introduced the term "Goodpasture's syndrome". Originally the term "Goodpasture's syndrome" signified all cases of pulmonary-renal syndrome with necrotizing glomerulonephritis combined with pulmonary hemorrhage.

With the advent of the possibility of more thoroughly examine the nature of renal involvement, including through immunofluorescence method, the term was applied only in cases where PRS is caused by antibodies to the glomerular basement membrane (GBM) kidney, since only under these conditions due to the cross-reaction of anti-GBM antibody and antigen kidney basement membrane of pulmonary alveoli, develops combined kidney and lung damage [19].

Wegener's granulomatosis (auto-immune antineutrophil cytoplasm antibody (ANCA)-positive vasculitis) was first described in 1931. H.Klinger and F.Wegener (1936, 1939) identified the disease as an independent syndrome with characteristic triad of symptoms: necrotizing granulomatous vasculitis of the upper respiratory tract, glomerulonephritis and systemic necrotizing vasculitis of small-caliber arterial disease and venous [2].

Thanks to modern research PRS is defined as a combination of respiratory and renal failure, resulting from an autoimmune-mediated diffuse alveolar hemorrhage (DAH) and rapidly progressive glomerulonephritis [20, 25].

Involved in the pathogenesis of the syndrome are not only several types of immunological damage, but other mechanisms, such as the appearance is not immune antibody BMK and antineytrofil cytoplasmic antibodies, immune and thrombotic microangiopathies [25].

The main type of lung injury in most cases, the PRS is a vasculitis of small vessels, characterized by necrosis and destructive

inflammation of arterioles, venules and alveolar capillaries. This gives the impression of perfusion and the integrity of the walls of the pulmonary capillaries, allowing blood to flow from the vessels into the tissue in the alveolar space. Clinical manifestation process is DAH [7]. A distinctive feature of quickly progressing glomerulonephritis in PRS is fibrinoid necrosis of glomeruli , with the formation of " crescents ". Kidney biopsy is described as focal segmental necrotizing glomerulonephritis. Violation of glomerular capillary walls with the passage of immune cells and fibrin deposition in Bowman's space forming crescents . Destruction crescent Bowman space leads to the loss of renal function [4].

DAH represents a broad clinical spectrum. It may develop acutely over a few days, or more insidiously, and may present as a mild illness or as fulminant respiratory failure. Features such as dyspnoea, haemoptysis, anaemia and hypoxia are neither sensitive nor specific. They may be attributed to complications of active vasculitis or its treatment, such as fluid overload or infection, and not all patients with DAH present with haemoptysis and/or dyspnoea. This simple radiography of the lungs is very sensitive but nonspecific method. Obtaining lung histology may be considered the gold standard test for diagnosing DAH secondary to small-vessel vasculitis. Clinical features of acute renal failure are non-specific and can include oliguria, peripheral or pulmonary oedema and hypertension. Serum creatinine may not always be elevated at presentation in PRS. Urine should be sent for dipstick analysis, microscopy and protein:creatinine ratio estimation. Proteinuria does not reach the nephrotic level. In the course of urine microscopy revealed dysmorfni erythrocytes and erythrocytic cylinders, confirming glomerular source of bleeding. Ultimately, a renal biopsy should be carried out to confirm the diagnosis of focal and segmental necrotising glomerulonephritis (FSNGN) [18, 28].

The most common specific causes of PRS in adults is ANCA-associated vasculitis (antyneytrofilnymy associated with cytoplasmic autoantibody vasculitis, Wegener's granulomatosis) and is caused by

antibodies to BMK (ABMK) kidney disease, which accounts for 56-77,5 12,5-17 % and , 5 % of PRS [4 , 20].

ANCA-associated vasculitis (AAV) is composed of three separate nosological forms: from polianhiyitom granulomatosis, microscopic polianhiyit and eosinophilic granulomatosis with polianhiyitom (formerly Chargah-Strauss syndrome), the incidence of which in Britain is under 9.7 , 8 and 2.7% per million population. Usually affects people aged 65 years and older. In 8-36 % of patients with ANCA- associated vasculitis occurs SAC [5, 16].

DAH is one of the earliest precursors of mortality in patients with AAV because they increase the relative risk of mortality by 8.6 times. Factors that increase the mortality of these patients during the first month include end-stage renal disease, age and a high rate of creatinine. Most patients who are treated with DAH require dialysis treatment . The relapse rate during the DAK disease ranges from 10 % to 31 % [10, 29].

Incidence of anti-GBM disease is about one case per million population. 60-80 % of patients with anti-GBM disease with clinical manifestations of simultaneous impression of the lungs and kidneys. Goodpasture prognosis is favorable , survival is 90% if patients do not require dialysis treatment early. Having DAH is a risk factor of premature mortality. Level crescents on biopsy correlated with initial renal function and its effect on subsequent changes [18, 23].

Double-positive disease represents a sub-group of AAV and anti-GBM disease where both antibodies are present. Five to fourteen per-cent of ANCA-positive patients have detectable anti-GBM, and 30–43% of anti-GBM-positive patients have detectable ANCA. The predominant type of ANCA in double positive ANCA disease is the presence of antibodies to myeloperoxidase (82%). All registered patients with double positive disease have renal involvement, and 41-83 % have concurrent pulmonary involvement. In patients with severe renal failure at the onset of kidney function recovery is unlikely. We suggest that this damage GBM in AAV creates antigens to which

antibodies are produced . This is confirmed by the fact that the number of double-positive patients are different from classical antibodies against components of GBM. However, the double- positive patients are ANCA-negative rather than the typical AAV and relapses relatively rare [8].

But also there are some less common causes of PRS , which constitute less than 10 % of all cases [3, 6, 14, 24, 26]. Antiphospholipid syndrome (APS) is a disease characterised by vascular thrombosis, recurrent miscarriages and the presence of antiphospholipid antibodies: lupusanticoagulant, anticardiolipinantibody or anti-β_2 glycoprotein-I antibody. APS associated with other autoimmune diseases, particularly lupus vasculitis and rheumatoid arthritis [12, 24].

DAH is a rare manifestation of lupus vasculitis (LV). It occurs either in the presence of capillaritis or with minimal inflammatory response and undamaged lung structure. DAH is more likely to occur as an initial feature rather than later in the disease course. Lupus nephritis coexists in 40–100% of patients, and haematopoietic system involvement occurs in more than 90% of patients [14].

IgA vasculitis (IgAV) or previously Henoch-Schönlein Purpura is a small-vessel vasculitis commonly associated with IgA nephropathy. Ninety percent of cases occur in those under 10 years old. IgAV classically consists of the triad of a purpuric rash, abdominal pain and arthritis, though other features can be present. DAH is a rare complication of IgAV, seen more often among adults [26].

Cryoglobulins are immunoglobulins that precipitate when exposed to lower temperatures. Cryoglobulinaemic vasculitis (CV), usually containing a monoclonal IgM and a polyclonal IgG, leads to systemic small-vessel vasculitis. A clinical picture similar to CV can occur in association with hepatitis C virus (hepatitis C virus-associated cryoglobulinaemic vasculitis) or as a cancer-associated vasculitis (particularly with lymphoma). DAH occurs in 3.2% of cases of CV, and is associated with membranoproliferative glomerulonephritis in 90% of cases. DAH is most commonly associated with the mixed immuno-

globulin subtype of CV. Constitutional symptoms include purpura, arthralgia, fever and neuropathy. [6].

Leads to the PRS, but quite rare, diseases such as Behcet's disease, rheumatoid vasculitis, mixed connective tissue disease, systemic sclerosis, poststreptokokovyy glomerulonephritis, dermatomyositis and polymyositis. In these cases, kidney damage is not directly due to lung disease [3, 9, 15, 19 , 21, 22].

Regardless of etiology, PRS remains a difficult clinical condition with high morbidity and mortality [11]. Since there are no specific clinical features for the diagnosis required a high index of suspicion. At the first suspicion of the diagnosis of PRS should be appropriate immunological tests and kidney biopsy.

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РЕЗЮМЕ

СУЧАСНИЙ ПОГЛЯД НА ПУЛЬМОРЕНАЛЬНИЙ СИНДРОМ

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Резюме. Пульморенальный синдром описывают как сочетание почечной и дыхательной недостаточности, обусловленные аутоиммунно-опосредованным быстро прогрессирующим гломерулонефритом и диффузным альвеолярным кровотечением соответственно. Пульморенальный синдром связан с высокой заболеваемостью и смертностью, а своевременная диагностика позволяет значительно улучшить результаты. Поскольку клинические признаки пульморенального синдрома не являются специфичными для установления диагноза в большинстве случав требуется высокий индекс подозрения и иммунологическое тестирование. Наиболее частыми причинами пульморенального синдрома являются ассоциированный с антинейтрофильными цитоплазматическими антителами васкулит и заболевания вызваные антителами к базальной мембране клубочков.

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Пульморенальний синдром описують як поєднання легеневої та ниркової недостатності, зумовлених аутоімунно-опосередкованим швидкопрогресуючим гломерулонефритом і дифузними альвеолярними кровотечами. Пульморенальний синдром пов'язаний зі значною захворюваністю та смертністю, але оперативний діагноз може значно покращити результати. Оскільки клінічна симптоматика неспецифічна, потрібний високий індекс підозри та імунологічне тестування. Найчастішими причинами пульморенального синдрому є асоційований з антинейтрофільними цитоплазматическими антитілами васкуліт і захворювання, викликані антитілами до базальної мембрани клубочків.

Ключові слова: пульморенальний синдром, дифузна альвеолярна кровотеча, швидкопрогресуючий гломерулонефрит, ANCA-асоційований васкуліт, захворювання, викликані антитілами до базальної мембрани клубочків нирки.

РЕЗЮМЕ

СОВРЕМЕННЫЙ ВЗГЛЯД НА ПУЛЬМОРЕНАЛЬНЫЙ СИНДРОМ

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Пульморенальный синдром описывают как сочетание почечной и дыхательной недостаточности, обусловленные аутоиммунным-опосредованными быстро прогрессирующим гломерулонефритом и диффузным альвеолярным кровотечением соответствен-

но. Пульморенальный синдром связан с высокой заболеваемостью и смертностью, а своевременная диагностика позволяет значительно улучшить результаты. Поскольку клинические признаки пульморенального синдрома не являются специфичными для установления диагноза в большинстве случав требуется высокий индекс подозрения и иммунологическое тестирование. Наиболее частыми причинами пульморенального синдрома являются ассоциированный с антинейтрофильными цитоплазматическими антителами васкулит и заболевания, вызванные антителами к базальной мембране клубочков.

Ключевые слова: пульморенальный синдром, диффузное альвеолярное кровотечение, быстропрогрессирующий гломерулонефрит, ANCA-ассоциированный васкулит, антитела.