CASE STUDY

MICROSCOPIC POLYANGIITIS – A VIEW OF THE PROBLEM THROUGH THE LENS OF A NEPHROLOGIST

DOI: 10.36740/WLek202104140

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ABSTRACT

The article presents two clinical cases of microscopic polyangiitis in patients with symptoms of glomerulonephritis with renal failure, which were preceded by such nonspecific symptoms as: abdominal syndrome, high blood pressure, arthralgia, myalgia, weight loss, uveitis, shortness of breath, general weakness. Clinical and laboratory-instrumental aspects of diseases are analyzed. Emphasized the feasibility of early diagnosis, adequate therapy appointment.

The aim of the article is to show that only with timely prescribing of pathogenetic therapy it is possible to achieve clinical and laboratory remission and, even, to cease hemodialysis sessions.

It was described two clinical cases of microscopic polyangiitis in patients with symptoms of glomerulonephritis with renal failure. Approaches to complex treatment of patients with the use of pathogenetic and the possibility of using renal replacement therapy were discussed. After verifying the diagnosis, all patients started immunosuppression with corticosteroids and cytostatics. It is shown that only with timely prescribing of pathogenetic therapy it is possible to achieve clinical and laboratory remission.

Clinical examples demonstrate to physicians that systemic vasculitis can often hide under the «mask» of other diseases and require timely diagnosis and immediate pathogenetic treatment.

KEY WORDS: microscopic polyangiitis, systemic vasculitis, glomerulonephritis, renal replacement therapy

Wiad Lek. 2021;74(4):1024-1031

INTRODUCTION

Systemic vasculitis (SV) is a heterogeneous group of diseases where ischemia and tissue necrosis occur as a result of inflammation of the blood vessels (primary or secondary to the underlying disease), in the pathogenesis of which involves mechanisms of both immune and non-immune genesis. Among this group of diseases are vasculitis with a predominant lesion of small and medium vessels, which include anti-neutrophil cytoplasmic antibody (ANCA) -associated. They are united by a variety of multifaceted lesions, rapid progression and, often, adverse effects. [1, 2, 3].

ANCA-associated «renal» vasculitis is a common problem in nephrology [4, 5, 6].

ANCA is a heterogeneous population of autoantibodies that react with various neutrophil cytoplasmic enzymes with proteinase-3 (PR3) and myeloperoxidase (MPO), rarely with lactoferrin, cathepsin I and others. The indirect immunofluorescence reaction reveals: 1) cytoplasmic ANCA (cANCA), which are more common in granulomatosis with polyangitis (60-90% of cases); 2) perinuclear ANCA (pANCA), which are more common in MPA (50-80% of patients) and less common in Crohn's disease, eosinophilic granulomatosis with polyangiitis (EGPA) (Cherdja – Strauss syndrome), NP, ulcerative colitis. Perinuclear glow is associated with MPO [7].

In the pathogenesis of ANCA-associated SV the leading role is played by the activation of the complement system by an alternative pathway with the formation of C5a, the interaction of C5a and C5aR. It leads to neutrophil degranulation [8, 9], to the secretion of anti-MRONG / anti-PR3NG, which damages the vascular endothelium of the microcirculatory bed, mainly in the skin, lungs and kidneys [10].

Microscopic polyangiitis (MPA) – necrotizing vasculitis with minimal or no immune deposits, with predominant vascular lesions of the microcirculatory bed (capillaries, venules, arterioles), rarely – small and medium-sized arteries. In this case, the clinical picture is dominated by the phenomena of necrotizing glomerulonephritis, skin lesions, rarely – pulmonary capillaries. It is noteworthy that pulmonary embolism of the pulmonary artery MPA is found 10 times more often than in classical nodular polyarteritis (NP) and twice more often than in granulomatous polyangiitis (GPA) (in the past – Wegener's disease) [11,12].

The diagnosis of MPA is based on complaints, clinical, immunological and morphological examination data. It is well known that diagnostic criteria are: fever, malaise, weight loss; arthritis, myalgia; changes in the kidney (often a rapidly progressing glomerulonephritis); skin manifestations in the form of erythema; abdominal syndrome, bleeding diarrhea; mono- or polyneuropathy; presence of pulmonary infiltrates (often with fatal bleeding) and detection of perinuclear autoantibodies to cytoplasmic components of neutrophils, antimyeloperoxidase in serum.

Renal impairment in MPA is manifested in the form of rapidly progressing glomerulonephritis with proteinuria (sometimes with nephrotic syndrome), micro- or hematuria, early renal failure (RF). Often patients are concerned cough, chest pain, sometimes – hemoptysis and pulmonary hemorrhage. In this case, radiographs of the lungs find infiltrative changes without decay sites, often with the development of pleurisy. In laboratory examination patients have moderate hypochromic anemia, neutrophilic leukocytosis, acceleration of erythrocyte sedimentation rate (ESR), increased levels of C-reactive protein (CRP) and creatinine.

According to the literature, the course of MPA has individual characteristicsHowever, the frequency of clinical symptoms with MPA varies. Myalgia, arthritis, arthralgia occur in 30-65%; purpura or erythema, contact bleeding – 40-58%, abdominal pain – 30-58%, lung damage – 57-100%, gastrointestinal bleeding – 20 – 30%, lesions of the eyes and ENT organs – in 30%, fever – 50%, arterial hypertension – 40-50%, isolated urinary – 70-90%, of which 50% of patients require renal replacement therapy (RRT). In 75% of patients exhibit high titer of pANCA/MPO [13, 14].

The difficulty of diagnosis is the need for a simple differential diagnosis, through a similar clinical picture, even within the ANCA-associated systemic vasculitis, the need for histopathological examination of skin, kidney or lung biopsy, the useing of not always available immunological tests.

ANCA – testing must be performed in accredited laboratories participating in quality assurance testing programs. In all cases, it is necessary to perform a biopsy of the kidney, which is the most reliable for establishing the nature and prevalence of inflammation, diagnosis and determination of vasculitis [15].

Renal lesions are typical of all ANCA-associated vasculitis, but the incidence of nephropathy is different: maximum (90%) with MPA and GPA (90%), rarely – with EGPA (20-45%). As a rule, kidney damage in MPA is accompanied by a sharp onset and a more aggressive course. It is essential to diagnose the disease as soon as possible and to start treatment in a timely manner. But in a third of patients do not detect antibodies at all, that is, a negative ANCA result does not rule out vasculitis in the presence of clinical signs of active disease [16].

The urgency of the problem is increasing due to the emergence of a certain tendency to increase these diseases.

CASE REPORT

THE CLINICAL CASE №1

Patient C., 52 years old, was admitted to the center of nephrology and dialysis of the Poltava Regional Clinical Hospital of N. Sklifosovsky (PRCH) 29/07/2019. At the time of hospitalization, she complained of shortness of breath with little exercise, increasing blood pressure (BP) to 150/100 mm Hg., dry mouth, general weakness. There was no history of kidney or lung disease, however, during the 6 months before the first clinical symptoms, there was a periodic increase in blood pressure up to 150/100 mm Hg. Considers herself sick since April 2017, when after eating fresh vegetables, she felt acute pain in the right half of her stomach. She was treated on her own, the condition improved, but a week later there was an attack of acute pain in the left half of the abdomen, noted urinary opacity. Subsequently, there were complaints of frequent urination at night (5-6 times), nausea, headache in the temporal area, dry mouth, fever to subfebrile numbers. From 05/05/2017 to 11/05/2017 were examined and treated inpatient at the place of residence with suspected secondary (paraneoplastic?) nephropathy. 07/05/2017 consulted by oncologist – oncology excluded, diagnosed with small uterine fibroids. General clinical examinations were performed, which revealed significant deviations: in the general analysis of urine (GBA) – proteinuria (0.158 – 1.79 g / l), leukocyturia (by ½ in the field of view (f/v)), erythrocyturia (12- 14 in f/v); in biochemical analysis of blood (BAB) – azotemia (increase of creatinine level to 438 μmol / l). The glomerulonephritis with acute kidney damage was diagnosed. Symptomatic treatment did not give effect.

Given the above complaints, changes in the results of analyzes, ineffectiveness of treatment, on May 11, 2017, the patient was referred for consultation to a nephrologist of PRCH, where she was hospitalized to the center of nephrology and dialysis for examination to clarify the diagnosis and treatment.

According to the analysis of medical records, changes in the objective status of the patient were noted: pallor of the skin, puffiness of the face, displacement of the left border of cardiac dullness by 1.5 cm outside the left mid-clavicular line, symptom of tapping moderately positive on both sides. In the general analysis of blood (GBA) – leukocytosis ($12x10^9$/l), anemia (Hb – 107 g/l, erythrocytes –$3,47x10^{12}$/l), acceleration of the erythrocyte sedimentation rate (ESR) – up to 34 mm/h; in the GUA there were signs of urinary syndrome (erythrocyturia (unchanged erythrocytes – for all f/v), leukocyturia (8-10 in f/v), cylindruria (hyaline 2-3 in f/v). In the urine analysis for Nechiporenko revealed erythrocyturia. Daily proteinuria (DP) was 1.4 g/d. At the same time, the level of creatinine and urea in the BBA increased to 505 μmol/l and 17.8 mmol/l, respectively, and the glomerular plasma filtration rate (PFR) according to the SKD-ERI formula was 11 ml/ min./1,73м^2. On the electrocardiogram (ECG) – deviation of the electric axis to the left, signs of blockage of the anterior branch of the left leg of the bundle branch, changes of the myocardium of the anterior-membranous area. Ultrasound examination of abdominal organs showed an increase in ultrasound echogenicity of the parenchyma of both kidneys with the presence of symptoms hypoechoic pyramids and reduction of parenchyma thickness of the right kidney up to 1.4 cm, left – up to 1.2 cm. Consulted by urologist, neurologist. Diagnosed cervical cystitis, dyscirculatory encephalopathy (hypertensive-dyshormonal) I st., with vegetative-vascular dysfunction.

Membrane stabilizing, detoxifying, anticoagulant, antihypertensive and anti-anemic therapy did not produce a pronounced effect. In the dynamics of laboratory param-

eters from 22/05/17, normalization of the indicators was noted, however, anemia progressed, ESR accelerated to 46 mm/h, creatinine and urea levels increased to 738.7 μmol/l and 22.5 mmol/l, respectively. DP – in the range: 1.4 – 1.1 g/d. 22/05/17 diagnosed with acute rapidly progressing glomerulonephritis, urinary syndrome. Taking into account the patient's complaints, the presence of changes in the results of laboratory and instrumental examinations indicated the ineffectiveness of the therapy and the high probability of the patient having systemic vasculitis with renal injury. In order to verify the diagnosis, it was recommended to send for consultation to the State Institution «Institute of Nephrology of the National Academy of Medical Sciences of Ukraine», where on May 24, 2017, the patient was consulted by a nephrologist, but refused the proposed nephrobiopsy..

31/05/2017 with complaints of intense pain in the lower leg muscles, shortness of breath, low physical activity, increased blood pressure, pronounced general weakness, the patient was re-admitted to the center of nephrology and dialysis. At the examination from 01/06/2017: in GBA – there were signs of anemia (er. – $3{,}0x10^{12}$ /l, Hb – 84 g / l), accelerated ESR – 42 mm/h, normal level of leukocyte indexes ($6{,}6x10^{9}$/l) on the background of shift of leukocyte formula to the left %; in BAB – azotemia (creatinine – 1161.8 μmol/l, urea – 35.0 mmol/l); the GUA retained the above-mentioned signs of urinary syndrome. Intensive detoxification, membrane stabilizing, anti-anemic and antihypertensive therapy was carried out. After a two-week course of treatment, the results of GBA showed a slowing of ESR to 20 mm / h, but there were signs of anemia (er. – $2{,}47 \cdot 10^{12}$/l, Hb – 73 g/l), leukocytosis ($11{,}1 \cdot 10^{9}$ /l) and lymphocytopenia (9%); there were no significant dynamics in BBA in the levels of creatinine and urea (1140 μmol / l and 33.7 mmol / l, respectively), hyperkalaemia (6.04 mmol / l) was first detected. DP – 1,63 g / d., DD – 1,5 l.

Data from the immunological examination of the patient from 06/02/17: increased titer of AT IgG ANCA to 1: 3200 (<1: 100 – negative result) and high-positive result of ANCA to MRO (6.1 R) (up to 1.0 – negative, more than 5.0 – highly positive result). Thus, the results of the study could be interpreted as verified systemic ANCA (MPA +) vasculitis.

Due to the presence of arterial hypertension, history of abdominal syndrome, rapidly progressing GN with the development of RF, anemia, elevated titer of AT IgG ANCA and ANCA to MRO by decision of the council of 08.06.2017 was diagnosed with: ANCA (MPO +) vasculitis with preference kidney. It is recommended to change the tactics of treatment of the patient. Methylprednisolone was administered at a dose of 32 mg / day and endoxan 50 mg / day, orally, in combination with NRT by acute hemodialysis (AHD). Fifteen days of combination therapy improved the patient's well-being, tended to decrease serum creatinine and urea (276 μmol / l and 11 mmol / l, respectively). The patient was advised to continue pathogenetic therapy at the above dose and to further carry out NRT by programmatic hemodialysis (PHD). However, due to the reduction of the diameter of the vein (1.0 mm) and artery (1.2 mm), the establishment of arterio-venous (AV) fistula proved impossible. Therefore, on June 23, 2017, the patient was consulted at the Institute of Surgery and Transplantology O.O. Shalimov, superimposed arterio-venous alosunt. Since June 27, 2017, the PGD has been started.

The six-month course of the above therapy led to an improvement in the patient's general, positive dynamics in laboratory parameters (serum creatinine: 250 – 210 – 180 μmol / l). Due to the effectiveness of the treatment, 01/01/2018, PGD sessions and cytostatics were canceled. The patient is recommended to continue taking medrol, at a dose of 32 mg / day, orally, with a gradual reduction of the dose by 2 mg every 2 weeks, until the minimum effective maintenance dose will be reached. At the time of discharge from the hospital, there was a decrease in ESR up to 16 mm / h, an increase in Hb up to 93 g / l, serum creatinine levels stabilized at 150 μmol / l.

Since then, the patient has felt satisfactory, the dose of methylprednisolone was gradually reduced to 4 mg / day, and from May 2019 completely stopped taking it..

In July 2019, after suffering SARS, the patient developed shortness of breath with little exercise, dry mouth, blood pressure was maintained at 160/100 mm Hg. against antihypertensive therapy, a general weakness. The examination revealed azotemia (creatinine 800 μmol / l). From 25/07/19 to 28/07/19 – re-hospitalization in therapeutic department at the place of residence. Evaluation of the results of laboratory tests revealed significant changes in indicators: in GBA – signs of progression of anemia (er. – $2.7 \cdot 10^{12}$ / l, Hb – 75 g / l), acceleration of ESR (19 mm / h); in BBA – expressed azotemia (creatinine – 902,6 μmol / l, urea – 26,8 mmol / l); in GUA – proteinuria (2.96 g / l). Symptomatic therapy was done. 29/07/19 was consulted by the regional rheumatologist and nephrologist. Diagnosed with: Systemic vasculitis: microscopic polyangiitis, stage II activity with kidney damage. CKD V: glomerulonephritis, nephrotic syndrome. Stage II hypertension, grade 3, the risk is very high. On the same day she was transferred to the Center for Nephrology and Dialysis of PRCH for further treatment.

Laboratory indicators at hospitalization: reduction of erythrocytes is revealed (2.8 × 1012 / l) and Hb (72 g / l), lymphocytes (14%); acceleration of ESR (17 mm / h); increase in creatinine (964.8 μmol / l) and urea (33.7 mmol / l). ECG data from 07/30/19: sinus rhythm, heart rate – 75 / min, electrical axis of the heart is rejected to the left. Reduced QRS voltage in standard and amplified leads, V1-V2. Blockage of the anterior branch of the left leg of the bundle branch. Ischemic type of repolarization disorders. Data fibrogastroduodenoscopy (FGDS) from 31/07/19. Conclusion: – chronic duodenal ulcer in remission. On rheoencephalography from 01/08/19, the hemispherical asymmetry (D> S) was detected; the volume blood flow of the right hemisphere is sufficient, the left is reduced; increased peripheral vascular resistance, arterial tone is unstable. Data of ultrasound from 01/08/19. Conclusion: presence of a small amount of free fluid in the pleural

cavities (in the right pleural cavity – ≈ V 40 ml, in the left ≈ V 15 ml), ultrasound – signs of nephritis, progression of nephrosclerosis (reduction of the size of the kidneys (right – up to 7,9x3,2 cm) , left – up to 8.0x4.4 cm) and thickness of their parenchyma (1.0 cm and 1.3 cm, respectively). Echocardiography (Echocardiography) of 02/08/19 showed a decrease in myocardial contractility, signs of left ventricular hypertrophy with type II diastolic dysfunction; enlargement of the cavities of both atria, compaction of the aorta, aortic valve; insufficiency of the mitral valve of the II degree, relative insufficiency of the tricuspid valve of the II degree, pulmonary hypertension of the I-II degree.

Consulted by related specialists: rheumatologist, hematologist, gastroenterologist. Diagnosed with: systemic vasculitis: microscopic polyangiitis, grade III activity. CKD V: rapidly progressing glomerulonephritis, urinary syndrome. Stage II hypertension, grade 3, the risk is very high. Secondary normochromic anemia of moderate severity. Peptic ulcer of the duodenum with deformity of the bulb, with high acid-forming gastric function in remission.

Treatment: Re-initiation of NRT sessions using PGD mode: 3 times a week for 4 hours on the background of pathogenetic (given the high degree of process activity) therapy. After a two-week course of prescribed therapy, there was a positive trend in creatinine (962.5 – 946.2 – 709.9 mmol / l) and urea (36.4 – 34.8 – 26.5 mmol / l) in serum, and PD decreased up to 2.73 g / d. 08/16/19 The patient was transferred for further treatment to the therapeutic department, at the place of residence.

THE CLINICAL CASE №2

Patient M., 48 years old, hospitalized for examination and correction of treatment at the Nephrology and Dialysis Center in November 2019 with complaints of periodic lumbar pain, general weakness.

From the anamnesis it is known that the patient considers herself ill since 2012, when after physical exertion she felt pain in the joints, especially – in the left knee joint. She consulted a family doctor at the place of residence, consulted by a traumatologist. Diagnosis: osteoarthritis of the left knee. Prescribed anti-inflammatory and chondroprotective therapy did not show a pronounced effect. In connection with the expressed pain syndrome, the patient went to a consultation at the State Institution «Institute of Traumatology and Orthopedics of the National Academy of Medical Sciences of Ukraine», where the diagnosis was confirmed and it was found that the joint was preserved, the patient did not need surgery. Recommended: Mucosate intramuscularly, according to the scheme for 6 months. From 2012 to 2013 the patient periodically received courses of non-steroidal anti-inflammatory drugs and chondroprotective agents. The severity of the pain in the joints decreased. However, since then, the patient has begun to notice an increase in blood pressure up to 160/100 mm Hg.

For four years the patient lost 15 kg. In the fall of 2016, symptoms of polyarthritis began to increase and the patient began to notice pain in the lumbar region, a change in the color of urine (such as «meat washes») against the background of fever to subfebrile numbers, and in parallel increased general weakness. After the examination at the place of residence, glomerulonephritis was diagnosed. To clarify the diagnosis and the purpose of treatment, the patient was hospitalized at the therapeutic department of the central district hospital of Lubny. Biochemical examination of the blood revealed for the first time signs of impaired renal function (blood creatinine level – 210 μmol / l), in the GUA – signs of urinary syndrome (proteinuria – 1,13 g / l and erythrocyturia (changed er. – by ½ f/v.). Appointed detoxification, antihypertensive and antibacterial therapy. After treatment, the pain in the joints decreased, but continued to be disturbed by the aching pain in the lumbar region, the creatinine levels increased to 400 μmol / l, and proteinuria and erythrocyturia were constantly detected in the urine. Consulted by a PRCH nephrologist and hospitalized at the Nephrology and Dialysis Center with a diagnosis of CKD II: glomerulonephritis, urinary syndrome, exacerbation. CKD I degree. Stage II hypertension, 2 degrees, risk is high.

At the time of admission, objective examination revealed swelling on the face, the shins, signs of left knee arthritis (painful on palpation, swelling, restriction of active and passive movements). The left border of cardiac dullness is displaced 1 cm outside the midclavicular line. Auscultatory – heart sounds are audible, short systolic murmur over apex, accent of II tone over aorta. BP – 150/75 mm Hg. (against the background of continuous antihypertensive therapy). The symptom of tapping is positive on both sides. DD – 3,0 l. At laboratory examination – signs of anemia of moderate severity, thrombocytosis, acceleration of ESR up to 68 mm / h .; in GUA – proteinuria (protein – 1.13 g / l), erythrocyturia (altered er. by 1/2 f/v., unchanged 10-20 in f/v.), moderate leukocyturia, cylindruria (hyaline 3-4, single granular and waxy in f/v), bacteriuria; elevated levels of creatinine and urea (268 μmol / l and 12.5 mmol / l, respectively) were maintained in the BBA. The speed of CFR according to the formula SKD-ERI was 54.9 ml / min / 1.73 m^2.

During the hospital stay the patient is thoroughly examined. On the chest Ro-gram – the pulmonary fields are transparent, in the basal departments of the lungs the pulmonary pattern is thickened and deformed, the roots are fibrous, the right sinus is free, the left is obliterated, massive left-sided pleural-diaphragmatic quadruplets. On the Ro-gram of the left knee joint in 2 projections – signs of osteoarthritis II st. Ultrasound revealed ultrasound – signs of nephritis, gallstones, moderate enlargement of the liver. Computed tomography (CT) CT data: CT revealed signs of decreased renal parenchyma density, small pelvic effusion, moderate hepatomegaly, pelvic lymphadenopathy. FGDS revealed congestive gastropathy; at fibrocolonoscopy – chronic left-sided colitis. When sowing urine on the microflora enterobacter 10^4 CFU. The performed sternal puncture of changes did not reveal. Immunological examination of blood for antibodies to double-stranded DNA, AB IgG showed a negative result. Consulted neurologist,

hematologist, gynecologist, gastroenterologist, pulmonologist, rheumatologist. The following diagnosis was established: CKD II: glomerulonephritis, urinary syndrome, exacerbation stage. CRF I degree. Stage II hypertension, degree 2, risk is high. Dysmetabolic encephalopathy of II degree with bilateral reflex-pyramidal insufficiency, moderate vestibulo-atactic syndrome, cephalic syndrome. Hypochromic anemia of unspecified genesis, thrombocytosis. Chronic gastroduodenitis in the acute stage. Duodenogastric reflux. Gallbladder dysfunction. Osteoarthritis: Stage II gonarthritis with reactive synovitis. FJI II. Appointed detoxification, membrane stabilizing, anticoagulant antihypertensive therapy, topical anti-inflammatory drugs.

The lack of positive dynamics in laboratory parameters is noteworthy. In the clinical picture, signs of glomerulonephritis (proteinuria – 0.79 – 0.5 g / l), erythrocyturia (altered erythrocytes by 1/2 – 1/4 f/v.), Moderate leukocyturia, cylindruria prevailed; in Nechiporenko urine analysis – leukocyturia (14250 in 1 ml), erythrocyturia (20000 in 1 ml), cylindruria (187 in 1 ml); DP – 1,62 g / d., In BBA – creatinine – 283 μmol / l, urea – 15,8 mmol, in the urine analysis according to Zimnitsky – hypoisostenuria, anemia (er. – $3,2x10^{12}$ / l, Hb – 73 g / l) and signs of systemic inflammation (moderate leukocytosis, ESR acceleration up to 73 mm / h.).

Due to the lack of positive effect of treatment, a consultation at the State Institution of the "Institute of Nephrology of the National Academy of Medical Sciences of Ukraine" is recommended, which the patient categorically refused.

She has since continued treatment at the place of residence. Three months after discharge from the hospital, the patient again experienced pain in the lumbar region, noted reddening of the urine, swelling in the face and legs increased, pain in the left knee joint increased. At the same time, the blood pressure periodically increased to 180/110 mm Hg. She was re-treated at the Center for Nephrology and Dialysis of PRCH. On physical examination: swelling of the left knee joint, active and passive movements are limited due to pain. Otherwise, there were no significant dynamics. Laboratory parameters still showed moderate anemia, moderate eosinophilia – 6-7%, ESR acceleration – 62-68 mm / h, signs of renal dysfunction (creatinine – 142 μmol / l) and urinary syndrome (proteinuria) – 0,365 g / l -1,62 g / d., eErythrocyturia (altered erythrocytes 20-35 in f/v, cylindruria (60 in 1 ml)). On the Ro-gram of the left knee joint in 2 projections – signs of osteoarthrosis II degree. After the course of treatment the patient was discharged in satisfactory condition.

However, in September 2017, the patient's condition worsened significantly: redness of the sclera of the left eye appeared, dizziness developed, moderate pain began in the epigastric region. Consulted by an optometrist and diagnosed with left eye uveitis. Outpatient treatment did not give effect. Due to the further deterioration of the condition, she was hospitalized at the center of nephrology and dialysis. During the treatment there was a slight improvement in clinical and laboratory parameters. GBA increased the number of red blood cells ($4.01x10^{12}$ / l) and Hb (106 – 111 g / l), slowed ESR (50 – 37 mm / h), but no significant changes occurred in the GUA. Nitrogen metabolism was normalized in the BBA (creatinine – 101 μmol / l, urea – 6.2 mmol / l), other indicators also within normal values. The rate of GF is 85.1 ml / min / 1.73 m3; tubular reabsorption (TR) – 95.1%. Acute-phase blood counts: rheumatoid factor, antistreptolysin-O – negative, but C-reactive protein was positive – 8.6 mg / l. According to ultrasound: right kidney 11,8x3,7 cm, parenchyma – 0,9 cm, cup-bowl complex compact, partially doubled, parenchyma moderately enhanced, microliths; left kidney – 9,1x4,0 cm, parenchyma – 1,1 cm, cup-bowl complex is structurally preserved, parenchyma moderately enhanced, microliths. Conclusion: ultrasound – signs of nephritis. Microliths in the kidneys. Pathology of the liver, spleen, pancreas was not detected.

Consulted by an ophthalmologist (09/22/17, 09/25/17, 09/26/17): Diagnosis: Left eye uveitis. Secondary (post uveal) glaucoma OS.

Given the weight loss of the patient, the presence of hypertension, glomerulonephritis with renal failure, recurrent uveitis, anemia, increased content of C-reactive protein, inefficiency of symptomatic drug therapy in the patient was suspected presence of systemic vasculitis. Immunological examination of the patient's blood was performed to verify the diagnosis.

Increased titers of IgG antibodies to MPO> 8 (<1.0 – negative) and antibodies to double-stranded DNA were detected. To clarify the diagnosis, the patient was referred to the State Institution «Institute of Nephrology NAMS of Ukraine» for the purpose of nephrobiopsy. However, the patient flatly refused and was discharged to continue outpatient treatment at the place of residence.

From February to November 2018, the patient was repeatedly treated by an ophthalmologist with a diagnosis of slow-moving uveitis, secondary glaucoma, complicated by cataracts of the left eye. Pterigium I degree of both eyes – there was no effect. It was periodically inspected at the place of residence. As a result of clinical research methods leukocytosis, acceleration of ESR (45-68 mm / h), mild anemia, changes in urine (proteinuria – 0.46-0.95 g / l), erythrocyturia (unchanged er. – 25-35 in f/v were preserved), leukocyturia (10-6 in f/v). In the analysis of urine according to Zymnitsky: specific gravity of urine – 1005-1012, DD – 2650 ml. She was treated at the place of residence, repeatedly consulted by a PRCH nephrologist.

In November 2018, the patient's condition suddenly worsened: growing shortness of breath, pain in the lumbar region, frequent urination. She was referred to a nephrologist and re-admitted to a Nephrology and Dialysis Center.

In the objective status, compared with the data of the previous hospitalization, a pronounced deformity of the left knee joint, sharp restrictions of active and passive movements in the left knee due to the pronounced pain syndrome, attracted attention. The results of laboratory examinations revealed signs of renal dysfunction (creatinine – 172 μmol / l, urea – 10 mmol / l, GF rate was 72.8 ml / min / 1.73m3, KR – 93.1%); urinary syndrome (trace

proteinuria, erythrocyturia (1200 in 1 ml), mild anemia and increase in cholesterol (CL) up to 7.79 mmol / l. Ultrasound: signs of increased echogenicity of the renal parenchyma. Symptomatic treatment was performed.

The presence of hypertension, weight loss, eye damage (uveitis), muscle damage (myalgia), joint damage (osteoarthritis), anemia, constant changes in the urine (erythrocyturia, proteinuria), increased creatinine, and repeated confirmation of increased levels of antibodies to MPO (> 8) allowed to make a diagnosis: Systemic vasculitis: microscopic polyangiitis with renal involvement. Stage II hypertension, degree 2, high risk. CHD: diffuse cardiosclerosis. CHF 0 degree. FC I. Hypercholesterolemia.

She was consulted by a nephrologist at the Institute of Nephrology of the National Academy of Medical Sciences of Ukraine, and a rheumatologist from the State Institution of Cardiology. An additional immunological blood test showed positive blood test results p-ANCA (perinuclear) 1:40 (reference values 1:<10). Diagnosed with ANCA (MPO+) vasculitis with predominant renal involvement. Pathogenetic therapy was prescribed. Since then, the patient has been receiving endoxan 500 mg and methylprednisolone 12 mg daily (oral), telmisartan under the control of BP.

In October 2019 she was consulted by a rheumatologist of the State Institution «Institute of Cardiology named after academician M.D. Strazhesko»of the National Academy of Medical Sciences of Ukraine. The patient is advised to reduce the dose of methylprednisolone to 10 mg / d.

In November 2019, the patient again noted a change in the color of urine to «red», a general weakness. The examination revealed proteinuria – 1.0 g / l, in which case the patient was re-hospitalized to the center of nephrology and dialysis of PRCH for examination and correction of treatment.

On initial physical examination: skin and mucous membranes without features. Peripheral lymph nodes are not enlarged. Deformation of the left knee joint with restriction of active and passive movements. Moderate edema around the articular tissue of the left knee. Swelling of the face. The left border of cardiac dullness is displaced outward from the middle-clavicular line by 1 cm. Auscultative: heart tones are audible, short systolic murmur over apex, accent II tone over aorta. BP up to 140/100 mm Hg.

At examination: proteinuria (protein – 0,174 g / l), unchanged erythrocytes – 3-8 in f/v., Leukocytes – 0-2; in the analysis of urine by Nechiporenko: erythrocyturia – 7800 in 1 ml; in the urine analysis according to Zymnitsky – hypostenuria (specific gravity 1004-1011), DD – 1500 ml, nocturia. DP – 0,342 g / day. In the BBA – increase of creatinine level to 134 μmol / l, CL – 7,83 mmol / l, triglycerides – 2,75 mmol / l; atherogenic index – 3.5. In GBA: ESR – 13 mm / h, leukocytes – $4{,}93x10^9$ / l, lymphocytopenia (10%), Hb – 120 g / l, erythrocytes – $3{,}90x10^{12}$ / l, moderate thrombocytosis (334x109 / l). The patient received prednisolone 10 mg, azathioprine 100 mg / d., Orally, in the morning, after meals and symptomatic (antihypertensive, detoxification, nephroprotective) therapy.

As a result of the treatment, the patient's condition improved significantly, positive dynamics in laboratory parameters were noted: the level of creatinine in the BBA decreased to 101 μmol / l, CL – to 6.4 mmol / l. In GUA – proteinuria – 0.04 g / l, ep. – 2 – 3 in f/v, in Nechiporenko urine analysis: erythrocyturia decreased to 2540 / ml. It is recommended to continue pathogenetic therapy with azathioprine 100 mg / d, with a gradual decrease in the dose of methylprednisolone per ¼ tablet once every two weeks to 5 mg / d.

Microscopic polyangiitis is a rare necrotizing systemic vasculitis without immunoglobulin deposits associated with antineutrophil cytoplasmic antibodies. In the overwhelming majority of cases is characterized by lesions of the vessels of the microcirculatory bed, but there is a possibility of lesions of the arteries of small and medium diameter.

Usually manifestation of the disease begins with pulmonary-renal syndrome, namely: hemorrhagic alveolitis and necrotizing glomerulonephritis. However, the analysis of modern literature shows that it may have a very diverse beginning, different variants of the course with symptoms of damage to different organs that are characteristic of other SV. Practice shows that MPA is quite common in the practice of nephrologists.

It should be clearly understood that MPA is considered a fatal pathology. An important factor in determining the prognosis and quality of life of such patients is the timeliness of diagnosis, a clear differential diagnosis and the adequacy of medical care.

The difficulty of verification lies in the lack of clear classification criteria, the need for more extensive use of modern histological examination methods, with the mandatory use of immunological tests, which are not always available yet. Modern aspects of diagnostics include analysis of clinical manifestations, positive results of immunological studies of serum for detecting perinuclear autoantibodies to cytoplasmic components of neutrophils, antimyeloperoxidase in serum, antibodies to MPO-ANCA, histopathological examination of skin, kidney or lung biopsy specimen, signs of systemic inflammation and anemia in blood test, laboratory signs of rapidly progressing glomerulonephritis with development of renal failure.

As can be seen from a detailed chronological analysis of the course of MPA in the first case, we can state the gradual rate of progression of the disease with the development of such nonspecific symptoms as: increase in blood pressure, abdominal syndrome, fever to subfebrile numbers, nausea, dry mouth, headache, all of which were accompanied by symptoms suggestive of kidney damage, which were initially considered as glomerulonephritis, complicated by acute kidney damage. Differential diagnosis was made within paraneoplastic nephropathy and systemic vasculitis.

Ineffectiveness of the conducted symptomatic, membrane-stabilizing therapy, presence of arterial hypertension (AH), signs of systemic inflammation, anemia in the general blood test, proteinuria, hematuria, azotemia, positive results of immunological studies of serum for the diagnosis

of MPA vasculitis: microscopic polyangiitis, grade III activity, with kidney damage.

The appointment of patients with methylprednisolone at a dose of 32 mg / day and endoxane 50 mg / day, orally, in combination with the KRT method of acute, and further – program hemodialysis not only led to the control of the symptoms of the disease, but also allowed to renal replacement therapy stop taking cytostatics and gradually reduce glucocorticosteroid intake. This indicated the selection of the optimal treatment strategy. However, the unauthorized discontinuation of glucocorticosteroids in the future provoked a relapse and led to the need to resume the course of the above therapy.

In the second clinical case, concomitant joint lesions came to the fore, so the diagnostic search was initially aimed at clarifying the nature of joint syndrome and its treatment. However, weight loss, the symptoms of glomerulonephritis, which occurred only four years after the first signs of arthritis, and then – the presence of hypertension, eye damage (uveitis), muscle damage (myalgia), azotemia, anemia on the background of joint damage (osteoarthritis) suspect systemic vasculitis. Repeated positive blood test results for antibodies to MPO (>8) and p-ANCA (1:40) allowed to make the diagnosis: Microscopic polyangiitis with kidney damage. Pathogenetic therapy only (methylprednisolone 12 mg and endoxane 500 mg daily) for eleven months, followed by administration of methylprednisolone 10 mg and azathioprine 100 mg / d. led to a significant improvement in the patient's overall condition, a positive trend in laboratory parameters, which prompted nephrologists to gradually reduce the glucocorticosteroid dose to a minimum effective.

The following clinical examples demonstrate to physicians that systemic vasculitis is quite common in the practice of nephrologists.

CONCLUSIONS

Thus, the described clinical cases differ slightly in features of the debut and the course of the disease, but they also have common features, which were manifested by renal involvement with the development of renal failure, arterial hypertension and anemia.

Therefore, before deciding on the primary or secondary nature of glomerulonephritis, nephrologists need to carefully evaluate the entire complex of objective and subjective features, laboratory and instrumental examination data, identify symptoms of multiple organ lesions, signs of disease progression.

In the case of the detection of additional signs that may indicate systemic pathology, it is always advisable to consider the possibility of the presence of kidney damage in patients, as a symptom of another disease, which is accompanied by similar symptoms, especially systemic vasculitis. Moreover, it is extremely important to be able to recognize them in time and to send these patients for further immunological examination and for nephrobiopsy, since the prospects of effective treatment and quality of life will depend on this.

Thus, clinical examples demonstrate to physicians that systemic vasculitis can often hide under the «mask» of other diseases and require timely diagnosis and immediate pathogenetic treatment.

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The article was prepared in accordance with the plan of research work of the Department of Internal Medicine № 2 with occupational diseases of the Ukrainian Medical Stomatological Academy (Poltava) «Investigation of the assessment of the combined effect of cardiovascular risk factors on the comorbid course of arterial hypertension, coronary heart disease and chronic kidney disease, features of prevention and rehabilitation.» State registration № 0119U102851.

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Conflict of interest:
The Authors declare no conflict of interest.

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Received: 10.12.2020
Accepted: 02.03.2021

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article