DOI 10.25789/YMJ.2022.78.33

УДК 616.1/.9

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A CLINICAL CASE OF ANCA-ASSOCIATED SYSTEMIC VASCULITIS IN A NINE-YEAR-OLD SAKHA CHILD

ANCA-associated vasculitis (AAV) is a group of diseases characterized by chronic immune inflammation of the small vessel wall, a polymorphic clinical picture with frequent involvement of the lungs and kidneys and the presence of circulating autoantibodies to neutrophil cytoplasm (ANCA). The article presents a clinical case of ANCA-associated systemic vasculitis with lung and kidney involvement.

Keywords: ANCA, vasculitis, inflammation, lung, kidney, child.

Introduction. Systemic vasculitis is a group of acute and chronic vasculitis, the most important pathomorphological features of which are considered to be inflammatory and necrotic lesions of the vascular wall [7]. ANCA-associated vasculitis is a systemic necrotizing vasculitis associated with antibodies to neutrophil cytoplasm (ANCA). ANCA vasculitis is represented by two major variants - granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

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The annual incidence is 20 cases per 1 million population worldwide [12]. In Europe and the United States, the prevalence of AAV is 1-2 cases per 100,000 population [2,4].

A definite association with the carrier of Staphylococcus aureus (HB - in aggravation), medications (EGPA), genetic factors has been established: The presence of HLA-DPB1*0401 (with which an increased risk of granulomatous disease in Europe is associated), polymorphism of genes encoding proteinase 3 (PR3) and its major inhibitor α1 - antitrypsin (SERPIN A1), which predisposes to hyperproduction of antibodies to proteinase-3[5]. Necrotizing inflammation of small and medium caliber vessels causes severity and multi-organ lesions in AAV.

The disease is characterized by high mortality due to damage of vital organs. Against the background of adequate immunosuppressive anti-rheumatic therapy in adults, the 5-year survival rate, according to some authors, is 70-75% [10,1].

Involvement of the kidneys in the pathological process is typical for all ANCA vasculitides. Clinically, renal damage manifests itself as a rapidly progressing nephritic syndrome [10,1]. ANCA-vasculitis belongs to renal diseases with the least favorable prognosis due to severe rapidly progressive drug-induced glomerular damage in the form of focal necrotizing inflammation of the glomerular capillaries, as well as rapidly progressive fibroplastic changes [11,9,1].

In children, the relevance of the problem is due to the high frequency of glomerulonephritis development [3,6,12]. Glomerulonephritis in AAV in children is a frequent and major manifestation, proceeding severely with a high risk of acute kidney damage with the outcome in terminal renal failure [6].

In this pathology, only timely clinical and morphological, immunological diagnosis and subsequent adequate therapy are the main factors of disease prognosis [1].

Clinical example: Girl A. born in 2012, a child of 1 pregnancy. On-time delivery, operative. Birth weight 3750, length 51 cm. Breast-feeding until the age of 1 year. She was growing and developing according to her age. Rare colds were registered.

Debut of the disease at the age of 4 years in May 2016, the child had a rash on the face, with the accession of a purulent infection. A district pediatrician diagnosed her with streptoderma. Treatment was prescribed: externally - levomikol ointment, lycopid in a dose of 1mg per day for 10 days.

Since 14.05.2016, the temperature rose to 38.0-38.5C°, cough, outpatient treatment was prescribed by the district pediatrician: bromhexin, nebulizer therapy with berodual 10 drops 2 times a day for 10 days, Sumamed in an age dosage. Since 30.06.2016 there was improvement: cough less often, temperature normalized. Since 29.07.2016 cough intensified, temperature increased to 39C°, pain and limitation of movement in knee and ankle joints appeared. Paraclinically: accelerated erythrocyte sedimentation rate (ESR) up to 60 m/hour (normal: 2-8 mm/hour). Chest X-ray of the chest organs dated 3.08.2016: Left-sided polysegmental pneumonia.

The patient was hospitalized by emergency indications on 8.08.2016 to the pulmonology department of RC RC RC №1-NCM in a serious condition with phenomena of respiratory failure of degree 2: respiratory rate up to 70 per min, fever up to 39.0ºC, pronounced signs of intoxication and arthritic syndrome.

Paraclinically: sedimentation rate 98 mm/hour (the norm: 2-5 mm/hour), neutrophil leukocytosis -12.3x109/l (the norm: 5-9.5 200x109/l), iron deficiency

anemia - blood hemoglobin 103 g/l (the norm: 105-145 g/l).

Computed tomography of the chest organs of 8.08.2016: multiple polymorphic foci with indistinct contours, with a tendency to fusion and formation of infiltrates, mainly in the lower and middle parts of the lungs. Focal infiltrative changes in both lungs, probably bilateral polysegmental bronchopneumonia.

Abdominal ultrasound - diffuse changes of both kidney parenchyma with thickened sinuses.

The patient was prescribed ceftriaxone, fluconazole, caspofungin, pentaglobin with insignificant positive dynamics.

Dynamics of chest CT scan data:

- 15.08.2016: partial resorption of foci in the lungs and restoration of pneumatization;

- 1.09.2016: lung infiltration density decrease in the lower lobe of the left lung. Without clear dynamics in the upper lobe of the left lung, in the right lung.

Paraclinically: from 1.09.2016: COE 63 mm/hour, anemia, hemoglobin level 90 g/L; hyperfibrinogenemia 7.5 g/L (normal: 2-4 g/L). In single urine portions, proteinuria from 1 to 1.75 g/l.: microhematuria changed to macrohematuria, cylinduria. Anti-dsDNA (antibodies to double-stranded DNA) IgG - 36.5 (normal 0 to 25), total ANCA - 3.24 (normal to 1.0).

Clinical diagnosis: ANCA-associated systemic vasculitis with lung and kidney damage.

Since 2.09.2016 he has been receiving methylprednisolone 12 mg/day. Since September 13, 2016, she has been receiving mycophenolate mofetil 250 mg/day, also received deaggerant therapy, captopril, inhalation with pulmicort. The child was hospitalized in SPbGPMU. Nephrobiopsy of the kidneys was performed: picture of ANCA-associated glomerulonephritis, focal variant, with cellular-fibrous semilunions (37%), with segmental and global sclerosis (49%), tubulointerstitial nephritis with minimal inflammatory activity, without necrotizing capillaritis. Baseline therapy was changed to cyclophosphamide at an age-appropriate dose of 1000 mg/m2/month (6 months total).

Computed tomography of the chest organs dated January 11, 2017: positive dynamics was noted due to a decrease in the size and density of the thickened areas of the left lung. Due to failure to achieve remission, therapy with rituximab at a dose of 500 mg, 2 injections every 2 weeks, change of baseline therapy with cyclophosphamide to mycopherolate mofetil (MMF) was prescribed. First administration of rituximab in 500 mg dosage on February 28, 2017, second administration on March 14, 2017 at the place of residence. Due to pronounced B-cell depletion and development of hypoimmunoglobulinemia, a six-month course of therapy with intravenous immunoglobulin (IVIG) drugs 1 g/kg -1 once a month was administered, a gradual reduction of methylprednisolone dosage was performed.

In summer 2017 the patient had no infectious diseases, received a full course of IVIG, methylprednisolone at a dosage of 6 mg/day. In October 2017, the patient received a course of rituximab in a dosage of 500 mg intravenous drip. At the end of November 2017, against the background of an acute respiratory infection, proteinuria up to 1 gram in a single portion of urine was observed. The dosage of MMF drug was recalculated, the dose of methylprednisolone was decreased, treatment with VBIH 1 g/kg once a month was continued.

In the next six months, there were recurrences of proteinuria in the field of acute respiratory infections; no clinical manifestations of vasculitis were noted. The patient grew by 3 cm and added 2 kg.

In June 2018, MMF therapy was continued, against the background of decreasing the dose of methylprednisolone, a course of VBIH treatment was prescribed for 6 months.

In November 2018, another administration of rituximab once in a dosage of 500 mg, since January 2019 prednisolone was completely abolished. There were no pathological changes in clinical and biochemical tests, proteinuria in single urine tests was up to 0.3 g/l. The patient grew by 6 cm, added 2 kg. Severe hypoimmunoglobulinemia IgA - 0.3 mg/ml (normal: 0.7-3.0 mg/ml), IgG - 3.5 mg/ml (normal: 8.0-16.0 mg/ml); IgM - 0.94 mg/ml (normal: 0.6-2.0 mg/ml); IgE - 0.5 ME/ml (normal: 0.0-100.0 ME/ml) persisted.

Computed tomography of the chest organs on 10/27/221: Focal interstitial changes in the lungs, no changes in the dynamics of 2020. Increased size of the thymus gland. Consultation of ophthalmologist on 10/27/2021: OU - Hyperopia of 1st degree. Initial complicated posterior capsular cataract. Retinal angiopathy.

Discussion: Our article describes a case of early debut of AAV (at the age of 4 years) as HPA with predominant kidney and lung involvement. The peculiarities of our case were early debut, absence of upper respiratory tract (URT) involvement. A multicenter retrospective study showed that the median time to diagnosis of AAV was 1.6 months for IPA and 2.1 months for HPA, with a maximum delay in diagnosis of up to 39 and 73 months, respectively [8]. The median age of debut was 12 and 14 years, with the earliest cases reported in the study being 1 and 2 years, respectively [8]. Among children with HPA, up to 30% may not have an AFD lesion, whereas MPA is usually 100% without an AFD lesion. Joint syndrome is about 1.5 times more common in patients with HPA. Renal damage is more frequent and severe in patients with MPA, they have a more frequent nephrotic syndrome and a higher need for renal replacement therapy [8]. Pulmonary involvement, on the contrary, is more typical for HPA, and is represented by cough, pulmonary bleeding, pleurisy, presence of nodules, infiltrative changes and decay cavities on lung radiological examination. Abdominal symptoms are more typical for MPA, while ENT lesions (chronic destructive otitis media, septal perforation, orbital and sinus granulomas, chronic sinusitis, granulomatous lesions of the larynx and trachea) are typical for GPA [8]. Cutaneous lesions: nodules, hemorrhages, purpura, ischemic necrosis are more common in patients with MPA. Nonspecific symptoms (fever, myalgia, intoxication, weakness, weight loss >10%) and increased CRP are more typical for patients with HPA. Among the immunological tests, the detection rate of antibodies to MPO (p-ANCA) was 55% for IPA patients and 27% for HPA patients, whereas antibodies to proteinase-3 (c-ANCA) were more common in HPA patients (67%) than in IPA patients (17%). At the same time, 26% of children with SMI and 5% of children with HPA were negative for all ANCA types [8]. Among treatment approaches, corticosteroids (97%) and cyclophosphamide (76%) were the main therapeutic agents; methotrexate, azathiaprine, and mofetil mycophenolate were used less frequently. Plasmapheresis was used in 21% of cases [8]. Rituximab was used in 12% of children with AAV.

Conclusions: AAV in children is a rare pathology with little coverage in the available scientific literature. The peculiarity of the case is an unusually early debut, the need for anti-B-cell therapy due to the lack of effect of hormonal-cytostatic therapy.

The work was performed as part of the research project "Physical development and health of the child population in the Far North (case study of Yakutia)" (state registration number: 1021062411641-9-3.2.3) under the state order of the Russian Ministry of Education and Science (FSRG-2020-0016).

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A SEVERE CLINICAL CASE REPORT OF A NOVEL CORONAVIRUS INFECTION (COVID-19) OF A PATIENT WITH DIABETES MELLITUS

DOI 10.25789/YMJ.2022.78.34

УДК 616.36-002.2-004

The article describes a clinical case of a severe course of a novel coronavirus infection (COVID-19) in a woman with comorbid pathology from the practice of the infection department of the Yakutsk Republican Clinical Hospital (YRCB). Type 2 diabetes mellitus, obesity, and arterial hypertension in an elderly woman were predictors of the severe course of a new coronavirus infection, which led to the development of ARDS and caused the death of this patient.

Keywords: COVID-19, viral pneumonia, diabetes mellitus, obesity, "cytokine storm", Yakutia.

Introduction. According to March 14, 2022, the total number of COVID-19 cases worldwide is more than 458 million, with more than 6 million deaths.

People with serious comorbidities are at a higher risk of severe disease caused by COVID-19 [1]. For example, an analysis of 1,099 diabetic patients hospitalized with COVID-19 showed that the severe course of infection (16.2%) was almost 3 fold more common than the mild course (5.7%) [2].

Regarding mortality, according to the results of the Chinese Center for Disease Control and Prevention, among 44,672 patients diagnosed with COVID-19, the mortality rate among people with diabetes was also significantly higher (7.3%) than in the general population (2.3%) [3].

In type 2 diabetes mellitus (T2DM), both humoral and cellular immunity are affected as a result of primary immune impairment. Poor glycemic control, in turn, impairs the immune response to viral infection and potential bacterial infection in the lungs. In addition, T2DM is associated with obesity, a risk factor for severe infection through systemic inflammation, bronchopulmonary pathology, and sleep apnea. Moreover, in DM the frequency of comorbidity and the presence of vascular pathology is high: cardiovascular disease, chronic heart failure (CHF), chronic kidney disease (CKD), diabetic foot, etc. [4, 5, 6].

Discussion: The article presents a clinical case of a novel coronavirus infection in the presence of many risk factors of a severe form of the disease, which resulted in a fatal outcome.

Patient P., 73 years old, first symptoms appeared on December 4, 2021 - fever up to 38.5°C, weakness, chills, pains in joints, body aches and pains. On December 6, 2021, she called a physician, and on December 7, 2021, a PCR test was taken for SARS CoV-2 RNA. During the outpatient phase of treatment, arbidol and antipyretic drugs was prescribed.

The patient had concomitant diseases: type 2 diabetes mellitus, grade 3 arterial hypertension, grade 1 obesity

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