A CLINICAL CASE REPORT: STROKE IN A YOUNG PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS ON THE BACKGROUND OF SECONDARY ANTIPHOSPHOLIPID SYNDROME

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Abstract. A clinical case report: stroke in a young patient with systemic lupus erythematosus on the background of secondary antiphospholipid syndrome. Shkrobot S.I., Milevska-Vovchuk L.S., Duve Kh.V., Naumova L.V., Budarna O.Yu. The article describes a clinical case report of a young patient with ischemic stroke on the background of antiphospholipid syndrome (APS). The uniqueness of this case lies in the complex diagnostic search that we performed. On admission, the patient had general cerebral, general infectious and focal syndromes. We suspected encephalitis due to the peculiarities of the onset of the disease and the results of computed tomography. However, after the results of lumbar puncture, the diagnosis of encephalitis required careful differential diagnosis. We performed an extensive diagnostic search. Based on clinical-laboratory, instrumental and immunological data the patient had the following final diagnosis: “Ischemic cardioembolic stroke in the right middle cerebral artery pool (15.10.17) (ICD 11: 8B11.5). Acute period with left pyramidal reflex insufficiency and changes in magnetic resonance imaging. Systemic lupus erythematosus (ICD 11: 4A40.0), subacute course, activity II, with the lesion of skin (transient erythematous rash), kidneys (proteinuria, transient impaired renal function), lungs (bilateral pleurisy with immunological disorders). Secondary APS (ICD 11: 4A45) (Acute iliofemoral thrombosis, May 2017; chronic thrombosis of the inferior vena cava, iliac veins, positive IgG to cardiolipin, beta 2 glycoproteins). Thus, we have to link thrombotic complications in young patients with APS and to examine the patients for antiphospholipid antibody presence.

For the first time the main cause of acquired thrombophilia anti-phospholipid syndrome (APLS) was described by a British scientist G. Hughes in the early 1980s. He called this state "sticky blood syndrome."
Today, this term refers to a chronic autoimmune vaso-occlusive process, accompanied by the development of multiple organ ischemia and, in some cases, multiple organ failure, due to recurrent thrombosis in small vessels of internal organs on the background of circulation of lupus or antiphospholipid antibodies (APLA) in the blood [2].

Despite the relevance and severity of this multidisciplinary problem in the modern literature, we find little data on the epidemiology and prevalence of APLS. It is known that about 82% of people diagnosed with APLS are women (according to the European study EUROAPLS); APLS in them is five times more common than in men, but their presence in the serum does not always indicate APLS. Between 10 and 15% of women with habitual miscarriage suffer from APLS. According to the results of the Alliance for Clinical Trials and International Networking (APLS ACTION), about 14-17% of people under the age of 50 diagnosed with stroke and 11% of those diagnosed with myocardial infarction have APLS. Clinical manifestations of this syndrome are observed in 30% of patients with lupus antibodies and in 30–50% of patients with moderate or elevated levels of APLS. A single detection of APLS in the blood is not a basis for a final diagnosis. Besides patients with APLS, APLA is also found in patients with infectious diseases (due to viral and bacterial mimicry) during drug treatment with methyldopa, combined oral contraceptives and even in healthy people [7].

There are several clinical variants of APLS.

- **Primary** APLS occurs in patients without background autoimmune pathology in 7-12% of cases.
- **Secondary** APLS is identified in 88–93% of patients with rheumatic, autoimmune and infectious diseases, as well as malignant tumors on the background of usage of hormones, psychotropic drugs, high doses of \( \alpha \)-interferon, etc.
- **Catastrophic** APLS is associated with the development of multiple system's and multiple organs' disseminated thrombosis at the level of the microcirculatory bed with a high titer of APLS.
- **Neonatal** APLS is a rare pathology of the newborn that develops during the transmission of thrombotic factors by transplacental route from mothers with high titer of APLA.

The laboratory criterion of APLS is the presence of at least two of the three markers, which is determined at least twice with an interval of at least 12 weeks after the appearance of clinical signs (lupus antibodies, antibodies to cardiolipin, and \( \beta \)-2 glycoprotein). A rational approach to the diagnosis of APLS according to these criteria can be described as "1+1":

- APLS is diagnosed only when one clinical and one laboratory criterion are met.
dizziness while changing body position. The detailed history revealed that on October 10, 2017, the patient noticed a fever up to 38°C, a severe headache and a sore throat, but she did not ask for any special medical help. Five days later, in the morning, she revealed facial asymmetry and speech disorders. An ambulance was called; they recorded increased blood pressure up to 180/110 mm Hg. The patient was admitted to the hospital.

A detailed history revealed that in January 2017, the patient had a pastose face and swelling of the extremities. In March 2017, according to the records in the outpatient card, there were inflammatory changes in the general blood analysis (increased erythrocytes sedimentation rate to 58 mm/h). From May 18, 2017 to June 02, 2017, the patient was treated in the vascular surgery department with the diagnosis of acute left iliofemoral deep vein thrombosis. She was prescribed rivaroxaban 15 mg twice a day for a long time. At the end of September 2017, the patient decided to cancel drug taking.

Objectively, on initial examination, the patient is in a relatively satisfactory state. The skin and visible mucous membranes are pale and relatively clean. Insignificant pastiness of the face and palms. The temperature is 38°C. Heart activity is rhythmic; tones are clear. Blood pressure: 140/90 mm Hg, pulse rate: 76 beats per minute. Respiration is vesicular. The abdomen is soft and not painful.

The assessment of neurological status revealed a smoothed left nasolabial fold, drooping of the left corner of the mouth, increased muscle tone in the left upper extremity, hyperreflexia in the left extremities, and the presence of pathological signs on the left (Pusep, Babinsky, lower Rossolimo, Strumpel).

We also found inflammatory changes (leukocytosis, shift of the leukocyte formula to the left, increased erythrocytes sedimentation rate) in complete blood counts at the time of admission.

Computer tomography of the brain (15.10.17): hypodense area in right parietal lobe (12*20 mm). Conclusion: Encephalitis?

Thus, based on the presence of general cerebral, general infectious and focal syndromes, and taking into account the gradual development of the disease and the results of CT in the patient, we suspected encephalitis.

Magnetico-resonance imaging of the brain (16.10.17): brain infarction in the right frontal lobe (right middle cerebral artery pool). There are ischemic zones in both the frontal and right parietal and left occipital lobes of the brain.

Because ischemia in the young patient was observed not only in one but in several areas and occurred on the background of a general infectious syndrome, encephalitis was not excluded, and its complications (ischemic zones in both frontal, right parietal and left occipital lobes of the brain) were suspected.

The patient underwent a lumbar puncture. The results of cerebrospinal fluid: protein: 0,91 g/l, glucose: 2,5 mmol/l, cytology: 6 cells.

The diagnosis of encephalitis required careful differential diagnosis.

The patient underwent the following examinations:

- Biochemistry: glucose – 4.3 mmol/l, blood urea: 9.2 mmol/l, cholesterol: 4 mmol/l, total protein: 59 g/l, alanine aminotransferase: 0.68 IU/l, aspartate aminotransferase: 0.38 IU/l.
- Prothrombin: 91.7; recalcification time: 90 sec; fibrinogen: 3.99 g/l thrombotest: VI, Fibrinogen: +; Platelets: 141 109/L; Clotting time: start – 4.05 sec, end: 4.20 sec.

- Blood test for rheumatoid arthritis:
  - Rheumatoid factor: 12 IU/ml, reactive protein: 96 mg/L.
  - General urine analysis: straw color, specific gravity: 1020, protein: 1 g/l, glucose: -, white blood cells: -, red blood cells: +.
  - General urine analysis according to Nechyporenko (18.10.17): white blood cells: 9.75, red blood cells: 14.5.
  - Wasserman reaction (blood test) (18.10.17) – negative.
  - Blood analysis for TORCH-infection (17.10): increased titer of IgG to Herpes virus, Cytomegalovirus, Toxoplasmosis.
  - Blot-analysis for borreliosis (17.10) revealed elevated levels of IgG antibodies to Borrelia (p41, p39, p58, OspC, p21, p19, p18, IgG).
  - Electrocardiography (18.10.17): moderately reduced metabolic processes in the myocardium of the right ventricle, with a tendency to tachysystole.

Specialists’ consultations:

- Hematologist (19.10): Normochromic anemia, moderate severity. Recommended: test for iron content, total iron binding capacity, ferritin, sternal puncture.
- Tests revealed: decreased total iron-binding capacity of the blood (40.3 mcg/dL), increased levels of ferritin (905.92 ug/L).
- Sternal marrow puncture (20.10): increased levels of blasts (2.0), myelocytes (16.0), metamyelocytes (18.6), promegaloblasts (0.6), basophilic megaloblasts.
(4.0), polychromatophilic megaloblasts (8.0 ), oxyphilic megaloblasts (7.3).

The megakaryocyte sprout is preserved.

Nephrologist (18.10): secondary nephropathy with impaired renal nitrogen excretory function.

Rheumatologist (18.10): recommended echocardiography, package for systemic connective tissue diseases, beta 2 microglobulin, immunoglobulin E, repeated computer tomography of the thoracic cavity, abdominal cavity with contrast to detect lymph nodes.

Echocardiography (20.10.17): the size of the heart's walls and chambers is normal. Mitral valve fibrocalciosis, with regurgitation. The aortic valve is normal. Global and segmental myocardial contractility are normal.

Blood tests for systemic diseases (18.10): elevated DNA levels of double-stranded (ANA–Screen) IgG antibodies (>300), positive antinuclear antibodies (ANA–Screen), elevated levels of chromatin (ANA–Screen), elevated levels of SS-B (ANA–Screen) (3.2), SS-A52/60 (ANA–Screen)>8).

Blood test for anti-phospholipid antibody syndrome (18.10): elevated levels of cardiolipin IgG (52.3 PL unites), elevated beta2 glycoprotein (70.3 PL unites).

Computer tomography of the abdominal cavity, retroperitoneal space and pelvis (23.10.17): chronic thrombosis of the inferior vena cava, common iliac and right external iliac vein. Moderate pelvic lymphadenopathy.

Re-consultation of a rheumatologist (24.10): Based on the presence of dermatological syndrome (transient erythematous rash), kidney involvement in the pathological process, presence of thrombosis (according to the results of an abdominal computer tomography scan), positive immunological markers of systemic diseases (antinuclear antibodies, anti-DNA double-stranded IgG antibodies, beta 2 glycoprotein), lesions of the reticuloendothelial system (lymphadenopathy) and lung pathology (bilateral pleuritis), the patient was diagnosed with:

Systemic lupus erythematosus (ICD 11: 4A40.0), subacute course, activity II, with the lesion of skin (transient erythematous rash), kidneys (proteinuria, transient impaired nitrogen excretory function of the kidneys), and lungs (bilateral pleuritis with immunological disorders syndrome). Secondary antiphospholipid syndrome (ICD 11: 4A45) (acute ileofemoral thrombosis, May 2017; chronic thrombosis of the inferior vena cava, iliac veins, positive IgG to cardiolipin, beta 2 glycoprotein).

Thus, on the basis of clinical-laboratory, instrumental, and immunological data, the patient had the following final diagnosis: "Ischemic cardioembolic stroke in the right middle cerebral artery pool (15.10.17) (ICD 11: 8B11.5). An acute period with left pyramidal reflex insufficiency and changes on magneto-resonance imaging. Systemic lupus erythematosus (ICD 11: 4A40.0), subacute course, activity II, with the lesion of skin (transient erythematous rash), kidneys (proteinuria, transient impaired nitrogen excretory function of the kidneys), and lungs (bilateral pleuritis with immunological disorders syndrome). Secondary antiphospholipid syndrome (ICD 11: 4A45) (acute ileofemoral thrombosis, May 2017, chronic thrombosis of inferior vena cava, iliac veins, positive IgG to cardiolipin, beta 2 glycoprotein).

Treatment included antibacterial therapy (Ceftriaxone), anti viral therapy (aciclovir), detoxification therapy (megulamine sodium succinate, hydroxyethyl starch, chloropyramine), and metabolic and vascular therapy (thiocytic acid, vitamin B1 in combination with vitamin B6 and/or vitamin B12, ATP, deproteinized calf blood haemoderivative, citicoline).

The patient was prescribed a long course of antiplatelet therapy under the control of laboratory blood tests.

According to the current recommendations, the treatment of patients with APLS is based on the appointment of indirect anticoagulants (warfarin) and antiplatelets (low doses of acetylsalicylic acid). In this case, the INR (international normalized ratio) should be maintained at a level of 2-3 in venous thrombosis and more than 3 – in arterial. Plasmapheresis, high doses of glucocorticoids (including pulse therapy), and cytostatics are used in the treatment of "catastrophic" APLS [5].

After the treatment, the patient's state improved: the paresis of facial muscles regressed. The indicators of laboratory tests stabilized.

In the literature, we have found such uncommon causes of stroke in young adults (nonatherosclerotic angiopathy due to cervicocephalic arterial dissection, cerebral amyloid angiopathy, moyamoya disease, fibromuscular displasia, migraine-induced stroke, hematoletic conditions such as hypercoagulable state due to deficiencies of protein S, protein C, or antithrombin; factor V Leiden mutation, acquired hypercoagulable state (eg, cancer, pregnancy, hormonal contraceptive use, exposure to hormonal treatments such as anabolic steroids and erythropoietin, nephrotic syndrome), antiphospholipid syndrome, hyperhomocysteinemia, sickle cell disease, Fabry disease, Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), Marfan syndrome, neurofibromatosis, inflammatory and infectious (vasculitis (primary angiitis of the central nervous system, Sjogren syndrome, Wegener’s granulomatosis, temporal arteritis, HIV, Varicella zoster virus) [10].
CONCLUSIONS

Thus, special care should be taken to link thrombotic complications in young patients with APLS and conduct research on the carrier of APLA. Further study of the relationship between the development of acute cerebrovascular disorders and APLS remains one of the top multidisciplinary problems in modern medicine. It is necessary to unite the efforts of different specialists – cardiologists, neurologists, rheumatologists, immunologists, etc.

Contributors:

Shkrobot S.I. – conceptualization;
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Duve Kh.V. – administration;
Naumova L.V. – investigation;
Budarna O.Yu. – investigation.

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REFERENCES


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