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M.S. Savvina, V.M. Argunova, M.F. Afonskaya,
M.P. Slobodchikova, Y.A. Munkhalova

VENOUS THROMBOSIS OF THE LOWER EXTREMITY IN A 13-YEAR-OLD PATIENT

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A clinical case of the venous thrombosis of the lower extremity in a 13-year-old patient is represented in the article, the thrombosis occurred in the course of post-COVID syndrome (enzyme-linked immunosorbent assay for SARS-CoV2 by 18.09.2024 detected 50000 BAU/mL. Onset of the disease acute fever up to 38C, abdominal pain. Diagnostic laparoscopy performed in the central district hospital. Diagnosis: right ovarian apoplexy, cystic ovaries, adhesions, anemia (hemoglobin - 75 g/l, dizziness, weakness). Prior to that, she was examined in Yakutsk, autoimmune thyroiditis was diagnosed. On the 6th day after laparoscopy, fever up to 39,2C, pain in the popliteal pits and lower legs appeared. Transferred to the childrens department of the central district hospital, from there sent to the admission and diagnostic department of the pediatric center RH1. Electroneuromyography revealed signs of progressive muscle damage. Transferred to the cardiorheumatology department for further examination and treatment. Laboratory data showed an increase in all inflammatory markers (CRP, D-dimer, ferritin). Ultrasound imaging revealed occlusive thrombosis of the sural veins of both lower extremities. Received low molecular weight heparin, anticoagulants, aspirin, diclofenac as treatment. The adequate therapy resulted in positive dynamics.

Keywords: thrombosis, thromboembolism, coronavirus, children, vessels, veins

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Introduction. Thrombosis is the formation of the blood clots in the blood vessels both in the arteries and the veins. Venous thromboembolism is most com-

mon and results in fatalities in the adult population. However, it is uncommon and rare among children and adolescents. Its estimated prevalence varies from 0.5 to 1.9 per 10,000 children population. Those children diagnosed with blood clotting disorders are at the highest risk [2,8].

Deep vein thrombosis can be complicated with thromboembolism and post-thrombotic syndrome. Most of the thromboses are associated with central venous catheterization. The other factors are traumas, surgical interventions, post-traumatic disorders, hereditary and acquired thrombophilic conditions, such as the presence of the factor V Leiden mutation, protein C and protein S deficiencies, disorders of the intestines, kidney, circulatory system, infections, rheumatic diseases, antiphospholipid syndrome and many others. The other causes of thrombosis are the inherited abnormalities (inferior vena cava agenesis, atresia, occlusion or uncomplete substitution) [3,6].

As a rule, the onset of deep vein thrombosis in children is asymptomatic, though there can be swollen upper

and lower extremities, elevation of body temperature, weakness, erythema, positive Homan's sign (pain response in the dorsiflexion of the foot). The diagnosis of venous thrombosis is confirmed by Duplex ultrasonography with color Doppler imaging; contrast venography, computed tomography, angiography and MRI are less common [2,4,8,9].

Despite all the mentioned causes post-COVID and multisystemic inflammatory system should be added, as they manifest by vasculopathy and hemostasis. The pathogenesis of SARS-CoV-2 affects the vascular endothelium, disturbs hemostasis that result in risk of clot formation [10]. The patients after COVID-19 show high indices of D-dimmer and fibrinogen which increase clot formation [3,9].

The clinical case. The female patient K., aged 13, was admitted to the department of cardio-rheumatology of the Pediatric Center of the Republican hospital #1, M.E. Nikolaev National health center. She complained of weakness, pains in the lower extremities when walking, nausea and dizziness.

SAVVINA Maya Semyonovna – Ph.D., senior staff scientist of the laboratory of pediatric health level monitoring, Yakutsk Scientific Center of Complex Medical Problems, maya_savvina@mail.ru; **ARGUNOVA Vera Maichna** – rheumatologist of the Department of Cardiorheumatology, M.E. Nikolaev Pediatric center, Republican hospital No.1, senior non-staff rheumatologist of the Far-Eastern federal district. cardiorevmatologsakha@mail.ru; **AFONSKAYA Marina Viktorovna** – a rheumatologist of the department of cardiorheumatology M.E. Nikolaev Pediatric center, Republican hospital No.1, senior non-staff rheumatologist of the Republic of Sakha (Yakutia); **SLOBODCHIKOVA Maya Pavlovna** – a senior lecturer of the department of foreign languages with the course of Latin language, St. Petersburg state pediatric medical university; **MUNKHALOVA Yana Afanasyevna** – Ph.D., head of the Department of Pediatrics and Pediatric Surgery, Medical Institute M.K. Ammosov Northeastern Federal University

Case history: She lost consciousness a month before the admission to the Pediatric center, the patient was admitted to the neurological department of the Central regional hospital. On examination no neurological abnormalities were revealed. Thyroid profile changes as well as changes in the thyroid gland were noticed. On the 13-th day after the onset of the disease she was discharged from the hospital with the diagnosis of autoimmune thyroiditis. At home she felt pains in the abdomen, the body temperature increased up to 38C. The diagnostic laparoscopy was carried out. She was diagnosed with apoplexy of the right ovary, cystic changes in the ovary, peritoneal adhesion, anemia (hemoglobin – 75g/L). To increase the level of the hemoglobin the erythrocyte mass was transfused on the 16th day. On the 2nd day after blood transfusion the body temperature increased up to 38-39C, the fever lasted for a week. On the 20-th day she experienced pains on the calves and lower legs.

The results of the tests showed: LDH – 896Un/L (N-250 Un/L), CRP-30.0 mg/L (N-5mg/L); coagulogram: time – 12.5 sec. (N: 6+-1.6), Protromb.index -97% (N:89+-4.2), PT – 1.02 (RI:0.8-1.14), PLT – 200-280 (RI: 160-380), ferritin – 192 mcg/L (7-140).

Past medical history: chicken-pox, acute respiratory diseases.

Family history: Her mother is 40, she suffers from chronic bronchitis, pyelonephritis, hypertension, bronchial asthma in close relatives. Her father is 39, with no medical conditions.

On admission, the patient's condition was moderately severe. There was marked weakness. Appetite and sleep were not disturbed. Clinically, swollen lower extremities, which were more marked at the lower legs, were noticed, the vascular pattern was expressed on the skin of the lower legs. The other organs and the systems had no abnormalities.

Local status: the patient limps, the patient cannot crouch. She has difficulties with tiptoeing and walking on heels. The muscles of the thigh and lower legs are painful on palpation.

Complete blood count on admission: increase erythrocyte sedimentation rate – 50mm/h, (N-4-15mm/h), neutrocytosis – 72% (N-40-65%), granulocytosis – 63,3x10E9/l (N-4.5-13,0x10E9/l), hemoglobin – 92g/l (N-115-150g/l). During the treatment, all blood counts returned to normal, hemoglobin increased to 114g/l.

Blood chemistry is presented in Table 1.

The coagulogram on the 33rd day of the disease showed that: free protein S was 55.00% (normal ranges are 50.00-134.00), antithrombin III was 110.00% (normal ranges are 96.00-126.00), protein C – 126.00% (normal ranges are 68.00-125.00);

The coagulogram on the 61st day of the disease showed that: prothrombin index was 100.00% (normal ranges: 70.00-140.00), Prothrombin time was 12.30 sec. (normal ranges: 13.50-17.00), INR was 1.00 (normal range: 0.81-1.13), fibrinogen was 3.71 g/L (normal range: 2.12-4.33), aPTT/PTT was 30.60 sec. (normal range: 30.80-41.40);

The coagulogram on the 89th day of the disease showed that: prothrombin index was 100.00% (normal range: 70.00-140.00), Prothrombin time was 12.80 sec (normal range: 13.50-17.00), INR was 1.00 (normal range: 0.81-1.13), fibrinogen was 4.49 g/L (normal range: 2.12-4.33), aPTT/PTT was 30.70 sec (normal range: 30.80-41.40).

Enzyme-linked immunosorbent assay for SARS-CoV2 by 18.09.2024 detected IgG>5000.0 BAU/mL.

The main values of thromboelastography are represented in the table 2.

The result of the lower extremities ultrasound scan is represented in the table 3.

Table 1

Biochemical blood test dynamics

The day of the disease	AST (Un/L) Normal value is up to 40	ALT (Un/L) Normal value is up to 37	Albumin (g/L) Normal level: 38-54	D-dimer (mcg/mL) Normal range: 0.16-0.39	Ferritin (mcg/L) Normal range: 7-140	LDH (Un/L) Normal range: 250-295	C-RP (mcg/L) Normal range is up to 5mcg/L
The 33-nd day	17.70	9.70	32.80	3.48	192	896.0	30.0
The 42-th day	16.10	9.90	-	1079.82	-	158.40	
The 52-nd day	38.70	64.20	42.80	799.93	46.10	-	
The 55-th day	43.90	58.40	38.10	-	39.50	136.50	
The 61-st day	21.30	25.30	38.90	349.57	24.80	117.30	
The 70-th day	39.50	41.30	43.40	1.42	-	165.30	
The 79-th day	16.20	15.60	43.50	0.27	29.10	125.30	1.25
The 89-th day	16.50	15.60	43.30	-	-	132.70	2.09

On the 32-nd day of the onset she was referred to the diagnostic department of the Pediatric center of the Republican hospital #1, the National health center. Later she was admitted to the department of cardio-rheumatology for further examination and treatment.

Anamnesis: The patient is a second child born after the second pregnancy; the pregnancy had no abnormalities during its course. It was a spontaneous vaginal delivery at due time. Her birth weight was 3750 g, height 52 cm.

Table 2

Thromboelastography (TEG) data on the 42nd day of the disease

The procedure code	TEG parameter	Measurement	Result	Normal value
1002237	Clot formation	min	2.30	Up to 6 min
1002377	Reaction time	min	8.00	Up to 12 min
1002302	Maximum amplitude	mm	56.70	50 mm
1002252	Maximum clot strength	mm	58.10	40-65

Table 3

The results of the ultrasound scan of the veins of the lower extremities

The day of the disease	The 33 rd	The 52 nd	The 67 th	The 90 th
Medical assessment report	Occlusive deep vein thrombosis of the both lower extremities	Non-occlusive deep vein thrombosis of the lower extremities with-out expressed floating parts. There is moderate infiltration in subcutaneous adipose tissue of the both lower legs. Inguinal lymphadenitis of the both sides.	Ultrasound signs of the partial re-canalization of the right femoral vein, deep veins of the lower leg. Occlusing thrombosis of the right femoral vein, deep veins of the both lower legs.	Ultrasound signs of the partial canalization of the popliteal veins of the both sides. Non-occlusive thrombosis of the external iliac vein, common femoral, great saphenous vein on the both sides.

Electromiography was carried out on the 33rd day. The medical finding: the motor point needling of the m. Tibialis anterior s. revealed the signs of progressive initial muscular disturbance: the potentials of the motor units showed expressed reduced time, amplitude (by 34.9%), all entirely polyphase, disperse, denervation / reinnervation process (DRP) is at the stage 2.

Secondary examinations on the 30th day of the disease revealed: 1) the syndrome of the median, ulnar, fibular and tibial nerves disorders was not detected on the both sides;

2) Motor point needling of m. Tibialis anterior s. revealed signs of initial muscular disturbance: the potentials of the motor units are reduced by 12.4%, polyphase, denervation / reinnervation process (DRP) was at stage 2 in comparison with the previous investigation (19.09.2024) positive dynamics is noticed: the amplitude of the potentials of the motor units (PMU) was normal, time of PMU increased, the polyphase index reduced.

Echocardiography of the 39th day of the disease revealed regurgitation of the tricuspid valve stage 1, unstable in the aortic valve – 1st stage. Mitral valve disease with minimum regurgitation. The heart cavities are not enlarged. Ejection fraction was 66%.

The ultrasound scan of the organs of the abdominal cavity and the kidneys was carried out on the 2nd day of the hospitalization. Findings: deformation of the gallbladder. Additional blood vessel was noticed in the right kidney.

Examination of the specialists.

An ophthalmologist revealed mixed astigmatism. Myopia of the 1st degree, complicated myopic astigmatism of the left eye. Retinal angiopathy of the both eyes.

A hematologist diagnosed thrombosis of the lower extremities. Secondary anti-phospholipid syndrome.

A vascular surgeon indicated no surgical treatment according to the objective

medical examination and findings of the instrumental investigations. Conservative treatment and follow up control examination are recommended.

A rheumatologist of the Federal center corrected the course of treatment, the patient was recommended to take etanercept 50 mg 1 per week, rivaroxaban 2.5 mg 2 times a day for 10 days, low-molecular heparin, aspirin, diclofenac and omeprazole.

Taking into account hyperinflammatory phenotype such as increased markers of inflammation (CRP, D-dimmer, LDH, ferritin) in the serum of the patient's blood etanercept was prescribed.

The condition was moderately severe on discharge. The patient does not complain of anything. She does not limp and she can crouch. She can tiptoe and go on her heels.

The patient is recommended a follow-up care in her local polyclinic and to apply for disability, walk moderately and wear compression stockings; physical trainings at school are contraindicated.

The hematologist and the vascular surgeon should be consulted again in a month. The patient should continue taking rivaroxaban in the recommended dose.

Discussion. We have presented the clinical case of a rare childhood disease, thrombosis of the veins of the lower extremities at the age of 13. The childhood thrombosis is always a great clinical issue due to the severity of its course and outcome. One of the main causes of the venous thrombosis in childhood is the central venous catheterization and a genetic predisposition [3,9]. The researchers revealed that the risk of thrombosis increases and results from the deficiencies in antithrombin III, protein C and protein S due to gene mutation, thrombophilia is one of the candidates [11]. According to the scientific data it is relatively rare complication of post-COVID syndrome. Moreover, multisystem inflammatory syndrome (MIS) can develop after COVID infection in children and ad-

olescents. According to the latest investigations of the recent years, the criteria of multisystem inflammatory syndrome (MIS-C) diagnosis were updated by the Council of state and territorial epidemiologists (CSTE) and the Center for disease control (CDC) of the USA this could allow to identify the disease from the other similar conditions. Thus, MIS-C is diagnosed in all patients under 21 years with COVID infection in the anamnesis which occurred within 60 days before or during the hospitalization, accompanied with high fever of 38C or above and lasting for any time. The only laboratory finding was an increased level CRP from 3.0 mg/dL and more. To diagnose MIS-C there should be at least two signs of the organ or system involved: affection of the heart, skin and mucous membranes, gastro-intestinal tract, hematologic changes in the laboratory findings and shock [1,5]. The risk of thrombosis increases in that case. Dysfunction of the platelets is most commonly associated with COVID-infection.

According to the researchers, who studied the link of COVID-19 and development of thrombosis in such COVID-patients, the infection results in thrombotic complications as there is accumulation of the proinflammatory factors. Pathogenesis of the thrombotic complication is associated with a complex of pathophysiological mechanisms which develop afterwards. Thus, viral respiratory infections including COVID-infections, are associated with platelet activation and hypercoagulation. The platelets display the receptors on the surface, which recognize the viruses and release lots of pro-inflammatory mediators, which are responsible for interaction of platelets with leukocytes and endothelial cells initiating coagulation and activation of different interleukins [11]. In that case an increased inflammatory and coagulant activity takes place, which results in thrombosis [7,11].

Conclusion. This clinical case shows that there are long-lasting post-COVID effects, which was asymptomatic when it was complicated by thrombosis. The

main feature of the disease manifestation is its comorbidity course in the child. The description of this case underlines the importance of early diagnosis and adequate therapy administration to treat such patients.

The authors declare no conflicts of interest.

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