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CLINICAL CASE OF DELAYED TREATMENT OF VISCERAL LEISCHMANIASIS

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Abstract: This article provides brief information about the etiology, epidemiology, clinical picture, diagnosis and etiotropic therapy of visceral leishmaniasis. Also, the article presents a clinical case of Mediterranean-Central Asian (childhood) visceral leishmaniasis in a 5-year-old boy. The development of the clinical picture of the disease, laboratory and instrumental research methods are described in detail. For the purpose of etiotropic therapy, the patient was prescribed Sol. Meglumine antimonate (Glucantim) according to a regimen that gave a good therapeutic effect.

Key words: visceral leishmaniasis, L. infantum, diagnosis, Sol. meglumine antimonate.

Materials and methods: This study included 1 patient with leishmaniasis and various examinations were conducted including immunochromotographic test , ultrasound examination of the liver and others.

Relevance. The causative agent of leishmaniasis is the protozoan parasite Leishmania, which is transmitted by infected female mosquitoes through the bite. There are 3 main forms of the disease: visceral leishmaniasis (also known as kala-azar and is the most severe form of the disease), cutaneous leishmaniasis (the most common) and mucocutaneous leishmaniasis.

Leishmaniasis is endemic in more than 98 countries, where over 350 million people are at risk. An estimated 1.3 million new cases of leishmaniasis occur worldwide each year: 0.3 million of these are visceral leishmaniasis and 1 million are cutaneous leishmaniasis (CL). As with other neglected tropical diseases, leishmaniasis has not received adequate attention in health policy, and consequently the public visibility of the problem is disproportionate to its burden .

Visceral leishmaniasis (VL), known as kala-azar, is usually fatal in 95% of cases if left untreated. The disease is characterized by irregular attacks of fever, weight loss, hepatosplenomegaly and anemia. Most cases of the disease have been recorded in Brazil, East Africa and India. There are an estimated 50,000 to 90,000 new cases of VL each year worldwide, but only 25–45% of these are notified to WHO. In 2020, more than 90% of new cases notified to WHO were reported in 10 countries: Brazil, China, Ethiopia, Eritrea, India, Kenya, Somalia, Sudan and Yemen. Thus, visceral leishmaniasis is one of the parasitic infections with the highest epidemic potential and mortality.

Two clinical forms of leishmaniasis are widespread and endemic throughout the WHO European Region: VL and CL. According to WHO, the only causative agent of VL in the European Region is Leishmania infantum, the main reservoir is domestic dogs, and the carrier is a number of species of mosquitoes of the genus Phlebotomus. In all endemic countries in the WHO European Region, there is underreporting of VL cases, ranging from mild to moderate. The annual incidence of VL is estimated to be between 1100 and 1900 cases. The most affected countries are Georgia, Spain, Albania, Italy, Turkey, Tajikistan and Azerbaijan .

In accordance with the peculiarities of etiology, epidemiology and clinical picture, visceral leishmaniasis of the Old World is divided into: Indian kala-azar and Mediterranean-Central Asian (childhood) leishmaniasis. Sporadic cases of Mediterranean-Central Asian (childhood) visceral leishmaniasis are recorded in the republics of Central Asia and Transcaucasia.

The incubation period for VL usually ranges from 20 days to 6 months, but can last up to several years. The onset of symptoms is usually subacute, with a slow progression of symptoms such as malaise, fever, weight loss and splenic pain that continue over a period of months. At the same time, cases of acute, rapidly progressing disease are also observed, especially among children under 5 years of age. The patient often appears pale due to anemia. The spleen is enlarged and usually compacted, slightly painful, but with a high degree of splenomegaly the pain can be more pronounced. Liver enlargement is usually less pronounced .VL is a more dangerous disease than other forms of leishmaniasis and can be fatal if the disease is not diagnosed and treated promptly. The risk group includes children under 5 years of age.

The classic method for diagnosing VL is the detection of parasite amastigotes by microscopy. Typically, samples taken from the bone marrow or spleen are used, and the overall sensitivity of the methods ranges from 53% to 86% and from 93% to 99%, respectively. One of the rapid diagnostic tests is immunochromatographic test strips using the rK39 antigen. This test is easy to perform, inexpensive, and can be used for early diagnosis of VL at the peripheral and central levels. The sensitivity of the rK39 antigen varies depending on the geographical region, but is considered to be quite high .

Since the late 1940s, the traditional treatment for VL has been pentavalent antimony (Sb5+) preparations. Pentamidine was introduced in 1952 and was used primarily as a second-line agent until its use was discontinued due to toxicity. In the 1980s, the now traditional amphotericin B deoxycholate (ABD) was introduced, followed by the introduction of lipid formulations of amphotericin B with high efficacy and low toxicity. In 2003, miltefosine was developed as an oral drug for the treatment of VL, followed by paromomycin (aminosidine) in 2005, a cheap and effective parenteral drug that can be easily administered by intramuscular (IM) injection.

For the treatment of VL caused by L. infantum in the countries of the Mediterranean basin, the Middle East and Central Asia, WHO makes the following recommendations: the preferred option is liposomal Amphotericin B: 3-5 mg/kg daily, IV drip for 3-6 days until total dose 18-21 mg/kg; alternatively, pentavalent antimony preparations: 20 mg Sb5+/kg per day IM or IV for 28 days; third option Amphotericin B deoxycholate: 0.75-1.0 mg/kg per day, IV drip, daily or every other day 20-30 doses until a total dose of 2-3 g is reached .

Clinical case review. A sick child I., 5 years old, a citizen of Tajikistan, was admitted for inpatient treatment to the clinic of the Republican Specialized Scientific and Practical Medical Center for Epidemiology, Microbiology, Infectious and Parasitic Diseases with a diagnosis of visceral leishmaniasis. Date of admission: 09/10/2021.

Complaints upon admission: according to the mother, an increase in body temperature to 39°C, general weakness, lethargy, lack of appetite, pale skin, enlarged abdomen, shortness of breath, weight loss.

From the epidemiological history: according to the mother, they live in the city of Istaravshan, Sughd region of the Republic of Tajikistan, located in the northern part of the Republic of Tajikistan, in the foothills of the Turkestan Range. The onset of the disease is not associated with anything. But, it notes cases of visceral leishmaniasis among residents in this region.

History of the disease. According to the mother, the child has been sick for 1.5 years. The disease began in March 2020. He became acutely ill, his body temperature rose to 39°C, weakness and lethargy appeared. The parents consulted a pediatrician and outpatient treatment was prescribed for ARVI, but at the end of treatment the patient's condition did not improve, the fever persisted, anemia progressed, and

weakness and lethargy increased. The child received outpatient treatment several times. After 6 months from the onset of the disease, the patient's parents contacted an infectious disease specialist to clarify the diagnosis. After a comprehensive examination, based on clinical and epidemiological data, a preliminary diagnosis of "Leishmaniasis?" was made, but a myelogram was not performed. At that time, the clinic did not have etiotropic drugs available due to the COVID-19 pandemic. Only symptomatic and pathogenetic treatment was prescribed. The patient did not receive etiotropic therapy.

In April 2021, the patient was once again hospitalized in the infectious diseases clinic due to deterioration of his condition. The progression of anemia continued, the fever persisted, weakness and lethargy increased, the abdomen sharply increased due to hepatosplenomegaly, and he continued to lose weight. Due to the lack of etiotropic drugs, the patient was prescribed only symptomatic therapy, which was carried out for 37 days.

After the opening of the borders between Uzbekistan and Tajikistan on 09/06/2021, parents and their child arrived at the Republican Specialized Scientific and Practical Medical Center for Pediatrics in Tashkent for examination and treatment with complaints: fever, shortness of breath, abdominal enlargement, general weakness, lethargy, lack of appetite , pale skin, anxiety, weight loss. The patient was hospitalized to clarify the diagnosis.

General blood test dated 09/06/2021: hemoglobin – 49 g/l, erythrocytes – 2.2 x 1012/l, leukocytes – 2.1 x 109/l, s/i – 15%, lymphocytes – 80%, monocytes – 5 %, platelets – 60 x 109/l, ESR – 75 mm/h.

Biochemical blood test dated 09/06/2021: ALT-16 units, AST-42 units, total bilirubin - 12.9 µmol/l, direct bilirubin - 2.6 µmol/l, indirect bilirubin - 10.3 µmol/l, blood glucose - 6.0 mmol/l, total protein - 75 g/l, creatinine - 28 µmol/l, urea - 4.3 mmol/l.

The test for HIV infection is negative.

HBsAg and anti-HCV are negative.

Blood type – 0 (I), Rh+.

Myelogram analysis from 09/07/2021: blast cells - 0.2%, promyelocytes - 0.6%, myelocytes - 38%, metamyelocytes - 5.2%, band cells - 8.0%, segmented cells - 9.6%, eosinophils - 2.0%, lymphocytes - 12%, monocytes - 2.4%, pronormocytes - 0.8%, basophilic normocytes - 5.8%, polychrome normocytes - 39.6%, oxyphilic normocytes - 9.4%, leuko- erythroblastic ratio is 1:1.3, amastigote forms of Leishmania were found in the preparation.

Within 5 days the patient was prescribed the following medications: Sol. Dicinoni 1.0 iv, Contriver 10,000 iv, Sol. Acidi ascorbinici 5%-5.0 i.v. According to vital indications, a blood transfusion with red blood cells was performed.

On September 10, 2021, after a consultation of specialists from the center (pediatrician, hematologist, hepatologist) and stabilization of the general condition, by agreement, the patient was transferred to the clinic of the Republican Specialized Scientific and Practical Medical Center for Epidemiology, Microbiology, Infectious and Parasitic Diseases (RSSPMCEMIPD) for further treatment with a diagnosis of : leishmaniasis, visceral form, hepatosplenomegaly.

Anamnesis of life. Child from pregnancy II, birth II, at term, body weight - 3200 g, height - 52 cm. The neonatal period was uneventful. Past illnesses: ARVI, anemia. No allergic reactions were observed. The mother denies the presence of hereditary diseases.

Objective examination data. The general condition of the patient is serious, which is due to severe intoxication syndrome and anemia. The patient's weight is 15 kg. Body temperature – 37.5°C. Psychomotor development corresponds to age. The skin and visible mucous membranes are pale, the

nasolabial triangle is cyanotic, and the peripheral lymph nodes are slightly enlarged. Subcutaneous tissue is poorly developed. Skin turgor and elasticity, as well as muscle tone, are preserved. The chest is cylindrical, breathing through the nose is free. Respiration rate - 24 per minute. In the lungs, a shortening of the pulmonary sound is determined by percussion, and dry and moist rales are heard on auscultation against the background of hard pulmonary breathing. Heart sounds are muffled, heart rate is 126 beats/min, the pulse is rhythmic, normal tension and filling. The tongue is moist and covered with a white coating. The abdomen is enlarged in volume, soft, painful on palpation. The liver protrudes 3.0 cm from under the edge of the costal arch. The spleen is enlarged to the small pelvis. Urination is free and regular. Chair - 1 time per day, decorated.

The following laboratory and instrumental research methods were carried out in the clinic of the Russian National Research Medical and Medical Institute of Medical and Clinical Hospital:

General blood test dated September 10, 2021: hemoglobin – 84 g/l, red blood cells – 2.85 x 1012/l, leukocytes – 4.6 x 109/l, platelets – 134 x 109/l, ESR – 18 mm/h.

Biochemical blood test dated September 11, 2021: ALT - 0.80 mmol/l, AST - 0.40 mmol/l, total bilirubin - 20.0 µmol/l, direct bilirubin - 3.0 µmol/l, indirect bilirubin - 17 .0 µmol/l, blood glucose - 4.6 mmol/l, total protein - 52.4 g/l, creatinine - 85.1 µmol/l, urea - 8.3 mmol/l.

VSK from 09/11/2021: start 2 min. 01 sec. end 2 min. 19 sec.

General stool analysis dated September 11, 2021, without any features.

General urine analysis dated September 11, 2021 - protein - 0.033, epithelium - 2-3/1, leukocytes - 4-8/1, erythrocytes - 6-7/1, hyaline casts - 0-2/1.

Ultrasound examination of the abdominal organs revealed signs of hepatosplenomegaly and portal hypertension.

Based on clinical symptoms, laboratory test results and myelogram results, the patient was diagnosed with Leishmaniasis. Visceral form, severe course. Complication: hepatosplenomegaly, stage II anemia.

The patient was prescribed treatment in accordance with the current clinical standard of the Ministry of Health of the Republic of Uzbekistan. For the purpose of etiotropic therapy, the patient was prescribed Sol. meglumine antimonate, under the trade name Glucantim according to the following regimen: 1st day - 250 mg (0.8 ml), 2nd day - 500 mg (1.6 ml), 3rd day - 750 mg (2.4 ml), from the 4th day to 1000 mg (3.2 ml) IM for 28 days. In parallel, the following drugs were also prescribed: Sol. Dicinoni IM 1.0 ml x 2 times a day for 7 days, Sol. Acidi ascorbinici 5% IV 4.0 ml x 1 time per day for 10 days, IV Thiotriazoline 2.0 ml x 1 time per day for 10 days, Cefepime IM 450 mg x 2 times a day for 7 days, Veroshpiron 25 mg, 1 tablet 1 time a day for 10 days, Asparkam, 1 tablet 2 times a day for 10 days, Flucanazole 50 mg, 1 tablet 1 time a day for 3 days , Fersinol drops 10 drops x 2 r.i.d. within 20 days.

In the following days, during treatment, a repeat laboratory examination was carried out.

General blood analysis:

from 09/17/2021: Hb - 75 g/l, erythrocytes -3.41x1012/l, leukocytes - 2.5x109/l, lymphocytes - 31.8%, platelets -153x109/l, ESR - 13 mm/h.

from 09.30.2021: Hb - 81 g/l, erythrocytes - 3.59x1012/l, leukocytes - 2.8x109/l, lymphocytes - 29.8%, platelets - 162x109/l, ESR - 13 mm/h.

from 10/7/2021: Hb - 88 g/l, erythrocytes - 3.64x1012/l, leukocytes - 3.1x109/l, lymphocytes - 27.4%, platelets - 168x109/l, ESR - 12 mm/h.

Blood clotting time:

from 09/17/2021: start 2 min 39 sec, end 3 min 00 sec.

from 09/30/2021: start 3 min 40 sec, end 3 min 58 sec.

from 10/7/2021: start 3 min 30 sec, end 4 min 06 sec.

With the therapy, the child's condition gradually improved. There was a gradual normalization of the size of the liver and spleen and positive dynamics of laboratory parameters. The general condition of the child at the time of discharge on October 9, 2021 was satisfactory.

Conclusion:

During the coronavirus pandemic, many diseases have been forgotten and relegated to the background, while the burden of other neglected diseases, such as visceral leishmaniasis, continues to be recorded today. This clinical case analysis will help trainee doctors remember such a forgotten disease as visceral leishmaniasis. At the present stage, it is necessary to eliminate and timely combat this disease, organize full access to health care services, with sufficient provision of diagnostic tools and a full supply of etiotropic drugs.

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