The girl with fever and jaundice

A patient M., 8 years old, came to see a pediatrician on the 8th day of the disease with complaints of jaundice, of the sclera and skin, weakness, loss of appetite.
***From the medical history*: at the onset of the disease, fever went up to 39,5 °C without catarrhal phenomena. On the 5th day the fever stopped, since the 6th day of the disease, ochrodermia, sclera, acholic stool have developed. The child has not been vaccinated.**
***During the examination on the 8th day of the disease*: satisfactory condition, no fever, no signs of intoxication. The skin was pale, jaundiced, mucous membranes icteric. The tongue was coated with white bloom. Palpation showed enlarged liver and spleen. Other organs and systems did not have any specific features. In the clinical blood analysis: leukocytes — 8,12 th/mkl (the norm is 5,6-11,5 th/mkl), neutrophils — 1,02 th/mkl (the norm is 1,8-8 th/mkl), lymphocytes — 5,88 th/mkl (the norm is 1,5-6,5 th/mkl), platelets — 236 th/mkl (the norm is 150-440 th/mkl), ESR — 22 mm/h (the norm is 2-20 mm/h). The concentration of C-reactive protein — 3,98 mg/l (the norm is up to 5 mg/l). In the biochemical analysis of the blood: increase in transaminase, bilirubin, alkaline phosphatase activity (table). The antibodies to hepatitis A, B and C were negative. According to the ultrasound examination of the abdomen: hepatosplenomegaly, symptoms of diffuse perivascular process and parenchymal reaction process in the liver, secondary changes in pancreas.**
***During the examination on the 11th day of the disease*: no fever, the tonsils were coated with white abundant bloom, the cervical lymph nodes were swollen, there was a difficulty in nasal breathing. Jaundice decreased, stool was colored. The dynamics of biochemical indicators is presented in table 1.**

Table. The dynamics of biochemical indicators of the blood of patient M.

Biochemical blood analysis	Units of measurement	Normal values	The result on different days				
			8	11	14	21	27
Alanine aminotransferase	IU/l	<40	631	505	1 074	711	265
Aspartate aminotransferase	IU/l	<42	487	281	1 053	347	105
Total bilirubin	mkmol/l	3,7 - 20,5	26,7	18,1	15,5	16,2	18,1
Direct bilirubin	mkmol/l	<5,1	13,9	7,4	5,3	3,1	3
Gamma-glutamyl transferase	IU/l	5 - 35	136	142	104	74	54
Lactate dehydrogenase	IU/l	91 - 225	588	486	722	378	221
Alkaline phosphatase	IU/l	60 - 400	564	381	547	415	328

What is your possible diagnosis?

1. Viral Hepatitis A
2. Viral Hepatitis B
3. Infectious mononucleosis
4. Autoimmune hepatitis

Correct answer: 3. Infectious mononucleosis

Hepatitis A is characterized by acute onset of the disease, fever, weakness, loss of appetite, dyspeptic symptoms. Jaundice appears later; the patient feels better. The source of infection is a person. The virus is transmitted primarily through household contacts, through hands contaminated with faeces, as well as through food and drinking water. To confirm the diagnosis of hepatitis A, it is necessary to conduct a serological blood test for the presence of specific antibodies of class M (anti-HAV IgM). The generation of antibodies begins before the disease manifestation, their concentration increases in the acute phase. After 3-6 weeks of the disease, this class of antibodies in blood is no longer detected. Anti-HAV IgM were not detected in the blood of our patient.

Viral hepatitis B is characterized by more gradual progression of the disease, normally, absence of fever (low-grade fever is possible), long incubation period, there is no improvement of the general condition of the child during the development of jaundice (the condition can even worsen). Infection occurs when the blood of an infected person gets into the child through damaged skin and mucous membranes, for instance, through medical instruments during operations, blood transfusions, injections, dental procedures 3-6 months before the onset of the disease. The girl's parents denied the possibility of such infection. The determinative criterion in the diagnosis of hepatitis B is the detection of antibodies to the surface antigen HBsAg in the blood. The synthesis of the antibodies begins soon after the infection with their disappearance from circulation in the blood 1 month after the onset of jaundice. Identification of HBsAg in later periods indicates a prolonged or chronic illness. In this patient's blood, no antibodies to the surface antigen were found.

Autoimmune hepatitis is a chronic disease of unknown etiology, which is characterized by progressive lesions of the liver. Approximately, in 1/3 of all cases the onset of the disease is characterized by acute hepatitis with fever, general weakness, hepatosplenomegaly, jaundice, cytolysis and cholestasis syndrome, so clinicians should consider the diagnosis of autoimmune hepatitis in any patient with acute hepatitis or acute liver failure. The examination of such patients should include the identification of specific autoantibodies to autoimmune hepatitis of 1st and 2nd type. No autoantibodies were identified in our patient.

On the day of the first doctor visit, the patient's major symptoms of the disease were syndromes of cytolysis and cholestasis, developed due to febrile fever, hepatosplenomegaly, therefore viral and autoimmune hepatitis were the first to exclude. Pathogenetic therapy with ursodeoxycholic acid drug was prescribed. On the 11th day of the disease, typical symptoms of infectious mononucleosis appeared: the tonsils were coated, lymphadenopathy, difficulty in nasal breathing. The diagnosis was confirmed by the detection of antibodies of class M to capsid protein of Epstein-Barr virus (EBV): Anti-VCA IgM>160 IU/ml. As a rule, indicative clinical picture of the disease can be observed at the end of the 1st week of disease. In this clinical case, infectious mononucleosis was diagnosed with a delay, only in the 2nd week of the disease, because during the first doctor visit the possibility of EBV-etiology was not considered due to the absence of lymphadenopathy.

The infection with EBV occurs in early childhood. Those, who were not infected in childhood, are infected in their teens. Further in the course of life of the virus is constantly released into saliva. About 90% of people are carriers of the virus as a lifelong latent infection of B lymphocytes (in the pool of long time living B memory cells). The initial contact with the virus may happen asymptomatically, with minor symptoms of acute respiratory viral infection, but, in most cases (50-75%) — in the form of infectious mononucleosis. The infection is anthroponotic, the source of the disease can be both asymptomatic patients and patients with typical forms of the disease. Infection occurs

through airborne droplets, mainly through saliva. There also exist a hemotransfusion and a sexual way of transmission.

Primary infection and virus replication occur in lymphoid oropharynx formations, where virions invade hematogenously into other organs with lymphoreticular tissue, including peripheral lymph nodes, liver and spleen. Under the influence of the virus B, lymphocytes proliferate and turn into large atypical lymphocytes (mononuclear cells). The virus persists lifelong in the oropharynx epithelium of infected individuals, therefore, virus excretion in saliva and blood cell culture by polymerase chain reaction is useless for diagnosis.

The main indications of infectious mononucleosis include fever, swollen lymph glands, especially in the neck, oropharyngeal lesion (the tonsils are enlarged and coated), nasopharynx (difficulty in nasal breathing due to hypertrophy of the adenoids), hepatosplenomegaly. The disease may begin acutely with fever and full symptom picture by the end of the 1st week of the disease, or gradually, when during 2-5 days low-grade fever is indicated, malaise, minor catarrhal phenomena. In addition to the leading symptoms exanthema, enanthema, periorbital edema may occur. Hepatosplenomegaly is observed very often. The liver and spleen begin to enlarge since the first day of the disease, the maximum size is reached to the 10th day. Sometimes in the midst of the disease jaundiced skin and sclera appear. Laboratory examinations can diagnose leiko- and lymphocytosis, atypical mononuclear cells (>10%), neutro- and thrombocytopenia, increase in the activity of liver enzymes, hyperbilirubinemia (40%). Serological diagnosis is based on the detection of heterophilic antibodies or IgM to capsid protein of Epstein-Barr virus, which are detected during the acute phase of the disease and during 1-2 months after the recovery. Since the first days of the disease, antibodies of IgG start developing in the blood, and they remain for the whole life, therefore, the detection of anti-IgG to Epstein-Barr virus in children is of no use (under 1 month — maternal antibodies, later — the indication of the infection) .

In most cases, infectious mononucleosis goes away on its own. Sometimes it can progress heavily with liver and kidney lesion. Complications are very rare. They include cranial nerves lesion, hemolytic anemia, ruptured spleen, obstruction of the upper airway, myocarditis, nephritis, pneumonia. Deaths are also extremely rare (central nervous system lesion, ruptured spleen, superinfection).

There is no specific treatment for infectious mononucleosis. Symptomatic treatment is prescribed. However, in heavy cases with prolonged febrile fever in case of the appearance of obstructive sleep apnea, some experts recommend a short course of glucocorticoids (prednisone, 1-2 mg/kg per day up to 3-7 days). Our patient had a positive dynamics during the treatment with hepatoprotective drug (ursodeoxycholic acid).

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Recommended list of sources

1. Bennett NJ. Pediatric Mononucleosis and Epstein-Barr Virus Infection. 2015 [cited 2016 Jan 12]. Available from: http://emedicine.medscape.com/article/963894-overview.

2. *Педиатрия: национальное руководство. В 2-х т.* М.: ГЭОТАР-Медиа. 2009. Т. 2. С. 570-582. [Pediatrics: national leadership. In 2 v. Moscow: GEOTAR-Media; 2009. pp. 570-582. (In Russ).]

3. Учайкин ВФ, Нисевич НИ, Шамшева ОВ. *Инфекционные болезни у детей: учебник*. М.: ГЭОТАР-Медиа. 2011. С. 232-240, 257-292. [Uchaikin VF, Nisevich NI, Shamsheva OV. *Infectious diseases in children: a textbook*. Moscow: GEOTAR-Media; 2011. pp 232-240, 257-292. (In Russ).]

4. David CW. *Autoimmune Hepatitis. 2015* [cited 2016 Jan 12]. Available from: http://emedicine.medscape.com/article/172356-overview.