UDC 616.36-002:578; 578.8 https://doi.org/10.33619/2414-2948/56/18

CO-INFECTION OF HEPATITIS A AND HERPES SIMPLEX VIRUS: A CASE REPORT

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КОИНФЕКЦИЯ ВИРУСОВ ГЕПАТИТА А И ПРОСТОГО ГЕРПЕСА: ОТЧЕТ О СЛУЧАЕ

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Abstract. Hepatitis A is a self-limiting disease where fulminant hepatitis and death occur in a small proportion of patients. Fulminant hepatic failure is more common in patients with underlying liver diseases, such as chronic hepatitis B and C, co-infection with more than one genotype of hepatitis A at the same time, non-alcoholic fatty liver disease or alcoholic steatohepatitis, in advanced age and with dependence on intravenous drugs. We present a case of infection of hepatitis A and herpes simplex virus that lead to acute liver failure. In this rare case, the importance of attention to the first manifestations of the disease in diagnosing severe cases of hepatitis A in adults is emphasized. At the same time, HSV hepatitis can also be the cause of fulminant hepatic insufficiency. Therefore, patients with severe hepatitis A need an early examination for HSV infection, and empirical treatment with acyclovir should begin at early stage.

Аннотация. Гепатит А является самоограничивающимся заболеванием, при котором молниеносный гепатит и смерть возникают у небольшого числа пациентов. Молниеносная печеночная недостаточность чаще встречается у пациентов с основными заболеваниями печени, такими как хронический гепатит В и С, коинфекция с более чем одним генотипом гепатита А одновременно, неалкогольная жировая болезнь печени или алкогольный стеатогепатит, в пожилом возрасте и в зависимости от внутривенных наркотиков. Мы представляем случай заражения гепатитом А и вирусом простого герпеса, которые приводят к острой печеночной недостаточности. В этом редком случае подчеркивается важность внимания к первым проявлениям заболевания при диагностике тяжелых случаев гепатита А у взрослых. В то же время гепатит ВПГ также может быть причиной молниеносной печеночной недостаточности. Следовательно, пациенты с тяжелым гепатитом А нуждаются в раннем обследовании на наличие инфекции ВПГ, и эмпирическое лечение ацикловиром должно начинаться на ранней стадии.

Keywords: hepatitis A, herpes simplex virus, acute liver failure.

Ключевые слова: гепатит А, вирус простого герпеса, острая печеночная недостаточность.

Т. 6. №7. 2020
https://doi.org/10.33619/2414-2948/56

Introduction

Hepatitis A infection occurs worldwide and its global estimations are 1.5 million of cases each year [1]. Hepatitis A virus can cause acute liver failure and death (in approximately 0.2% of clinical cases) and this risk increases with age and the presence of chronic liver disease. Viral hepatitis A is food- and water-borne infection that can result in acute outbreaks in communities with unsafe water and poor sanitation. They do not result in chronic infection or chronic liver disease and there is no specific treatment. Prevention is done through improved sanitation, food safety and vaccination [2].

The Kyrgyz Republic is a high endemic area for hepatitis A, representing up to 60.5% of cases overall of viral hepatitis according to the Epidemiological Surveillance largely due to enteral spread of contaminated food and water or direct person-to-person contact. In the country the children incidences of hepatitis A dominate traditionally, but in the periods of epidemic outbreaks the adult proportion becomes higher. The tendency towards growing up of hepatitis A has been traced since 2001 with a predominant increase in incidences in the age groups of 15-19 years and 20-29 years (14.7% and 19.1%, respectively), reaching 60.3% during the epidemic outbreaks [3].

The course of hepatitis A may vary extremely. Children with general subclinical hepatitis have neither symptoms nor jaundice. These asymptomatic cases can be recognized by detecting antibodies to hepatitis A virus (HAV) only. Patients may develop anicteric or icteric hepatitis and have symptoms ranging from mild and transient to severe and prolonged, from which they recover completely or develop fulminant hepatitis and die. The severity of the disease increases with age at time of infection. Acute hepatitis A has four clinical phases: 1) an incubation or preclinical period, ranging from 10 to 50 days, during which the patient remains asymptomatic despite active replication of the virus; 2) a prodromal or preicteric phase ranging from several days to more than a week, characterized by the appearance of symptoms like loss of appetite, fatigue, abdominal pain, nausea and vomiting, fever, diarrhea, dark urine and pale stools; 3) an icteric phase, during which jaundice develops, patients often seek for medical help at this stage of their illness. The icteric phase generally begins within 10 days of the initial symptoms. Fever usually improves after the first few days of jaundice. Extrahepatic manifestations of hepatitis A are unusual. The mortality rate is low (0.2% of icteric cases) and the disease ultimately resolves. Occasionally, extensive necrosis of the liver occurs during the first 6-8 weeks of illness. In this case, high fever, marked abdominal pain, vomiting, jaundice and the development of hepatic encephalopathy associated with coma and seizures are the signs of fulminant hepatitis, leading to death in 70 - 90% of the patients. In these cases, mortality is highly correlated with increasing age, and survival is uncommon in patients aged 50 and over. Among patients with chronic hepatitis B or C or underlying liver disease, who are superinfected with HAV, the mortality rate increases considerably [4].

Case report

A 22-year-old woman was admitted to the republican clinical infectious disease hospital on August 14, 2017 with a one-week history of vomiting, weakness, lethargy, abdominal and epigastrium pain jaundice. She had acute onset of infection with increased temperature, dyspeptic symptom joined, then abdominal pain and vomiting began. She went to a Family Medical Center and there she was sent for treatment to the hospital.

In history of disease she told about her work as a bookbinder in the printing house, she had constant contact with toxic substance (paints, solvents). During the last month of work, there was a lack of appetite, nausea. A week before the illness' start she had a rest in Issyk-Kul Lake area.

On admission, the patient’s T° was 37.0°C, the condition was mild severe with asthenic syndrome, abundant vesicles on the skin around the mouth and nose, intense icteric discoloration of the skin and sclera, an increase of liver size on 1.5-2.0 cm. Consciousness was clear, the patient

Т. 6. №7. 2020
https://doi.org/10.33619/2414-2948/56

answered the questions adequately. Vesicular breathing and heart sound were muffled, rhythmic. Pain in the epigastrium and right hypochondriac area was determined by palpation of the abdomen. Vesicles on the skin around the mouth and nose disappeared in three days.

Laboratory data on admission: a high level of total bilirubin – 221.3 μmol/liter (norm up to 20,5 μmol/l), due to conjugated fraction of 161.1 μmol/liter, elevated ALT in 15 times (1,55 μkat/l) in comparison with the upper limit of the norm (0,01-0,1 μkat/l), the prothrombin index decreased up to 66%. During the following week jaundice and weakness decreased and appetite increased, but sub febrile fever repeated every other day (37,4°C to 38ºC). Serology for hepatitis A (anti-HAV IgM) was positive. She was provisionally diagnosed as a case moderate hepatitis A and was managed with supportive parenteral fluids.

In one week, the level of total bilirubin raised to 343.1 μmol/liter, conjugated fraction – up to 223.5 μmol/liter, unconjugated fraction – up to 120 μmol/liter. ALT activity reached 1,78 μmol/liter.

On the 26th day of the disease, the patient's condition worsened, weakness, loss of appetite appeared again, ascites joined. Prothrombin index decreased to 60%.

On the 29th day of the disease there were signs of encephalopathy and edematous-ascetic syndrome, Tº was 38ºC. The size of the liver began to decrease and prothrombin index was undetectable. Repeated investigations showed a disorder in the blood coagulation system: APTT (activated partial thromboplastin time) – 60,7sec (control range 24-34 sec), prothrombin time – 30 sec (control 12-20 sec), INR (international normalized ratio) – 2,18 (control 0,9-1,2), fibrinogen – 48,2 mg/dl, serum albumin – 34,3 g/l. Other investigations results including hepatitis B surface antigen, serology for hepatitis E, C, D were negative. Repeated IgM anti hepatitis A virus was positive. Serology for HSV type 1 and 2 IgM titer was higher by 3 times (correlation coefficient = 3.73), IgG exceeded by 7 times (correlation coefficient =7.31). Plasma transfusion, parenteral fluids were continued and acyclovir was added to treatment but her clinical and laboratory parameters continued to get worse. On the 38th day of the disease coma and DIC syndrome were developed.

Pathoanatomical diagnosis: Acute viral hepatitis of mixed genesis: hepatitis A and herpetic hepatitis, fulminant form. Complications: acute hepatic insufficiency with the development of hepato-renal syndrome, hepatic encephalopathy and hemorrhagic syndrome, which is confirmed by morphological studies.

Discussion

We present an unusual case of acute liver failure (ALF) due to co-infection of hepatitis A and herpes simplex virus (HSV) infection.

HAV causes an acute self-limited disease with the likelihood of developing symptomatic hepatitis with jaundice more often in adults. High rates of hospitalization and complications of hepatitis A occur among the elderly people. Although the treatment and outcome of acute hepatitis A is largely beneficial, but with the development of HAV infection with acute liver failure, accompanied by the presence of coagulopathy and encephalopathy, up to 50% of patients may die or require emergency liver transplantation. People older than 50 years may have high fatality ratios (1.8%). Therefore, it is important to identify patients with hepatitis A with an unfavorable prognosis in early stages although it is difficult because of the low prevalence of ALF in the general population [5; 6].

Fulminant hepatic insufficiency is more common in patients with underlying liver disease, such as chronic infection of hepatitis B and C, co-infection with more than one HAV genotype at the same time, non-alcoholic fatty liver disease (NAFLD) or alcoholic steatohepatitis (ASH), also in advanced age and with dependency on intravenous drugs [7; 8].

HSV hepatitis is an uncommon cause of ALF, in 0.8% of all cases and only 2% of all viral hepatitis. It is mostly seen in immunocompromised individuals and pregnant women in their third

trimester following an orogenital HSV-1 or HSV-2 infection. HSV hepatitis is a difficult diagnosis to establish. It should be considered in the differential diagnosis of any case of severe hepatitis with concomitant fever, abdominal pain and elevated values of liver function tests with or without jaundice. The diagnosis with liver biopsy is the gold standard; HSV PCR with a simultaneous increase in aminotransferases can serve as a substitute for markers for diagnosis [9; 10].

In presented case, the patient was admitted with symptoms of hepatitis and oral mucocutaneous lesions of HSV. Lesions disappeared in 3 days. Lab test showed positive anti-HAV IgM then supportive care started. Patient condition became worse, symptoms of fulminant hepatitis: fever, coagulopathy and encephalopathy were presented. On the 29th day of hospitalization, serology was performed for HAV, HBV, HCV and HSV: anti-HAV IgM and anti-HSV type 1 and 2 IgM and IgG were detected, exceeding the titers.

In conclusion, it should be assumed that HSV hepatitis is highly suspected as the cause of fulminant hepatic insufficiency. Therefore, patients with severe HAV need an early examination for HSV infection and empirical treatment with acyclovir should begin in early stage.

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Работа поступила
в редакцию 09.06.2020 г.

Принята к публикации
14.06.2020 г.

Ссылка для цитирования:

Akhunbaev S., Kutmanova A., Gupta A. Co-infection of Hepatitis A and Herpes Simplex Virus: A Case Report // Бюллетень науки и практики. 2020. Т. 6. №7. С. 158-162. https://doi.org/10.33619/2414-2948/56/18

Cite as (APA):

Akhunbaev, S., Kutmanova, A., & Gupta, A. (2020). Co-infection of Hepatitis A and Herpes Simplex Virus: A Case Report. *Bulletin of Science and Practice, 6*(7), 158-162. https://doi.org/10.33619/2414-2948/56/18