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FULMINANT HEPATITIS B – A CASE REPORT

Introduction: Acute liver damage has a fulminant clinical course and lead to the patient's death within a period of several days. The disease is not common, but for this reason there are no large clinical studies or relevant statistics on the incidence of this disease. The most widely accepted definition implies coagulation disorder and any degree of encephalopathy in a patient without previous liver disease and a disease duration of less than 26 weeks. This timing of the disease applies to patients with Wilson's disease, autoimmune hepatitis, or vertically acquired viral hepatitis B (1). The most common causes of acute liver damage are toxic damage caused by paracetamol, viral and autoimmune hepatitis. Other toxic substances, herbal and nutritional supplements may be the cause of this disease, too (2). Drugs are the most common causative agents in Western Europe. Hepatitis A, B, C and E viruses are the most common causative agents in developing countries. Cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes viruses (HV) and varicella zoster virus (VZV) are possible causes as well (3).

Among viral fulminant hepatitis, hepatitis B virus (HBV) is the most common (4). There are two clinical forms – acute hepatitis B and reactivation of chronic hepatitis B. The diagnosis of fulminant hepatitis in chronic hepatitis B complicates the possible existence of previous cirrhosis caused by a chronic disease (5). Differentiation of these forms affects the understanding of the clinical course, therapy and prognosis (6).

The aim of this study was to present a severe clinical case of fulminant hepatitis B with a fatal outcome in a patient who was previously treated for bladder malignancy, and who developed acute renal failure during acute liver disease.

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Case report

The woman, aged 63, was admitted due to yellow discoloration of the skin and sclera and decreased diuresis. The symptoms – nausea and weakness started a few days earlier. The urine was darker, and the stool was lighter a couple of days before the reception.

The patient was diagnosed with bladder cancer two years earlier. A radical cystectomy with a ureterocutaneous stoma was performed. She regularly took the prescribed antihypertensive drug for several years. She did not smoke cigarettes or consume alcohol. Socioepidemiological data were not relevant.

The patient was conscious, oriented, afebrile, subicteric sclera and skin, cardiacly compensated, normotensive, with no visible skin changes at the reception. Auscultatory findings on the heart and lungs were normal, pulse 75/ min, blood pressure 135/85 mmHg. The abdomen was above the level of the chest, palpably painful below the right costal arch. The liver and spleen were not palpably enlarged. The ureterostomy was functional.

The diagnosis of acute HBV infection was made by evidence of HBsAg, HBeAg, antiHBc IgM antibody. Our patient had a lot of medical interventions, received blood products, and underwent invasive diagnostic and therapeutic treatments that are risc for HBV transmission. All procedures were performed in health facilities where precise protocols for the prevention of nosocomial infections are applied. HBsAg was determined three times over 12 months and was never detected in serum. This is additional data indicating that there is no reactivation of chronic HBV infection.

The analyzes excluded hepatitis A, C and E viruses (antiHAV IgM, antiHEV IgM, antiHCV), HIV virus (antiHIV At, HIV Ag), EBV, CMV (anti EBV IgM, antiCMV IgM), autoimmune hepatitis (ASMA, ANA, antiLKM1), Wilson's disease (value of copper in serum and urine).

Our patient's laboratory findings are shown in Table 1.

Table 1. Laboratory parameters of patients with fulminant hepatitis B

Laboratory analysis (normal)	Hospital admission	8th day of illness
WBC (3.4–9.7x10^9/L)	11.6	5.3
RBC (3.8–5.7x10^{12}/L)	3.0	4.2
Hb (11.9–17.8 g/dL)	8.7	9.8
PLT (150–450x10^9/L)	179	181
Glycemia (4.1–5.9 mmol/L)	5.5	6.5
Urea (3.2– 8.2 mmol/L)	52.3	51
Creatinine (44.2–97.2 umol/L)	795.9	681
Sodium (137–145 mmol/L)	122	129
Potassium (4.1–5.6 mmol/L)	4.2	3.8
Albumin (35–52 g/L)	30	22

Bilirubin total (5.1–17.0 mmol/L) conjugated (1.0–5.0 μmol/L)	144.5 77	286 112
AST (< 34 U/L)	821	1223
ALT (10 – 49 U/L)	1070	2583
GGT (< 40 U/L)	90	215
C reactive protein (< 10 mg/L)	44	14
aPTT (21–35 s)	31	44
PT (10–12 s)	12.8	18

Laboratory findings indicated an increase in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values, total and conjugated bilirubin, decreased albumin values, and coagulation disorders.

Enterococcus sp. sensitive to cephalosporins was isolated in urine culture. The dose of antibiotics (ceftriaxone) is reduced and adjusted to renal function.

Ultrasound examination revealed suspicion of acute acalculous inflammation of the gallbladder, which was not confirmed by further diagnosis. Computed tomography of the abdomen revealed easily reduced parenchyma of the right kidney and ascites in the abdomen. The description of other organs of the abdominal cavity was within physiological limits, as well as the distal parts of the chest.

X-ray of the lungs did not indicate pathological changes.

Immediately after admission, the patient was placed on a femoral dialysis catheter. Hemodialysis procedure was performed according to the proposal and plan of the nephrologist.

The patient was treated with hepatoprotective, general, symptomatic, antibiotic therapy and antiviral from the fifth day.

The patient becomes somnolent with flapping tremor on the third day after admission. Meningeal signs were negative. No pathological changes were detected by computed tomography of the endocranium. Encephalopathy progressed on the fourth day to the third degree, and on the sixth day to the fourth grade. Tachycardia occurs on the eighth day. On the ninth day of admission, gastrointestinal bleeding occurs, followed by cardiac arrest. There was no positive response to the applied measures and the disease ended in death on the same day.

Discussion

The hepatitis B virus is one of the most important causes of acute liver damage in Eastern European countries. This course of the disease can occur after an acute infection with this virus, or in chronic carriers of the virus in which reactivation occurs. Reactivation of the virus is usually induced by some immunosuppression of the host organism (7). The use of immunomodulators can lead to such immunosuppression

(8). An adult immunocompetent person with acute B viral hepatitis usually recovers spontaneously, while less than 4% of such cases develop acute liver damage (9).

Fulminant liver damage caused by HBV is characterized by the clinical picture of encephalopathy, jaundice and coagulation status disorders. Virus and antibody antigens are detected in the serum as a consequence of the body's immune response (10). An intense immune response can lead to rapid virus removal and acute liver damage. The innate immune response of hepatocytes detects the presence of the virus and inhibits its replication in the early phase of the immune response (11). Cytolottic immune mechanisms develop that induce aggressive elimination of the virus with consequent serious liver damage at a later stage. The result of this immune response is a high titer of antiHBc IgM antibodies. This was noticed by Oketani et al. (12). A high titer of the mentioned antibodies was also present in the serum of our patient.

A US study showed a higher incidence of acute liver damage in infection caused by hepatitis B virus subtype D (13). Our case does not support this conclusion, since we were not able to determine the subtype of the virus.

A change in the levels of endothelial nitric oxide, which leads to changes in vasodilation, an increase in free radicals and their toxic effect on the endothelium of blood vessels is additional explanation for the fulminant course of HBV infection. There is a mass activation of leading caspases. These cysteine proteases have essential roles in apoptosis, necrosis, and inflammation. The consequence is massive cell apoptosis (14).

Laboratory parameters of our patient indicate hepatocyte necrosis (aspartate aminotransferase, alanine aminotransferase) and liver function disorders – synthetic (albumin), cholestatic (bilirubin, gamma-glutamyl transpeptidase) and coagulation (PT, APTT). C-reactive protein was initially elevated, and with disease progression it decreased, consistent with decreased synthetic liver function (15).

Classification of jaundice in relation to the occurrence of encephalopathy implies hyperacute (shorter than 7 days), acute (7-28 days), or subacute (4-26 weeks) course (16).

Our patient had a hyperacute clinical course of the disease. The time between the onset of jaundice and the onset of encephalopathy, according to classifications based on these factors, makes our case of fulminant hepatic insufficiency (17).

Liver transplantation has been described in the vast majority of cases as the only successful therapeutic procedure (18). There was no possibility for such a therapeutic procedure in our case. Lamivudine has been used successfully in patients with acute liver damage caused by HBV, according Yu and and colleagues in their study (19). They detected a significant reduction in viral copies after lamivudine administration. It was a significant predictive factor in the survival of these patients. We started lamivudine therapy on the fifth day of the illness, when the drug became available to us. We cannot report a conclusion about the success of lamivudine in the treatment of the

patient, but also about the possible resistance of HBV to lamivudin, because we have not given it since the beginning of treatment. Earlier guidelines for the treatment of these patients included lamivudine, tenofovir, entecavir. Lamivudine was not omitted from the recommendations in later recommendations, the greatest importance was given to entecavir. (20, 21, 22). Zhao et al conclude that liver transplantation is the definitive therapeutic choice, while nucleoside analogues may improve survival in some patients (23). The recommendation for the use of human B immunoglobulin has also been changed and suspended over time (24, 25). There are also studies that report the success of therapeutic plasma modification in the survival of these patients (26).

Our patient also had acute renal failure (ABI) in addition to fulminant liver damage. Hadem et al analyzed patients with these disorders and observed that most patients with AFL also developed ABI. They conclude that the degree of liver dysfunction does not affect the occurrence of ABI. The correlation between AST and ABI stage indicates a hemodynamic compromise as a result of reduced venous flow, which can cause renal dysfunction (27). It has been shown that in acute liver damage the level of angiopoietin 2 is increased, which causes multiorgan damage. It is not completely clear how this enzyme leads to kidney damage (28).

The diagnostic procedures we applied to the patient did not indicate the occurrence of metastatic changes as a consequence of previous malignant bladder disease. It can be assumed that radical cystectomy led to a weakening of the immune response. There were no data that before and after this surgery, attention was paid to the immunonutrients recommended for these patients (29).

Conclusion

Acute liver damage caused by the hepatitis B virus is a serious disease that requires treatment in the intensive care unit and the transfer of the patient to the transplant center as soon as possible. Acute renal failure, as a possible complication, significantly complicates the clinical picture and prognosis. In some cases it is necessary to provide hemodialysis.

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