Slađana Pavić[1], Ljubisav Maričić[2], Mira Vujović[3], Ivan Janković[4], Aleksandra Pavić[5]

FULMINANTNI HEPATITIS B – PRIKAZ SLUČAJA

Sažetak

Uvod: Fulminantni hepatitis je teško akutno oboljenje jetre. Nastaje usled masovne nekroze hepatocita. Bolest tokom nekoliko dana progredira do letalnog ishoda. Uzročnici ovog oboljenja su najčešće toksične materije, autoimuni i virusni hepatitisi.

Cilj istraživanja je bio da prikažemo letalni slučaj fulminantnog hepatitisa uzrokovanog B virusom hepatitisa kod pacijentkinje sa lečenim karcinomom mokraćne bešike.

Prikaz slučaja

Pacijentkinja uzrasta 63 godine primljena je na lečenje zbog osećanja malaksalosti, mučnine i smanjene diureze. Dve godine ranije je imala operaciju uklanjanja mokraćne bešike zahvaćene malignim procesom. Pri prijemu je bila subikterična, urednog auskultatornog nalaza na srcu i plućima. Abdomen je bio palpatorno bolno osetljiv ispod desnog rebarnog luka, bez organomegalije. Ureterostoma je bila funkcionalna. Dijagnoza akutne HBV infekcije postavljena je na osnovu dokaza HBsAg, HBeAg, antiHBc IgM titra antitela. Laboratorijski nalazi su ukazali na povećanje vrednosti transaminaza, uree i kreatinina, ukupnog i konjugovanog bilirubina, snižene vrednosti albumina i poremećaj koagulacije. Lečena je hepatoprotektivnom terapijom, antibioticima i antivirusnom terapijom. Primenjena je i hemodijaliza. Od trećeg dana lečenja dolazi do pogoršanja opšteg stanja i pojave encefalopatije, koja je progredirala narednih dana. Bolest se pogoršala gastrointestinalnim krvarenjem i kardiološkim poremećajima i devetog dana završila smrtnim ishodom.

[1] Slađana Pavić, Odeljenje za infektivne i tropske bolesti Opšte bolnice Užice, Užice, Srbija, sladjanapj@gmail.com

[2] Odeljenje urologije Opšte bolnice Užice, Užice, Srbija

[3] Odeljenje nefrologije Opšte bolnice Užice, Užice, Srbija

[4] Odsek za radiologiju Opšte bolnice Užice, Užice, Srbija

[5] Medicinski fakultet Univerziteta u Beogradu, Beograd, Srbija

Zaključak: Fulminantno oštećenje jetre uzrokovano B virusom hepatitisa predstavlja teško oboljenje koje može komplikovati pojava akutne bubrežne insuficijencije. Prognoza bolesti je često nepovoljna, pa optimalno lečenje zahteva transplantaciju jetre.

Ključne reči: fulminantni hepatitis, hepatitis B virus, akutna bubrežna insuficijencija, letalni ishod

Abstract

Introduction: Fulminant hepatitis is a severe acute liver disease. It occurs due to massive necrosis of hepatocytes. The disease progresses to lethal outcome within a few days. The most common causes of this disease are toxic substances, autoimmune and viral hepatitis.

The aim of the study was to present a lethal case of fulminant hepatitis caused by hepatitis B virus in a patient with treated bladder cancer.

Case Outline: A 63-year-old patient was admitted for treatment due to weakness, nausea and decreased diuresis. She had surgery to remove her bladder, which was affected by a malignant process, two years earlier. On admission, she had a subicteric, orderly auscultatory finding. The abdomen was palpably painful below the right costal arch, without organomegaly. The ureterostomy was functional. The diagnosis of acute HBV infection was made by evidence of HBsAg, HBeAg and antiHBc IgM antibody titer. Laboratory findings indicated an increase in transaminases, urea, creatinine, total and conjugated bilirubin, decreased albumin values and coagulation disorders. The patient was treated with hepatoprotective therapy, antibiotics and antiviral therapy. Hemodialysis was performed as needed. Encephalopathy developed on the third day with further progression.The disease progressed with gastrointestinal bleeding and cardiac disorders and ended in death on the ninth day.

Conclusion: Fulminant liver damage caused by hepatitis B virus is a severe disease that can be complicated by acute renal failure. The prognosis of the disease is often unfavorable, so optimal treatment requires a liver transplant.

Key words: fulminant hepatitis, hepatitis B virus, acute renal failure, lethal outcome

Uvod

Akutno oštećenje jetre može imati fulminantni klinički tok i u periodu od nekoliko dana dovesti do smrtnog ishoda pacijenta. Oboljenje nije često, pa ne postoje ni velike kliničke studije, niti relevantna statistika o ovom oboljenju. Najšire prihvaćena definicija podrazumeva poremećaj koagulacije i bilo kog stepena encefalopatije kod

pacijenta bez prethodnog oboljenja jetre i trajanjem bolesti kraćem od 26 sedmica. Ova vremenska odrednica trajanja bolesti primenjuje se na obolele od Vilsonove bolesti, autoimunog hepatitisa ili vertikalno stečenog virusnog hepatitisa B (1). Uzroci nastanka akutnog oštećenja jetre najčešće su toksično oštećenje uzrokovano paracetamolom, virusni i autoimuni hepatitis. Uzročnici mogu biti i druge toksične materije, biljni i nutritivni suplementi (2). Dok su u zemljama zapadne Evrope najčešći uzročnici lekovi, u zemljama u razvoju su virusi hepatitisa A, B, C i E, ali i citomegalo virus (CMV), Epstein-Barr virus (EBV), herpes virusi (HV) i varicela zoster virus (VZV) (3).

Među virusnim fulminantnim hepatitisima najčešći je hepatitis uzrokovan hepatitis B virusom (HBV) (4). Postoje dve kliničke forme – akutni hepatitis B i reaktivacija hroničnog hepatitisa B. Postavljanje dijagnoze fulminantnog hepatitisa kod hroničnog hepatitisa B otežava moguće postojanje prethodne ciroze uzrokovane hroničnim oboljenjem (5). Razlikovanje ovih formi utiče na razumevanje kliničkog toka, terapiju i prognozu (6).

Cilj rada bio je da prikažemo težak klinički slučaj fulminantnog hepatitisa B sa smrtnih ishodom kod pacijentkinje koja je prethodno lečena zbog malignog oboljenja mokraćne bešike, a kod koje je tokom akutnog oboljenja jetre nastala i akutna bubrežna insuficijencija.

Prikaz slučaja

Ženska osoba, u starosnoj dobi od 63 godine, primljena je na lečenje zbog žute prebojenosti kože i sklera i smanjene diureze. Tegobe su počele nekoliko dana ranije, u smislu mučnine i malaksalosti. Par dana pre prijema primetila je zamućenje mokraće i svetliju boju stolice.

Dve godine ranije pacijentkinji je dijagnostikovan karcinom mokraćne bešike, učinjena radikalna cistektomija sa ureterokutanom stomom. Nekoliko godina unazad redovno je uzimala prepisani antihipertenzivni lek. Nije pušila cigarete, niti konzumirala alkohol. Socioepidemiološki podaci nisu bili od značaja.

Pri prijemu, pacijentkinja je bila svesna, orijentisana, afebrilna, subikteričnih sklera i kože, kardijalno kompenzovana, normotenzivna, bez vidljivih promena na koži. Auskultatorni nalaz na srcu i plućima je bio uredan, puls 75/min, krvni pritisak 135/85 mmHg. Abdomen je bio iznad ravni grudnog koša, mek, palpatorno bolno osetljiv ispod desnog rebarnog luka. Jetra i slezina palpatorno nisu bile uvećane. Ureterostoma je bila funkcionalna.

Dijagnoza akutne HBV infekcije postavljena je na osnovu dokaza HBsAg, HBeAg i antiHBc IgM titra antitela. Činjenica je da je naša pacijentkinja imala dosta medicinskih intervencija, primala krvne preparate, bila podvrgnuta invazivnim dijagnostičkim i terapeutskim tretmanima koji predstavljaju rizik za mogući prenos HBV. Sve procedure su sprovođene u zdravstvenim ustanovama u kojima se primenjuju

precizni protokoli za prevenciju bolničkih infekcija. Dodatni podatak koji ukazuje da se ne radi o reaktivaciji hronične HBV infekcije jesu prethodno rađene, tri puta tokom 12 meseci, analize HBsAg koji nijednom nije detektovan u serumu pacijentkinje.

Diferencijalno dijagnostički isključeni su virusi hepatitisa A, C i E (antiHAV IgM, antiHEV IgM, antiHCV), HIV virus (antiHIV At, HIV Ag), EBV, CMV (anti EBV IgM, antiCMV IgM), autoimuni hepatitis (ASMA, ANA, antiLKM1), Vilsonova bolest (vrednost bakra u serumu i urinu).

U tabeli 1. prikazani su laboratorijski nalazi naše pacijentkinje.

Tabela 1. Laboratorijski parametri pacijentkinje sa fulminantnim hepatitisom B

Laboratorijska analiza (normalna vrednost)	Pri prijemu	8. dana bolesti
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
Glikemija (4.1–5.9 mmol/L)	5.5	6.5
Urea (3.2–8.2 mmol/L)	52.3	36
Kreatinin (44.2–97.2 umol/L)	795.9	581
Na^+ (137–145 mmol/L)	122	129
K^+ (4.1–5.6 mmol/L)	4.2	3.8
Albumini (35–52 g/L)	30	22
Bilirubin ukupni (5.1–17.0 mmol/L) direktni (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 reaktivni protein (< 10 mg/L)	44	14
aPTT (21–35 s)	31	44
PT (10–12 s)	12.8	18

Laboratorijski nalazi su ukazali na povećanje vrednosti aspartat-aminotransferaze (AST) i alanin-aminotransferaze (ALT), ukupnog i konjugovanog bilirubina, snižene vrednosti albumina i poremećaj koagulacije.

U urinokulturi je izolovan *Enterococcus sp*. osetljiv na cefalosporinski antibiotik (ceftriaxone) kojim je lečena. Doza antibiotika je redukovana i prilagođena bubrežnoj funkciji.

Ultrazvučnim pregledom je postavljena sumnja na akutnu akalkuloznu upalu žučne kesice, što nije potvrđeno daljom dijagnostikom. Kompjuterizovanom tomografijom abdomena dijagnostikovan je lako redukovan parenhim desnog bubrega i slobodna tečnost u abdomenu. Opis ostalih organa trbušne duplje, kao i distalnih delova grudnog koša, bio je u fiziološkim granicama.

Radiografski snimak pluća nije ukazao na patološke promene.

Pacijentkinji je odmah po prijemu plasiran femoralni dijalizni kateter i sprovođena procedura hemodijalize, po predlogu i planu nefrologa. Odmah po prijemu započeta je hepatoprotektivna, kao i ostala opšta, simptomatska i već pomenuta antibiotska terapija, a od petog dana i antivirusna terapija.

Trećeg dana lečenja pacijentkinja postaje somnolentna, pojavljuje se flapping tremor, uz negativne meningealne znakove. Kompjuterizovanom tomografijom endokranijuma nisu viđene patološke promene. Četvrtog dana lečenja nastaje encefalopatija III stepena, uz dalju progresiju do IV stepena, koji je dijagnostikovan šestog dana lečenja. Od petog dana nastaje tahikardija, a devetog dana bolesti dolazi do gastrointestinalnog krvarenja, a zatim i srčanog zastoja. Nije bilo pozitivnog odgovora na primenjene mere i bolest se istog dana završila letalnim ishodom.

Diskusija

Virus hepatitisa B jedan je od najvažnijih uzroka nastanka akutnog oštećenja jetre u zemljama istočne Evrope. Ovakav tok bolesti može nastati nakon akutne infekcije ovim virusom, ili kod hroničnih nosilaca virusa kod kojih nastane reaktivacija. Ponovnu aktivaciju virusa obično indukuje neka imunosupresija organizma domaćina (7). Do takve imunosupresije može dovesti primena imunomodulatora (8). Odrasla imunokompetentna osoba sa akutnim B virusnim hepatitisom obično se oporavi spontano, dok manje od 4% takvih slučajeva razvije akutno oštećenje jetre (9).

Fulminantno oštećenje jetre uzrokovano HBV-om karakteriše klinička slika encefalopatije, ikterusa i poremećaja koagulacionog statusa. U serumu se detektuju antigeni virusa i antitela kao posledica imunološkog odgovora organizma (10). Intenzivan imunološki odgovor može dovesti do brzog uklanjanja virusa i nastanka akutnog oštećenja jetre. U ranoj fazi imunološkog odgovora na prisustvo virusa urođeni imunološki odgovor hepatocita otkriva prisustvo virusa i inhibira njegovu replikaciju (11). U kasnijoj fazi nastaju citolotički imuni mehanizmi koji indukuju agresivnu eliminaciju virusa uz posledično ozbiljno oštećenje jetre. Rezultat ovakvog imunog odgovora je visok titar antiHBc IgM antitela, što su u svom istraživanju uočili Oketani i saradnici (12). U serumu naše pacijentkinje takođe je bio prisutan visok titar pomenutih antitela.

Američka studija je pokazala veću učestalost akutnog oštećenja jetre kod infekcije uzrokovane podtipom D hepatitis B virusa (13). Naš slučaj ne podržava navedeni zaključak, s obzirom na to da nismo imali mogućnost da odredimo podtip virusa.

Dodatno objašnjenje za fulminantni tok HBV infekcije jeste u promeni nivoa endotelnog azotoksida, što dovodi do izmene vazodilatacije, povećanja slobodnih radikala i njihovo toksično dejstvo na endotel krvnih sudova. Pored toga, dolazi do masovne aktivacije vodećih kaspaza. Ove cistenske proteaze imaju esencijalne uloge u apoptozi, nekrozi, u inflamaciji. Posledično nastaje masivna apoptoza ćelija (14).

Laboratorijski parametri naše pacijentkinje ukazuju na nekrozu hepatocita (aspartat aminotransferaza, alanin aminotransferaza) i poremećaj jetrenih funkcija – sintetske (albumini), holestatske (bilirubin, gama-glutamil transpeptidaza) i koagulacione (PT, APTT). C-reaktivni protein je u početku bio povišen, a sa progresijom bolesti je došlo do njegovog smanjenja, u skladu sa smanjenom sintetskom funkcijom jetre (15).

Klasifikacija pojave žutice u odnosu na nastanak encefalopatije podrazumeva hiperakutni (kraće od 7 dana), akutni (7–28 dana) ili subakutni (4–26 sedmica) tok (16).

Naša pacijentkinja je imala hiperakutni klinički tok bolesti. Vreme između pojave ikterusa i nastanka encefalopatije, prema klasifikacijama zasnovanim na tim faktorima, čini naš slučaj insuficijencijom jetre fulminantnog toka (17).

Transplantacija jetre je u velikoj većini slučajeva opisana kao jedini uspešan terapeutski postupak (18). U našem slučaju nije bilo mogućnosti za hitnu transplantaciju jetre. Yu i saradnici u svom istraživanju iznose zaključak o uspešnoj primeni lamivudina kod pacijenata sa akutnim oštećenjem jetre uzrokovanim HBV-om (19). Detektovali su značajno smanjenje virusnih kopija nakon primene lamivudina i označili ga kao značajan prediktivni faktor preživljavanja ovih pacijenata. Mi smo terapiju lamivudinom započeli petog dana bolesti, kada nam je lek postao dostupan. S obzirom na to da lek nije uključen ranije, ne možemo izvesti zaključak o uspešnosti lamivudina u lečenju pacijenta, ali ni o mogućoj rezistenciji HBV-a na lamivudin. Ranije smernice za lečenje ovih bolesnika uključivale su lamivudin, tenofovir, entecavir, dok je kasnije lamivudin izostavljen iz preporuka, a najveći značaj je dat entecaviru (20, 21, 22). Zhao i saradnici iznose zaključak da je transplantacija jetre definitivan terapeutski izbor, dok nukleozidni analozi mogu poboljšati preživljavanje kod nekih bolesnika (23). Preporuka o primeni humanog B imunoglobulina vremenom je, takođe, promenjena i suspendovana (24, 25). Postoje i studije koje navode uspešnost terapijske izmene plazme u preživljavanju ovih pacijenata (26).

Naša bolesnica je, pored fulminantnog oštećenja jetre, imala i akutnu bubrežnu insuficijenciju (ABI). Hadem i saradnici su analizirali pacijente sa ovim poremećajima i uočili da je većina bolesnika sa AFL razvila i ABI. Tražeći objašnjenje, zaključuju da stepen disfunkcije jetre ne utiče na pojavu ABI. Korelacija AST i stadijuma ABI ukazuje na hemodinamski kompromis kao rezultat smanjenja venskog protoka, što može uzrokovati disfunkciju bubrega (27). Pokazano je da je kod akutnog oštećenja jetre povišen nivo angiopoetina 2, koji izaziva multiorganska oštećenja, ali nije do kraja razjašnjeno u kojoj meri ovaj enzim dovodi do oštećenja bubrega (28).

Dijagnostički postupci koje smo primenili kod pacijentkinje nisu ukazali na postojanje metastatskih promena kao posledice ranije maligne bolesti mokraćne bešike. Može se pretpostaviti da je radikalna cistektomija doprinela slabljenju odbrambenog sistema njenog organizma. Nije bilo podataka da je pre i nakon ovog hirurškog zahvata pažnja posvećena imunohranjivim sastojcima koji se ovim pacijentima preporučuju (29).

Zaključak

Akutno oštećenje jetre uzrokovano B virusom hepatitisa predstavlja teško oboljenje koje zahteva lečenje u jedinici intenzivne nege i što ranije prebacivanje pacijenta u transplantacioni centar. Akutna bubrežna insuficijencija, kao moguća komplikacija, značajno otežava kliničku sliku i prognozu i u nekim slučajevima je neophodno obezbediti hemodijalizu.

Sladjana Pavić[1], Ljubisav Maričić[2], Mira Vujović[3], Ivan Janković[4], Aleksandra Pavić[5]

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.

[1] Sladjana Pavić, Odeljenje za infektivne i tropske bolesti Opšte bolnice Užice, Užice, Srbija, sladjanapj@gmail.com

[2] Odeljenje urologije Opšte bolnice Užice, Užice, Srbija

[3] Odeljenje nefrologije Opšte bolnice Užice, Užice, Srbija

[4] Odsek za radiologiju Opšte bolnice Užice, Užice, Srbija

[5] Medicinski fakultet Univerziteta u Beogradu, Beograd, Srbija

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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