

Diabetes Mellitus Due to Liver Cirrhosis in 33-Year-Old Female

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ABSTRACT

Impaired glucose metabolism can occur in patient with chronic liver disease, either it is impaired glucose tolerance or diabetes mellitus (DM). DM due to liver cirrhosis is known as hepatogenous diabetes (HD). HD is different from type 2 DM in clinical signs and management.

A 33-year-old female came with chief complaint of fatigue since three days before admission. Patient also complained of nausea, vomiting, and increased abdominal circumference since one year ago. Patient was diagnosed with DM two months ago. From physical examination, anemic and ascites without signs of cirrhosis were obtained. Laboratory test showed mild anemia with hemoglobin levels 6.5 g/dL, elevated serum bilirubin and liver enzymes, decreased serum albumin, prolonged prothrombin time and elevated random blood glucose. Serologic test showed chronic hepatitis B with HBV DNA 1.61×10^4 copy/mL. The abdominal ultrasound result showed liver cirrhosis with ascites.

The patient was diagnosed with hepatogenous diabetes in liver cirrhosis due to chronic hepatitis B infection and anemia of chronic disease. The management of this patient was quite complex especially in administration of oral antidiabetic agent which could affect the liver function.

Keywords: *hepatogenous diabetes, liver cirrhosis, diabetes mellitus, chronic hepatitis B infection*

ABSTRAK

Pada penderita penyakit hati menahun dapat terjadi gangguan metabolisme gula, yaitu dari toleransi glukosa terganggu sampai diabetes melitus (DM). DM yang terjadi akibat komplikasi dari sirosis hati dikenal sebagai hepatogeneous diabetes (HD) atau DM tipe sirosis. DM tipe sirosis berbeda dengan DM tipe 2 baik dalam gejala klinis maupun tatalaksananya.

Seorang perempuan usia 33 tahun datang dengan keluhan utama badan lemas sejak tiga hari sebelum masuk rumah sakit. Pasien juga mengeluh mual, muntah, dan pembesaran perut sejak satu tahun yang lalu. Pasien diketahui menderita DM sejak dua bulan yang lalu. Pemeriksaan fisik menunjukkan keadaan anemis dan adanya asites tanpa disertai tanda-tanda sirosis. Pemeriksaan laboratorium menunjukkan anemia ringan dengan kadar hemoglobin 6,5 g/dL, peningkatan serum bilirubin dan enzim hati, penurunan kadar albumin, pemanjangan protrombin time dan peningkatan gula darah sewaktu. Tes serologis menunjukkan hepatitis B kronik dengan HBV DNA 1.61×10^4 copy/mL. Kesan sirosis hati dengan asites didapatkan pada hasil ultrasonografi abdomen.

Diagnosa kerja pasien ini adalah DM tipe sirosis pada sirosis hati akibat hepatitis B kronik dan anemia akibat penyakit kronik. Penatalaksanaan DM tipe sirosis cukup kompleks terutama dalam hal pemberian obat antidiabetes oral karena akan mempengaruhi fungsi hati.

Kata kunci: *DM tipe sirosis, sirosis hati, diabetes melitus, infeksi hepatitis B kronik*

INTRODUCTION

Hepatitis B is an infection of the liver caused by hepatitis B virus (HBV). Most adults usually suffer from hepatitis B infection and permanently recover. For some patients, predominantly in early age patient such as newborn or children, hepatitis B virus will remain in their body and may even progress into chronic liver infection.¹ Chronic hepatitis B infection can develop from asymptomatic, symptomatic, liver cirrhosis, or hepatocellular carcinoma.²

About 20-40% chronic liver disease will progress into cirrhosis in approximately 15 years later.³ Patient with cirrhosis can suffer resistance of insulin, from impaired glucose tolerance to diabetes mellitus (DM).^{4,5} DM originated from liver cirrhosis is known as hepatogenous diabetes (HD). HD is more likely in patients without risk factors for type 2 DM and the appearance of new onset hyperglycemia in the setting of cirrhosis.⁶ However there has been no descriptive studies done to determine the prevalence of HD.

Clinical progression of HD is different from that of type 2 DM (T2DM), where HD is less frequently associated with microangiopathy.⁷ There is no definitive test to differentiate T2DM with liver dysfunction from HD.⁴ Study by Kim et al suggested the use of 2 hours post prandial (2hPP) glucose/fasting plasma glucose (FPG) and fasting insulin level which are higher in HD ($p < 0.05$).⁸ DM in liver cirrhosis patient can occur subclinically because the fasting blood glucose (FBG) level in this patient is normal. In this case, patient should take the glucose tolerance test to detect the impaired glucose tolerance.⁷

CASE ILLUSTRATION

A 33-year-old female came with chief complaint of fatigue since 3 days before admission. Patient also complained of nausea, vomiting, and increased abdominal circumference since one year ago. Patient was diagnosed as DM two months ago by a primary care physician on the bases of polydipsia, polyphagia and polyuria with elevated capillary blood glucose (CBG) of 325 mg/dL. She was given metformin tablet 500mg twice daily, however was not compliant to treatment. Family history were unremarkable for hepatitis B and diabetes. Physical examination showed anemic and ascites without stigmata of cirrhosis. Laboratory test result showed normocytic normochromic anemia with hemoglobin level 6.5 g/dL, mild thrombocytopenia with platelet count 185,000/L, low serum iron 7 mg/dL, normal total iron binding capacity 255 µg/dL,

normal ferritin 102.38 mg/dL, low serum albumin 2.97 g/dL, mild increasing of liver enzymes (AST 60 u/L and ALT 64 u/L), hyperbilirubinemia (total, indirect and direct bilirubin of 1.8 mg/dL, 1.1 mg/dL and 0.7 respectively), prolonged prothrombin time (PT) 20.3 seconds, INR of 1.83, creatinine serum 0.5 mg/dL and elevated random blood glucose (RBG) 517 mg/dL. Serologic test result showed HbsAg positive, HbeAg negative, and HBV DNA 1.61×10^4 copy/mL. The abdominal ultrasound result showed liver cirrhosis with moderate ascites.

Based on clinical findings and laboratory results, patient was diagnosed with hepatogenous diabetes in liver cirrhosis child B due to chronic hepatitis B infection and anemia on chronic disease. The patient was treated using restriction of salt and fluids, protein 40 g/dL/day, short-acting insulin 3x12 U intravenously (IV), long-acting insulin 10 U IV at bed time, metformin tablet 500 mg thrice daily per oral, spironolactone tablet 100 mg twice daily per oral, lamivudine tablet 100 mg once daily per oral. After one week therapy, ascites was reduced and hemoglobin level, blood glucose, liver enzymes were improved.



Figure 1. Abdominal ultrasonography showed right liver lobe cirrhosis with ascites

DISCUSSION

Virology test results showed HBsAg positive, HBeAg negative, HBV DNA 1.61×10^4 copy/mL. There was no doubt that liver cirrhosis in this patient was the result of hepatitis B chronic infection (negative HBeAg). Progression of liver cirrhosis could be slowed down by giving nucleoside analog such as lamivudine. Association for the Study of Liver Diseases (AASLD) guideline practice recommended antiviral therapy for the patient with HBV DNA $> 2,000$ IU/mL or $> 10^4$ copy/mL. Treatment recommendation for decompensated hepatitis B liver cirrhosis is antiviral

drugs. Lamivudine is the first oral agent that is considered safe and effective in treating prolonged viremia in liver cirrhosis.^{2,10}

In this case, this patient had a history of diabetes since 2 months ago. Although it was rare for 33 years old patient to have type 2 DM. All of these things helped to make sure the diagnosis was diabetic type cirrhosis or hepatogenous diabetes. As the main pathogenesis is insulin resistance, patient was treated by insulin to regulate the blood glucose and metformin to reduce the resistance of insulin. Treating HD can be complicated because the liver dysfunction can increase response to the treatment by using standard dosage and higher risk of side effect if the drugs are metabolized in liver. For those reasons, many clinicians use insulin as a first line agent in treating diabetic patient with liver cirrhosis.⁴

Ascites occurred because of accumulation of fluid in peritoneal cavity as the results of portal hypertension, hypoalbuminemia, and hyperaldosteronemia. So, the ascites was treated by antialdosteron. Indication for albumin use in these cirrhotic patient are spontaneous bacterial peritonitis, hepatorenal syndrome, large volume of paracentesis, albumin level less than 2.5 g/dL with complication.¹¹

Viral infection, either acute or chronic, will cause anemia of chronic disease. Three major pathophysiology of anemia are impaired iron homeostasis, ineffective erythropoiesis, reduction of erythropoietin response. The normal or raising of ferritin level show increasing iron level in red blood cells because of immune activation. From the pathologic finding about chronic anemia disease, treatment can be done through the cure of main disease, use of erythropoietin, or blood transfusion.⁹

Lamivudine, spironolactone, metformin, and insulin could control cirrhosis due to hepatitis B, hepatogenous diabetes and chronic anemia.

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