[症例報告]A case of subacute type of fulminant hepatic failure treatedwith plasma exchange and hemodiafiltration

A case of subacute type of fulminant hepatic failure treated with plasma exchange and hemodiafiltration

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ABSTRACT

Fulminant hepatic failure (FHF) is known to have a poor prognosis, particularly in patients with a more gradual onset of hepatic encephalopathy (called subacute type). The presence of coagulopathy and the grade of hepatic coma are associated with a worsened prognosis. A 47 year-old woman with subacute type FHF was treated with a combination therapy of plasma exchange and hemodiafiltration, using a high-performance polymethyl metacrylate membrane. After this treatment, she regained consciousness and was stable in the lower hepatic coma grade for a long period (294 days). This survival period was longer than those of 340 patients with FHF who were treated with PE alone, and eventually died of FHF between 1983 and 1988 in Japan. *Ryukyu Med. J., 18(1, 2)37~40, 1998*

Key words: fulminant hepatic failure, plasma exchange, hemodiafiltration, hepatic encephalopathy

INTRODUCTION

Fulminant hepatic failure (FHF) has a very poor prognosis. The survival rate of FHF is reported to be 16.2% in Japan.[1] The prognosis is known to be poorer in the subacute type-FHF than in the acute type-FHF[2]. In Europe and the United States, patients with FHF are considered as candidates for liver transplantation. However, the consensus on liver transplantation has not been established in Japan as yet. Therefore, the main option in the treatment of FHF is artificial liver support, such as plasma exchange (PE). PE is a well-known technique of administering a large volume of fresh frozen plasma to treat bleeding tendency, without causing volume overload. However, this method is insufficient for controlling hepatic encephalopathy[3]. Recently, some investigators have reported that repeated hemodiafiltration (HDF) is useful for improving encephalopathy[1,4-6]. We treated a patient with subacute type-FHF with the combination therapy of PE and HDF, and the therapy prolonged survival.

CASE REPORT

A 47-year-old woman visited the Okinawa Red Cross hospital complaining of general fatigue and high fever, on March 28, 1991. She was initially diagnosed with common cold. However, 12 days later, jaundice developed, and she visited the hospital again, and was diagnosed with acute hepatitis. Thereafter, her laboratory data worsened rapidly, (total bilirubin 19mg/dl, prothrombin time 14%), and she was referred to our hospital.

She had no history of blood transfusion, acupuncture, or surgery. She was not a drinker, and none of her family members had liver diseases.

She was alert on admission. Physical examination revealed icteric sclera and slightly anemic palpebra and a distended abdomen with fluctuation. The liver, spleen and superficial lymph nodes were not palpable.

Ultrasound examination showed a severely atrophic liver and massive ascites, and no dilatation in the intrahepatic bile ducts.

Liver biochemical tests revealed albumin 2.4g/dl, total serum bilirubin 29.4mg/dl, asparate transaminase 73IU/l,

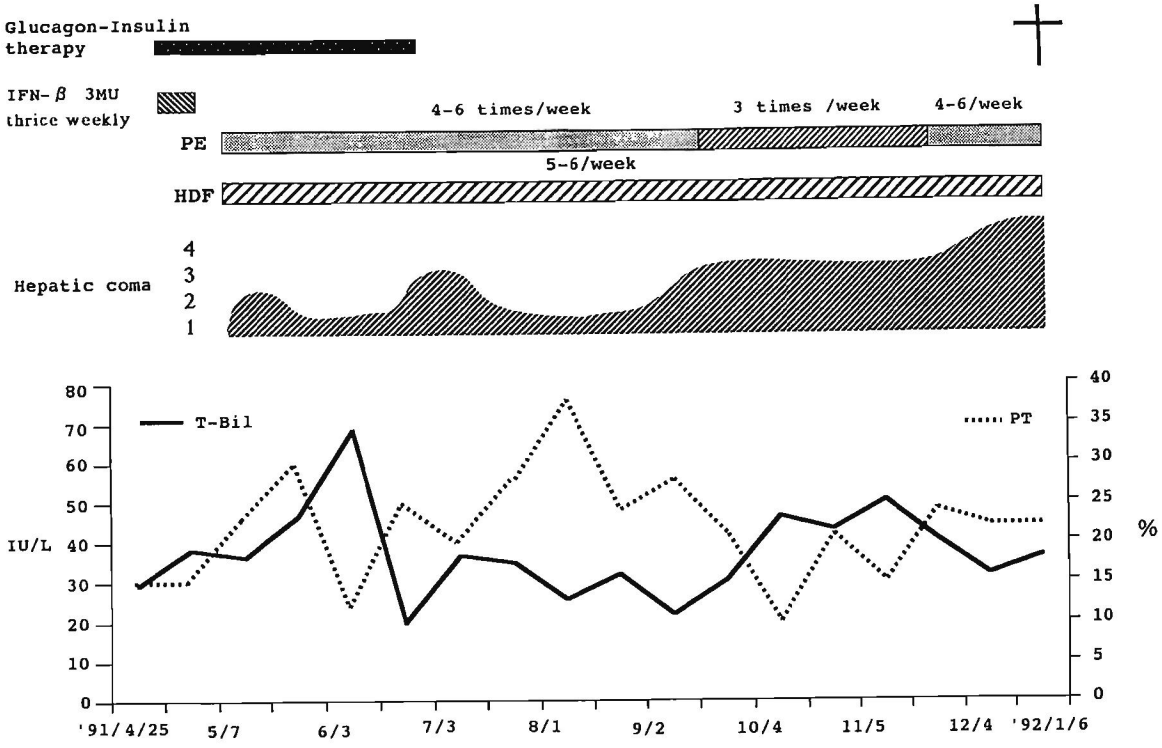

Fig. 1 Clinical course of the patient.
IFN; interferon, PE; plasma exchage, HDF; hemodiafiltration, T-Bil; total bilirubin, PT; prothrombin time, MU; million units.

and alanine transaminase 831U/l. The prothrombin time prolonged markedly (14%). Several hepatitis virus markers were negative. i.e. immunoglobulin M class-antibody to hepatitis A, hepatitis B surface antigen, immunoglobulin M class-antibody to hepatitis B core antigen, antibody to hepatitis C virus (HCV), HCV-RNA, and GB virus-C/Hepatitis G virus RNA. Antibodies to cytomegalovirus and herpes simplex virus were positive, but no significant elevation in antibody titers to these two viruses was noted during the follow-up period. Antinuclear and antimitochondrial antibodies were also negative.

After admission, she underwent glucagon-insulin therapy (Fig. 1).

The blood sample at admission was sent to another laboratory for HCV-RNA examination. Until the result of HCV-RNA was obtained, she was treated with three million units of interferon(IFN)-β thrice weekly. Two weeks later, because of negative HCV-RNA result, IFN therapy was discontinued.

On May 21, 1991, 55 days after onset, she showed Grade 2 hepatic coma (drowsiness, inappropriate behavior)[7] with flapping tremor. On the basis of the clinical course, she was diagnosed with subacute type-FHF.

The combination therapy of PE and HDF was started on May 23, 1991. PE and HDF were performed 4-6 times per week and 5-6 times per week, respectively (Fig. 1). A double-lumen catheter was inserted in the femoral vein. Fresh frozen plasma (3.2l) was given at each session. HDF using polymethyl metacrylate membrane (PMMA) filters ('Filtryzer BK-1.6p' TORAY · Medical, Tokyo, Japan) was continuously applied. Nafamostat mesilate was given as an anticoagulant during HDF.

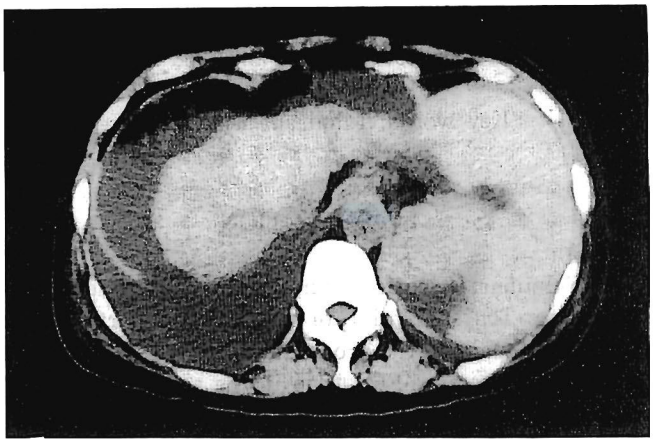

Fig. 2 Abdominal CT showed a severely atrophic liver, ascites, pleural effusion and splenomegaly (72nd days after onset of the disease).

At the start of the combination therapy, her consciousness level was Grade 2 hepatic coma. Two days after starting the treatment, her consciousness level recovered to Grade 1 hepatic coma (confused, alerted mood or behavior)[7]. She maintained Grade 1 consciousness level

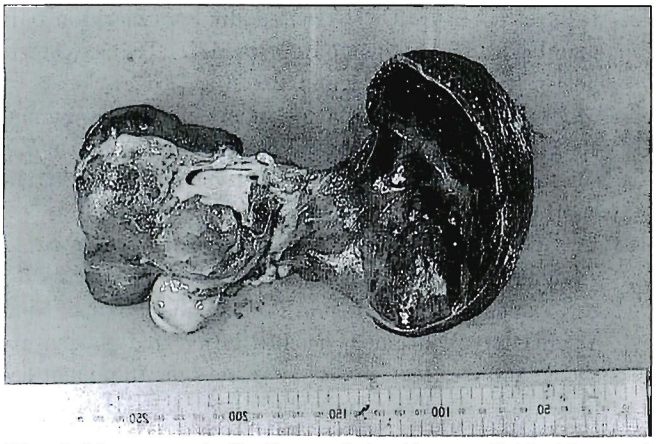

Fig. 3 Macroscopic findings of the liver, gall bladder and spleen at autopsy. Severely atrophic liver and markedly enlarged spleen are shown.

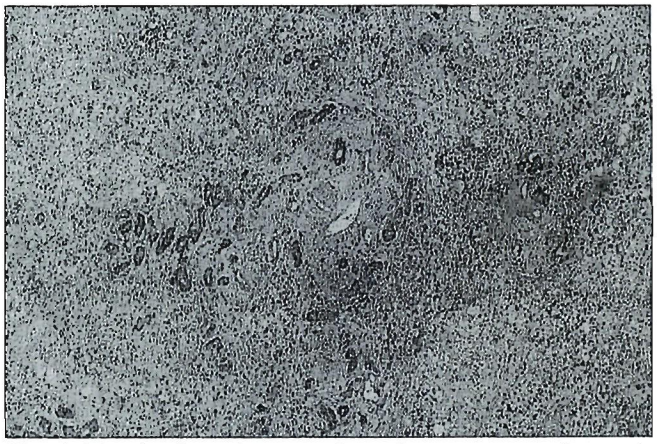

Fig. 4 Massive hepatic necrosis and no regenerative nodule were shown in microscopic examination (HE, X20).

during the next five months of the treatment and was able to communicate with her family.

On June 7, 1991, 72 days after onset of the disease, computed tomography showed a severely atrophic liver and splenomegaly. (Fig. 2)

Her consciousness level shifted to Grade 3 (marked confusion)[7] on September 2, 1991. On December 4, 1991, her consciousness level became Grade 4 (coma)[7], and the combination therapy did not improve her consciousness level any more. She died of liver failure on January 6, 1992. The survival duration was 294 days.

Autopsy showed an atrophic liver with a weight of 640g (Fig. 3). Histological diagnosis of the liver was massive hepatic necrosis with fibrosis (Fig.4).

DISCUSSION

The purpose of PE is to improve the coagulation defect and to remove the toxic substances inducing hepatic coma from circulation. Although PE is effective therapy for coagulopathy, hepatic coma is usually not improved by PE alone. Yosiba et al. had reported that middle-sized molecular substances were strongly related to hepatic coma. These substances are not sufficiently removed by PE alone[3].

Opolon et al. used a polyacrylonitrile (PAN) membrane to remove the middle-size molecular substances for the treatment of hepatic coma[8], and reported the recovery rate of hepatic coma to be 61.5%. Recently, some investigators found that an artificial liver support system, consisting of PE in combination with HDF, was effective in removing the middle-sized molecular substances[1,5,6]. Yoshiba et. al. reported that 65 (97.0%) of 67 patients with fulminant hepatic failure treated with the combination therapy gained normal consciousness, and 82.1% of those continued to be alert during the treatment[4]. Furthermore, another beneficial effect of HDF has recently been reported. This procedure was found to be useful in removing inflammatory cytokines (interleukin-6, tumor necrosis factor-alpha)[9].

The present patient received the combination therapy of PE and HDF using a PMMA membrane, and her consciousness level recovered for an extended period. She survived for 294 days from the onset of the disease. Takahashi et al. reported that the longest survival duration was 217 days among 340 patients with fulminant hepatitis, who were treated with PE alone, and who had eventually died between 1983 and 1988 in Japan[5]. From our experience, together with other observations in the literature[4,6,10], the combination therapy of PE and HDF might be more effective than PE alone.

Despite a clinically evident condition with severe atrophic liver disease, the patient survived longer period than expected. The liver was only 640g at autopsy. This suggests that the combination therapy was not enough to induce liver cell regeneration. Certainly, it is expensive and reqires paramedical support. However, the therapy may prolong the life of patients with FHF, therefore it can be performed.

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