

Hepatitis A Virus-related Late-onset Hepatic Failure: A Case Report

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Abstract

Late-onset hepatic failure, the least of the fulminant hepatic failures, has not occurred in patients with hepatitis A virus-related acute liver failure. We report a rare case of hepatitis A virus-related late-onset hepatic failure treated successfully by an emergent liver transplant.

A 58-year-old Japanese woman who presented with fever and general malaise was diagnosed as having jaundice and liver dysfunction by a positive serum test for anti-hepatitis A virus IgM, which ultimately led to a diagnosis of acute hepatitis A virus-associated hepatitis. Despite intensive treatment, her general condition was poor, and she developed a hepatic coma 79 days from the onset of the disease. Under a diagnosis of hepatitis A virus-related late-onset hepatic failure, she was given a living-donor liver transplant 82 days from the start of the disease. The resected native liver revealed submassive necrosis with marked cholestasis, compatible with late-onset hepatic failure. Today, 5 years after the transplant, she is alive and well with no signs of recurrent hepatitis A virus-hepatitis. This case should alert the physician to the clinical management of a patient with hepatitis A virus-related acute liver failure.

Key words: Hepatitis A virus, Fulminant hepatic failure, Late onset hepatic failure, Liver transplant

Liver transplant is not used in most instances of hepatitis A virus-related acute liver failure, because this entity resolves spontaneously more frequently than fulminant hepatic failure of other causes; thus, the decision to transplant or not is particularly difficult. Late-onset hepatic failure, the least-common type of fulminant hepatic failure, is defined as *fulminant hepatic failure with jaundice onset and encephalopathy emergence more than 8 weeks but less than 24 weeks*. To date, there have been no reports on a transplant case for hepatitis A virus-related late-onset hepatic failure. Here, we report a case with hepatitis A virus-related late-onset hepatic failure that was treated successfully by an emergent liver transplant. The relevant literature is also reviewed.

Case Report

Written consent was obtained from the patient for publication of an original report and any accompanying images. A 58-year-old Japanese woman presented at our emergency department with a moderate-grade fever and general malaise on June 4, 2005. She had been seen by her regular doctor who diagnosed it as a common cold. However, her subjective symptoms worsened, and she returned to the hospital, where jaundice and liver dysfunction were identified by a positive serum test for anti-hepatitis A virus IgM, which ultimately led to a diagnosis of acute hepatitis A virus-associated hepatitis. The results of other tests for markers of acute infection (including hepatitis B surface antigen, anti-HBc IgM, anti-VCA Epstein-Barr virus IgM, anti-cytomegalovirus IgM, anti-hepatitis C virus, and self-antibody antinuclear, and antimitochondrial-2) were negative. She had no history of alcohol intake or illicit drug use. Her autoimmune hepatitis score was 7 according to the scoring system from the International Autoimmune Hepatitis Group.¹

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Experimental and Clinical Transplantation (2011) 2: 150-152

After hospitalization consisting of conservative treatment, her transaminase levels improved; however, her bilirubin levels increased, and 3 courses of steroid pulse therapy with simultaneous administration of interferon- β (3 million units per week) were given. Although these treatments included 5 plasma exchanges, her condition gradually worsened, and she developed a hepatic coma, grade 3, with a convulsion that occurred 79 days after the onset of the disease.

She received a living-donor liver transplant on Aug 24, 2005, eighty-two days from the start of the disease. The donor was her blood type-identical, 34-year-old son, and his right lobe graft was used. Immunosuppression consisted of tacrolimus, low-dose steroids, and mycophenolate mofetil as previously described.²

The resected native liver weighed 1370 g, and pathological study revealed submassive necrosis with marked cholestasis, compatible with late-onset hepatic failure. Her postoperative course was uneventful, except for mild acute cellular rejection

(RAI = 4, P1, B0, V3) on day 12, which was successfully treated with steroid pulse therapy. Postoperatively, she tested positive for anti-hepatitis A virus IgM and IgG, but negative for hepatitis A virus-RNA. At the time of this writing, she is alive and well without any signs of recurrence of the original disease 5 years after her transplant. The results of her most-recent serum tests were positive for hepatitis A virus IgG, but negative for IgM.

Discussion

Hepatitis A virus-related acute liver failure accounted for 6.9% of the total fulminant hepatic failure patients, 12.0% of the acute type (n=316), and 1.9% of the subacute type (n=318).³ Because hepatitis A virus-related acute liver failure resolves spontaneously more frequently than does fulminant hepatic failure (due to other causes), as much as 72.7% of hepatitis A virus-related fulminant hepatic failure patients have been rescued, which is better survival when compared with those of other origins. Liver transplant has not been indicated for most patients; thus, the decision to transplant or not is particularly difficult in this population.

Late-onset hepatic failure is defined as *fulminant hepatic failure with jaundice onset and encephalopathy emergence more than 8 weeks but less than 24 weeks*. To date, there have been no reports of transplant cases of hepatitis A virus-related late-onset hepatic failure. Rezende and associates reported 19 patients with hepatitis A virus-related fulminant hepatitis—all of whom showed an acute or subacute pattern—not the late-onset type of hepatic failure (ie, with an interval ranging from 1 to 38 days between jaundice onset and encephalopathy).⁴

According to a recent report from the *Intractable Liver Diseases Study Group of Japan*, survival rates of patients without liver transplants were 53.7% in the acute and 24.4% in the subacute type; 11.5% in late-onset hepatic failure; and those who underwent liver transplant were 56.3%, 39.3%, and 23.4% (n=698).³ This shows that despite the worst survival in late-onset hepatic failure, liver transplant is also expected to improve an otherwise poor prognosis.

In our case, the possibility that interferon therapy was not adequate for this special patient and had an adverse effect on her clinical course, leading to an atypical manifestation of hepatitis A virus would not be completely ruled out.

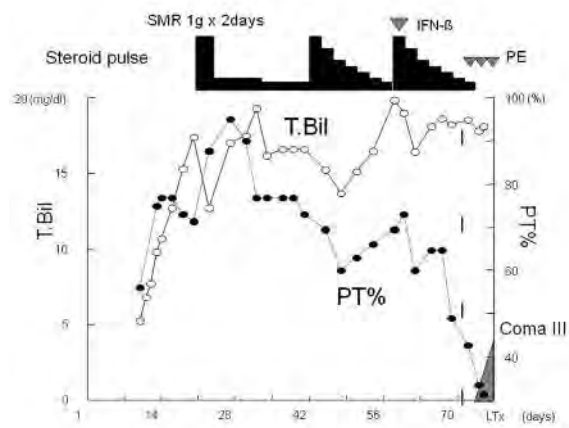


Figure 1. Clinical course before transplant.

Abbreviations: LTx, liver transplant; PE, plasma exchange; PT, prothrombin time; SMR, Solu-Medrol

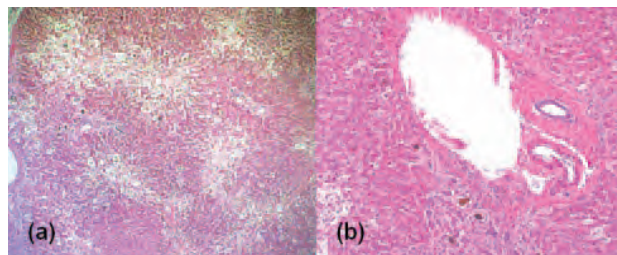


Figure 2. Microscopic examination of the explanted liver demonstrating (a) Submassive necrosis with marked cholestasis in the central vein region (hematoxylin-eosin, original magnification $\times 40$). (b) Periportal region showing changes compatible with late-onset hepatic failure, while inflammatory infiltration was not remarkable (original magnification $\times 100$).

With respect to posttransplant recurrence of hepatitis A virus, there have been 4 cases of recurrent hepatitis A virus infection to date, although it is generally believed that hepatitis A virus does not recur. Eisenbach and associates reported a patient whose hepatitis A virus-RNA reappeared after it had disappeared in the serum and feces, and hepatitis recurred 80 days after the transplant.⁵ Hepatitis A virus also has been reported to resemble acute rejection in that both conditions respond well to steroid pulse therapy. Care should be taken when faced postoperatively with liver dysfunction.

To the best of our knowledge, this case is the first report of the development of hepatitis A virus-related late-onset hepatic failure treated successfully by an

urgent liver transplant. Careful consideration is needed when dealing with severe hepatitis A virus acute liver failure.

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