

CASE REPORT

Acute Pancreatitis Complicating Spontaneous Acute Exacerbation of Chronic Hepatitis B Virus Infection: Case Report and Review of the Literature

Kyo-Sang Yoo, Kyung-Hun Lee, Kyung Rim Huh, Won Sub Choi, Gang Jeon, Jun-Wook Ha, Kyoung Oh Kim, Cheol Hee Park, Taeho Hahn, Sang Hoon Park, Jong Hyeok Kim, and Choong Kee Park

Department of Gastroenterology and Hepatology, Hallym University College of Medicine, Anyang, Korea

Acute pancreatitis may complicate viral hepatitis B, as well as the other causes of viral hepatitis. There have been reports of acute pancreatitis complicating acute exacerbations of chronic hepatitis B virus infection, most of which were related to immunosuppressive treatment or organ transplantation. However, acute pancreatitis complicating spontaneous acute exacerbation of chronic hepatitis B virus infection is rare. We report a case of acute pancreatitis that developed while a spontaneous acute exacerbation of chronic hepatitis B virus infection was underway in a healthy carrier. (*Gut and Liver* 2009;3:64-66)

Key Words: Pancreatitis; Hepatitis B, Chronic

INTRODUCTION

Acute pancreatitis can complicate the course of viral hepatitis, especially in fulminating forms.^{1,2} While acute pancreatitis has been documented in acute hepatitis B virus (HBV) infections,^{2,4} the association between acute exacerbation of chronic HBV infection and acute pancreatitis has been poorly described. There have been only isolated case reports of acute pancreatitis complicating acute exacerbation of chronic HBV infection.⁵⁻⁸ Most of the cases were related to immunosuppressive therapy following organ transplantation, and a high incidence of pancreatitis in HBsAg seropositive liver transplant recipients has been also reported.⁶

However, acute pancreatitis complicating spontaneous reactivation of chronic HBV infection unrelated to the im-

munosuppressive therapy is rare. We have experienced a case of acute pancreatitis superimposed on spontaneous acute exacerbation of chronic HBV infection in a healthy carrier, and the case had rapidly improved along with improvement of the acute exacerbation of chronic HBV infection.

CASE REPORT

A 27-year-old male was presented with severe epigastric pain radiating to his back and vomiting lasting one day. He was known to be HBsAg positive for more than five years. The laboratory data for liver function checked a few months before the admission had been within normal range. He was a social drinker but had no history of drinking during the last several weeks. His body temperature was 36°C, his pulse 72 beats per minute, respiratory rate 18 breaths per minute, and blood pressure 90/60 mmHg. The physical examination revealed yellowish sclera, slightly decreased bowel sound, and severe tenderness on the epigastric area without guarding or rebound tenderness. The serum amylase level was 920 U/L; the lipase level 712 U/L; the aspartate aminotransferase (AST) level 752 U/L; the alanine aminotransferase (ALT) level 1,257 U/L; the alkaline phosphatase level 206 U/L; the gamma glutamyl transferase level 125 U/L; the total bilirubin level 4.1 mg/dL; and the direct bilirubin level 1.8 mg/dL. The white cell count was 5,600/mm³; the hemoglobin 15.5 g/dL; and the hematocrit 45.5%. The levels of glucose, calcium, blood urea nitrogen (BUN), crea-

Correspondence to: Kyo-Sang Yoo

Department of Gastroenterology and Hepatology, Hallym University Sacred Heart Hospital, 896, Pyeongchon-dong, Dongan-gu, Anyang 431-070, Korea

Tel: +82-31-380-6065, Fax: +82-31-386-2269, E-mail: stanyoo@hallym.ac.kr

Received on June 25, 2008. Accepted on November 24, 2008.

tinine, and electrolytes were normal. The results of serological markers for hepatitis B were as follows: positive for HBsAg, negative for anti-HBs, positive for HBeAg, negative for anti-HBe, and negative for anti-HBc IgM. The HBV DNA level was 978.3×10^3 copies. An abdominal computed tomography (CT) scan demonstrated mild pancreatic swelling and a scanty amount of fluid retention at the peripancreatic and anterior pararenal space around the head and proximal body of the pancreas. Abdominal ultrasonography showed diffuse swelling of the pancreas, but no evidence of gallstones in the gallbladder or bile duct.

The medical treatment including no oral alimentation, intravenous fluids, and pain control was started, and abdominal pain had been improved thereafter. Oral intake was started on the fifth hospital day after epigastric pain had been completely improved. Additionally, the elevated serum transaminase and pancreatic enzymes had progressively improved. At two weeks after admission, the AST level was 39 U/L; the ALT level 74 U/L; the total bilirubin level 2.1 mg/dL; serum amylase level 249 U/L; and the lipase level 111 U/L. Both HBeAg and anti-HBe were positive, and the HBV DNA had converted to negative. Then he was discharged from the hospital with a resolution of clinical symptoms and improvement of laboratory findings.

The follow-up laboratory data after three months were as follows: levels of transaminase were completely normalized. HBeAg was converted to negative and anti-HBe was converted to positive. The HBV DNA remained negative. No relapse of acute exacerbation of chronic hepatitis B and pancreatitis has been seen during the seven months follow-up.

DISCUSSION

Most of the case reports of acute pancreatitis complicating acute exacerbation of chronic HBV infection were related to immunosuppressive therapy, especially following an organ transplantation.⁵⁻⁷ Immunosuppressive therapy results in enhanced replication of HBV and depressed host immunity. The discontinuation of therapy causes a rebound of the immune system, resulting in the development of hepatitis.⁸

Acute pancreatitis has been reported in patients submitted to liver transplantation. In these cases, acute pancreatitis was more common in individuals with an active hepatic disease related to HBV (HBsAg positive) than in those with inactive infections (HBsAg negative and anti-HBc or anti-HBs positive) and could be the result of pancreatic infection by HBV itself.⁶ Moreover, im-

munosuppressive therapy, to which these patients are submitted, can play an important role, since it predisposes to higher levels of viral replication in organs where the virus can persist only in normal circumstances.⁷

The increase in hepatitis B viral replication also has been shown to occur in patients taking chemotherapy^{9,10} and corticosteroids.^{11,12}

However, acute pancreatitis that was developed in healthy HBV carriers with spontaneous acute exacerbation of chronic HBV infection is rare.

Yuen *et al.*⁵ have reported five cases of acute pancreatitis complicating acute exacerbation of chronic HBV infection, and they demonstrated that these cases carried a poor prognosis. Three patients of the five patients were not involved with immunosuppressive therapy or organ transplantation, but the level of HBV DNA was not available in two patients among them. Even though the authors assumed that acute pancreatitis might occur during the resolving phase of the acute exacerbation in those cases, the causal relationship between the acute pancreatitis and acute exacerbation of chronic HBV infection was uncertain. Only one patient had acute pancreatitis complicating the acute exacerbation of chronic HBV infection. However, the patient had chronic hepatitis B related liver cirrhosis with a history of encephalopathy and nonbleeding esophageal varices, and acute pancreatitis occurred along with rapid deterioration of liver function and renal failure. Acute pancreatitis in fulminant hepatic failure is fairly common and has been well documented in several series on the basis of histology or serology,^{1,13-18} but the occurrence of acute pancreatitis in nonfulminant viral hepatitis is very rare.

The present case was the only one with acute pancreatitis that was developed in conjunction with spontaneous acute exacerbation of chronic HBV infection in a healthy carrier. Other likely causes of acute pancreatitis such as alcohol ingestion and cholelithiasis were excluded in the present case. The pancreatitis had rapidly improved along with improvement of acute exacerbation of chronic HBV infection, and eventually the HBeAb became positive and the HBV DNA was not detected.

HBsAg has been found in the pancreatic acinar cell and in the pancreatic juice.¹⁹⁻²¹ The mode of infection of the pancreas is probably through the hematological and biliary route.

Two possible mechanisms are suggested whereby acute exacerbation of chronic HBV infection can cause acute pancreatitis. Firstly, there may be a direct cytotoxic effect of the HBV on the pancreatic cells. It is well documented that an increase in viral antigen is a triggering mechanism for acute exacerbation of chronic HBV infection.²² The in-

crease in the viral antigenic load may become toxic to the pancreatic cells. Cavallari *et al.* demonstrated that immunohistochemistry and *in situ* hybridization of the pancreas following autopsy showed the presence of HBsAg and HBV DNA in the cytoplasm of acinar cells, together with the picture of necrotizing pancreatitis in a liver transplant recipient with fatal necrotizing pancreatitis caused by HBV infection. They postulated that the destruction of the pancreas by HBV is probably due to the direct viral damage.⁷ Secondly, the immune response against HBV-infected hepatocytes in acute exacerbation may also be directed against HBV-infected pancreatic cells. It is possible that both mechanisms, direct viral toxicity and immunological attack, are responsible for varying degree in different patients.⁵

The cases of acute pancreatitis complicating spontaneous acute exacerbation of chronic hepatitis B have not been reported yet in Korea, even though Korea is one of the endemic areas of chronic hepatitis B. It is unknown why clinically evident acute pancreatitis complicating spontaneous acute exacerbation of chronic HBV infection is rare.

Acute pancreatitis could occur complicating the spontaneous acute exacerbation of chronic HBV infection; therefore, if the patient with acute exacerbation of chronic HBV infection complains of epigastric pain, the possibility of acute pancreatitis should be considered.

REFERENCES

- Ede RJ, Moore KP, Marshall WJ, Williams R. Frequency of pancreatitis in fulminant hepatic failure using isoenzyme markers. *Gut* 1988;29:778-781.
- Jain P, Nijhawan S, Rai RR, Nepalia S, Mathur A. Acute pancreatitis in acute viral hepatitis. *World J Gastroenterol* 2007;13:5741-5744.
- de Oliveira LC, Rezende PB, Ferreira AL, et al. Concurrent acute hepatitis and pancreatitis associated with hepatitis B virus: case report. *Pancreas* 1998;16:559-561.
- Parenti DM, Steinberg W, Kang P. Infectious causes of acute pancreatitis. *Pancreas* 1996;13:356-371.
- Yuen MF, Chan TM, Hui CK, Chan AO, Ng IO, Lai CL. Acute pancreatitis complicating acute exacerbation of chronic hepatitis B infection carries a poor prognosis. *J Viral Hepat* 2001;8:459-464.
- Alexander JA, Demetrius AJ, Gavalier JS, Makowka L, Starzl TE, Van Thiel DH. Pancreatitis following liver transplantation. *Transplantation* 1988;45:1062-1065.
- Cavallari A, Vivarelli M, D'Errico A, et al. Fatal necrotizing pancreatitis caused by hepatitis B virus infection in a liver transplant recipient. *J Hepatol* 1995;22:685-690.
- Ohshiro Y, Tawata M, Takasu N. Acute pancreatitis and exacerbation of hepatitis B following reduced dose of prednisolone. *QJM* 2003;96:868-869.
- Locasciulli A, Santamaria M, Masera G, Schiavon E, Alberti A, Realdi G. Hepatitis B virus markers in children with acute leukemia: the effect of chemotherapy. *J Med Virol* 1985;15:29-33.
- Lok AS, Liang RH, Chiu EK, Wong KL, Chan TK, Todd D. Reactivation of hepatitis B virus replication in patients receiving cytotoxic therapy: report of a prospective study. *Gastroenterology* 1991;100:182-188.
- Scullard GH, Smith CI, Merigan TC, Robinson WS, Gregory PB. Effects of immunosuppressive therapy on viral markers in chronic active hepatitis B. *Gastroenterology* 1981;81:987-991.
- Fujiwara K, Yokosuka O, Kojima H, et al. Importance of adequate immunosuppressive therapy for the recovery of patients with "life-threatening" severe exacerbation of chronic hepatitis B. *World J Gastroenterol* 2005;11:1109-1114.
- Launois JP, Cachin M, Levy C. Severe jaundice and acute hemorrhagic pancreatitis. *Ann Med Interne (Paris)* 1972;123:1051-1053.
- Vital Durand D, Trepo C, Bouletreau P, Chevalier-Queyron P, Grimaud JA, Motin J. Fulminant hepatitis B virus associated with acute pancreatitis. Report of two cases. *Ann Med Interne (Paris)* 1981;132:120-123.
- Ham JM, Fitzpatrick P. Acute pancreatitis in patients with acute hepatic failure. *Am J Dig Dis* 1973;18:1079-1083.
- Parbhoo SP, Welch J, Sherlock S. Acute pancreatitis in patients with fulminant hepatic failure. *Gut* 1973;14:428.
- Geokas MC, Olsen H, Swanson V, Rinderknecht H. The association of viral hepatitis and acute pancreatitis. *Calif Med* 1972;117:1-7.
- Wands JR, Salyer DC, Boitnott JK, Maddrey WC. Fulminant hepatitis complicated by pancreatitis. *Johns Hopkins Med J* 1973;133:156-160.
- Yoshimura M, Sakurai I, Shimoda T, Abe K, Okano T, Shikata T. Detection of HBsAg in the pancreas. *Acta Pathol Jpn* 1981;31:711-717.
- Shimoda T, Shikata T, Karasawa T, Tsukagoshi S, Yoshimura M, Sakurai I. Light microscopic localization of hepatitis B virus antigens in the human pancreas: possibility of multiplication of hepatitis B virus in the human pancreas. *Gastroenterology* 1981;81:998-1005.
- Hoefs JC, Renner IG, Askhcavai M, Redeker AG. Hepatitis B surface antigen in pancreatic and biliary secretions. *Gastroenterology* 1980;79:191-194.
- Maruyama T, Iino S, Koike K, Yasuda K, Milich DR. Serology of acute exacerbation in chronic hepatitis B virus infection. *Gastroenterology* 1993;105:1141-1151.