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*Case Report*

## A Homosexual Japanese Man with Acute Hepatitis Due to Hepatitis B Virus Genotype Ae, Concurrent with Amebic Colitis

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We report herein a case with acute hepatitis due to hepatitis B virus genotype Ae, concurrent with amebic colitis. A 39-year-old homosexual Japanese man was admitted to our hospital with jaundice. Laboratory tests showed an elevation of transaminase and positivity for hepatitis B surface antigen and IgM-type antibody to hepatitis B core antigen. The hepatitis B virus genotype was determined to be Ae. Furthermore, a mud-like stool with blood and mucous had sometimes been noted during the past 3 years, and amebic colitis was shown by colonofiberscopy during hospitalization. The patient was diagnosed with acute hepatitis B, concurrent with amebic colitis, and was successfully treated with lamivudine and metronidazole. In Japanese patients with acute hepatitis B virus genotype A infection, homosexual activity tends to be high. Furthermore, in Japanese homosexual men, amebiasis has been increasing. Thus, in Japanese patients with acute hepatitis B, a determination of genotype should be performed in order to investigate the route of transmission of hepatitis B virus, and a search for amebiasis should be performed in patients with acute hepatitis due to hepatitis B virus genotype A. Furthermore, education of homosexual men regarding hepatitis B virus, hepatitis B virus vaccination, and amebiasis is urgently required.

**Key words:** hepatitis B virus, genotype, homosexual, amebic colitis, lamivudine

Acute hepatitis B virus infection acquired in adulthood, has been recognized to be self-limited. Hepatitis B virus DNA is successfully cleared in more than 95% of adult patients with the acute infection [1].

The hepatitis B virus genotype has been determined to be associated with the clinical course of

patients with acute hepatitis B. Hepatitis B virus is classified into 8 genotypes exhibiting distinct geographic distributions [2, 3]. Throughout East Asia, including Japan, genotypes B and C are prevalent [2, 3].

Recently, infection with hepatitis B virus genotype A, which is prevalent in North Western Europe, North America, and South Africa, has become frequent in Japan. In Japanese patients with acute hepatitis B viral infection, the proportion of patients infected with hepatitis B virus genotype A was

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reported at 9% prior to 1991, but 55% after 1991 [4]. Furthermore, it has been reported that, prior to 1991, the main infectious route was post-transfusion hepatitis, but thereafter has been sexual transmission [5].

In this report, we describe the case of a homosexual Japanese man with acute hepatitis due to hepatitis B virus genotype Ae, concurrent with amebic colitis, who was successfully treated with lamivudine and metronidazole.

### Case Report

A 39-year-old Japanese man was admitted to our hospital on January 2005 due to jaundice, general fatigue, and anorexia. The patient was a homosexual man, who reported having sexual contact with multiple unidentified partners since the age of 33. A mud-like stool with blood and mucous had sometimes been noted during the past 3 years. Ten days previously, the patient had a sore throat. For the past week, he had felt general fatigue and anorexia, and for the past 5 days he had noticed the dark color of his urine.

On physical examination at admission, the patient's consciousness was clear, and the bulbar conjunctiva was icteric. Neither ascites nor pretibial edema was recognized. Laboratory data on admission were as follows: total bilirubin, 10.7 mg/dL; aspartate aminotransferase, 1,507 IU/L; alanine aminotransferase, 2,448 IU/L; albumin, 4.5 g/dL; and prothrombin activity, 89%. Tests for hepatitis B surface antigen and IgM-type antibody to hepatitis B core antigen were positive, although in a medical checkup administered in June 2004, hepatitis B surface antigen had tested negative. Serum hepatitis C virus-RNA, antibody to hepatitis C virus, antibody to human immunodeficiency virus, and *Treponema pallidum* hemagglutination tests were all negative. The patient was diagnosed with acute hepatitis B, and daily administration of 200 mg of lamivudine was initiated.

The genotype of the hepatitis B virus was analyzed using serum obtained on the day of admission and was stored at  $-40^{\circ}\text{C}$ . Informed consent for the analysis was obtained from the patient. The genotype of the hepatitis B virus was determined based on the complete genome sequence [6, 7], and was shown to

be Ae.

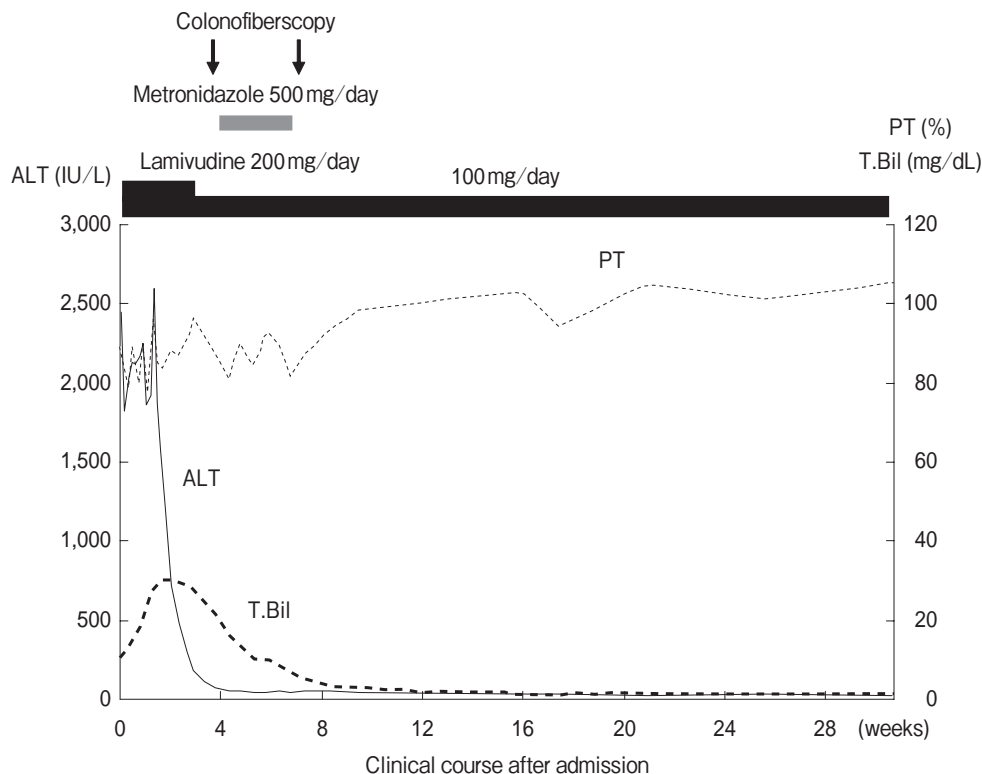
Two weeks later, the patient's serum alanine aminotransferase levels began to decrease, and his general fatigue and anorexia improved. The dosage of lamivudine was reduced to 100 mg/day 3 weeks after the introduction of lamivudine treatment. The normalization of serum levels of alanine aminotransferase was achieved 5 weeks after the introduction of lamivudine treatment. Hepatitis B e antigen disappeared from serum 12 weeks after the introduction of lamivudine treatment, and hepatitis B surface antigen was cleared 7 months after the introduction of lamivudine treatment (Fig. 1). However, antibody to hepatitis B surface antigen did not develop 14 months after the introduction of lamivudine treatment, and lamivudine treatment was continued.

Meanwhile, the peripheral hemoglobin concentrations fell gradually to 11.4 g/dL 4 weeks after admission, and colonofiberscopy showed multiple ulcers covered with whitish exudates in the cecum (Fig. 2A). Histological features showed mucosa with lymphocytic and eosinophilic accumulations, and trophozoites of *Entamoeba histolytica* ingesting red blood cells (Fig. 2C, D). The patient was diagnosed with amebic colitis, and daily administration of 500 mg of metronidazole was initiated. Colonofiberscopy performed after 3 weeks showed normal cecal mucosa (Fig. 2B). During the treatment of amebic colitis using metronidazole, no aggravation of the transaminases was recognized.

### Discussion

In the present case, the mode of transmission of hepatitis B virus was considered to be homosexual contact. Sexual transmission of hepatitis B virus is frequent among homosexual men because multiple partnerships are common and anal sex is inherently more traumatic than vaginal intercourse, fostering exposure to blood [8]. Thus, immunization against hepatitis B virus is recommended for homosexual men. However, the present case did not know anything about hepatitis B virus or hepatitis B virus vaccination. In Japan, education of homosexual men regarding hepatitis B virus and hepatitis B virus vaccination is urgently required.

Recently in Japan, approximately 30–40% of men with acute hepatitis due to hepatitis B virus genotype



HBs Ag (COI)	2000.0 (+)	2000.0 (+)	1018.8 (+)	24.9 (+)	1.1 (+)	0.4 (-)
anti-HBs (COI)	0.1 (-)	0.1 (-)	0.1 (-)	0.1 (-)	0.1 (-)	0.1 (-)
HBe Ag (COI)	958.8 (+)	13.0 (+)	2.5 (+)	0.2 (-)	0.1 (-)	0.1 (-)
anti-HBe (%)	0.1 (-)	47.6 (-)	76.4 (+)	91.8 (+)	91.3 (+)	88.8 (+)
HBV DNA (log <sub>10</sub> copies/mL)	6.8	3.7	3.3	<2.6	<2.6	<2.6

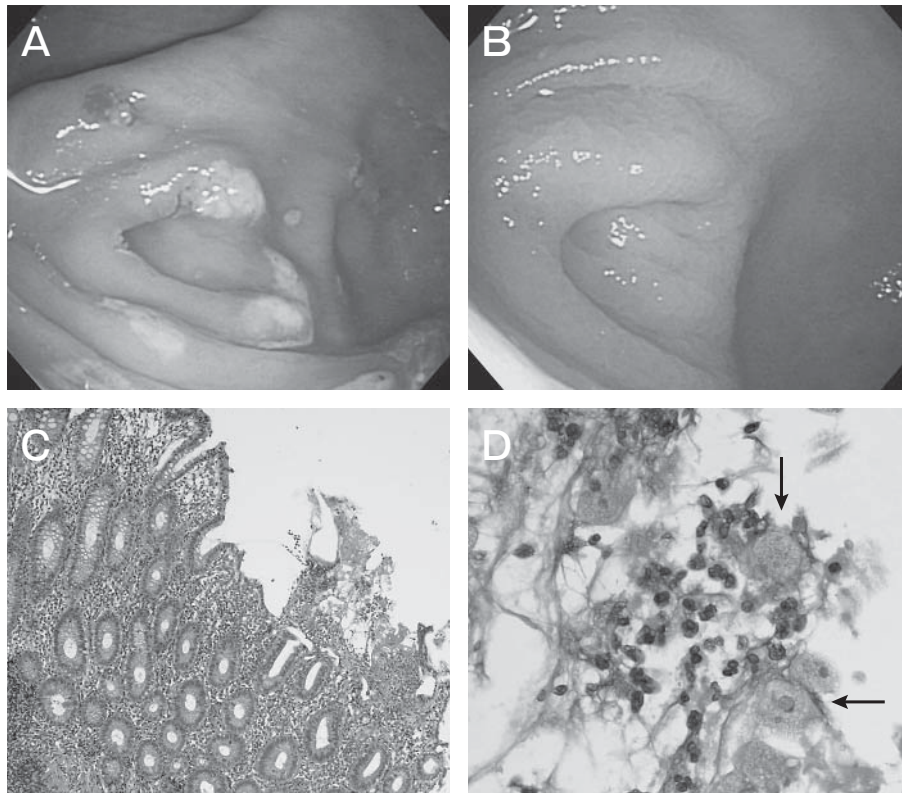
Fig. 1 Patient clinical course. ALT, alanine aminotransferase; anti-HBe, antibody to hepatitis B e antigen; anti-HBs, antibody to hepatitis B surface antigen; COI, cut off index; HBe Ag, hepatitis B e antigen; HBs Ag, hepatitis B surface antigen; HBV DNA, hepatitis B virus DNA; PT, prothrombin activity; T.Bil, total bilirubin.

A are reported to be homosexual [4, 9]. Among the human immunodeficiency virus type 1-positive population in Japan, approximately 90% of homosexual men infected with hepatitis B virus have genotype A [10]. In patients with acute hepatitis B viral infection, a determination of genotype should be performed in order to investigate the route of transmission of hepatitis B virus and to determine a medical treatment plan.

It has been reported that acute hepatitis due to hepatitis B virus genotype A tends to be persistent, compared with that due to other genotypes, and hepatitis B surface antigen is cleared in only a small proportion of patients receiving lamivudine treat-

ment, although approximately half of these patients respond with a loss of hepatitis B e antigen [9]. However, hepatitis B surface antigen was cleared with lamivudine treatment in the present case. Suzuki *et al.* [9] have reported that low maximum alanine aminotransferase levels (<500 IU/L) are predictive of the perpetuation of acute hepatitis due to hepatitis B virus genotype A. The clinical course of the present case was thus consistent with their report.

Although a randomized, prospective study of lamivudine in patients with acute hepatitis B has not been reported, lamivudine treatment has been reported to be safe and well-tolerated in these



**Fig. 2** Demonstration of amebic colitis by colonofiberscopy and histological features. **A**, Colonofiberscopy before treatment with metronidazole shows multiple ulcers covered with whitish exudates in the cecum; **B**, Colonofiberscopy after treatment with metronidazole shows normal cecal mucosa; **C**, Histological feature shows mucosa with lymphocytic and eosinophilic accumulations (HE; original magnification,  $\times 50$ ); **D**, Histological feature shows trophozoites of *Entamoeba histolytica* ingesting red blood cells (arrow, HE; original magnification,  $\times 400$ ).

patients [11, 12]. Furthermore, lamivudine treatment is considered to induce a prompt clinical, biochemical, serological, and virological response in immunocompetent patients with acute hepatitis B [11, 12]. We considered that, in patients with acute hepatitis due to hepatitis B virus genotype A, lamivudine should be administered upon diagnosis, in order to prevent the progression of acute hepatitis to fulminant hepatitis, and to achieve a normalization of transaminase levels and a clearance of hepatitis B virus infection, if they are not infected with a human immunodeficiency virus type 1.

In the present case, lamivudine treatment was continued even after hepatitis B surface antigen disappeared from serum. Yotsuyanagi *et al.* [13] have reported that, in the serum of patients after recovery from acute hepatitis B, free hepatitis B virus

persists at low levels in the window period when both hepatitis B surface antigen and antibody to hepatitis B surface antigen are absent from serum, although immunoglobulin-bound hepatitis B virus is predominant, and that free hepatitis B virus is not detectable after the seroconversion to antibody to hepatitis B surface antigen. The absence of free hepatitis B virus in serum generally indicates a loss of infectivity. Thus, we consider that lamivudine treatment should be continued until a protective titer of antibody to hepatitis B surface antigen develops.

Amebiasis is the second leading cause of death from parasitic disease worldwide, and an estimated 40,000–100,000 people die yearly from the disease [14]. Worldwide, most individuals with amebiasis are infected by ingestion of food or water contaminated with feces containing *Entamoeba histolytica*

cycts. However, in Japan, amebiasis is domestically transmitted by 2 populations: homosexual men and mentally handicapped persons, which is remarkably different from most other developed countries [15]. Recently, in Japanese homosexual men, amebiasis has been increasing [16]. In order to prevent the outbreak of amebiasis infection, the control of amebiasis in homosexual men is considered to be necessary.

In the present case, when metronidazole was initiated, the serum bilirubin levels were as high as 14.1 mg/dL. Metronidazole was prescribed for 3 weeks, and the serum bilirubin levels decreased to 5.0 mg/dL at the conclusion of metronidazole treatment. This is the first report that, in patients with acute hepatitis, metronidazole can be administered together with lamivudine to treat concurrent amebic colitis. Metronidazole may be well-tolerated, even in icteric patients with acute hepatitis B.

In summary, this report describes a homosexual Japanese man with acute hepatitis due to hepatitis B virus genotype Ae, concurrent with amebic colitis, who was successfully treated with lamivudine and metronidazole. In the present case, the mode of transmission of hepatitis B virus genotype Ae and *Entamoeba histolytica* was considered to be homosexual contact. In Japanese patients with acute hepatitis B virus genotype A infection, the statistical probability of homosexuality is high. Thus, a determination of genotype should be performed in order to investigate the route of transmission of hepatitis B virus, and a search for amebiasis should be performed in patients with acute hepatitis due to hepatitis B virus genotype A. Furthermore, education of homosexual men regarding hepatitis B virus, hepatitis B virus vaccination, and amebiasis is urgently required.

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