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Case report

A case of non-cirrhotic portal hypertension associated with anti-retroviral therapy in a Japanese patient with human immunodeficiency virus infection

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ABSTRACT

The diagnosis of non-cirrhotic portal hypertension (NCPH), a rare but potentially life-threatening complication in human immunodeficiency virus (HIV)-positive individuals, often occurs only after the emergence of fatal manifestations such as bleeding of esophageal varices. We herein report a female Japanese HIV patient who developed NCPH approximately 4 years after discontinuation of 65 months of didanosine (ddI) administration. The patient presented with severe ascites, bloody bowel discharge, extreme abdominal swelling, and symptoms of portal hypertension but no sign of liver cirrhosis. Examination revealed esophageal varices, oozing-like bleeding from a wide part of the colon, significant atrophy of the right lobe of the liver, and arterio-portal shunting and recanalization from the left medial segment branch of the portal vein to a paraumbilical vein, but no visible obstruction of the main trunk of the portal vein. Treatment for esophageal varices consisted of coagulation therapy with argon plasma after enforcement by endoscopic sclerotherapy and oral administration of β-blockers for elevated portal blood pressure. The patient has not experienced gastrointestinal bleeding in the approximately 5 years since the diagnosis of NCPH. Reviewing this case suggests the importance of suspecting NCPH in HIV patients with liver dysfunction of unknown etiology with a history of ddI and other purine analogs use, as well as the importance of controlling portal hypertension and esophageal varices in the treatment of NCPH.

1. Introduction

Non-cirrhotic portal hypertension (NCPH) is a rare but potentially life-threatening complication experienced by human immunodeficiency virus (HIV)-positive individuals [1]. This condition has become increasingly recognized as a cause of liver morbidity and mortality among HIV patients whose status is otherwise well-controlled. The most important predisposing factor to its development has been identified as exposure to didanosine (ddI). Although over 70 cases of NCPH in HIV patients throughout the world have been reported to date, few of these reports have concerned Asian patients [2]. Here we report the development of NCPH in a female Japanese HIV patient approximately 4 years after discontinuation of 65 months of ddI administration. To our knowledge, our patient represents the first case of NCPH diagnosed with liver biopsy in an HIV-positive individual in Japan.

2. Case report

A 35-year-old Japanese woman was admitted to our hospital with a large quantity of ascitic fluid and bloody bowel discharge. Although she was diagnosed of HIV infection in 1993 with CD4 count of 109 cells/mm^3, she did not present with AIDS. She did not have a history of excessive alcohol consumption.

After initiation of anti-retroviral therapy with azidothymidine (AZT) and lamivudine (3 TC) in 1999, the patient was referred to our hospital in 2000 and her anti-retroviral regimen was changed to stavudine (d4T), ddI, and nevirapine (NVP) therapy in preparation

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Table 1
Laboratory data at the onset of non-cirrhotic portal hypertension.

Blood cell count parameters			Blood chemistry parameters		
WBC	6700	Cells/μL	AST	83	IU/L
RBC	1.35	$\times 10^4$ cells/μL	ALT	82	IU/L
Hb	4.2	g/dL	LDH	271	IU/L
Hct	16.2	%	T-Bil	0.2	mg/dL
Plt	20.7	$\times 10^4$ cells/μL	ALP	268	U/L
Coagulation parameters			γ-GTP	54	U/L
APTT	33.6	sec	NH3	43	μg/dL
PT	15.9	sec	CPK	59	IU/L
PT-INR	1.26		Cre	0.5	mg/dL
PT	72.0	%	BUN	9	mg/dL
Fibrinogen	148	mg/dL	Na	139	mEq/dL
HIV parameters			K	4.1	mEq/dL
CD4 count	110	cells/mm^3	Cl	104	mEq/dL
HIV-RNA	<40	copies/mL	CRP	0.08	mg/dL

WBC: white blood cell; RBC: red blood cell; Hb: hemoglobin; Hct:hematocrit; Plt: platelet; APTT: activated partial thromboplastin time; PT: prothrombin time; PT-INR: prothrombin time-international normalized ratio; AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; T-Bil: total bilirubin; ALP: alkaline phosphatase; γ-GTP: γ-glutamyl transpeptidase; CPK: creatine phosphokinase; Cre: creatinine; BUN: blood urea nitrogen; Na: sodium; K: potassium; Cl: chloride; CRP: C-reactive protein.

for delivery. It had subsequently been changed to AZT, ddI, and NVP in 2004 and to tenofovir (TDF), 3 TC, and NVP in 2005. During this period, her level of HIV-RNA was below the detectable level (<50 copies/mL), and her CD4 count had been stable at around 100 cells/mm^3.

Since 2007, the patient's hemoglobin level had gradually decreased from 10 to 7 g/dL. We suspected that a gynecologic disorder was responsible for this decrease, and performed intravaginal ultrasonography. Although the result revealed a small amount of ascites of the floor of the pelvis, subsequent endocervical cytologic testing showed no signs of malignancy. The patient experienced temporary improvement upon administration of an oral and intravenous iron preparation, which was subsequently administered several times after gynecological inspection. While her serum vitamin B12 and folic acid levels were within normal ranges, her liver enzyme levels were slightly elevated. Despite the scheduling of more invasive means of examination, including gastrointestinal endoscopy, the patient refused to undergo them.

Three months after her visit to the gynecology department, the patient was admitted to the emergency room with massive ascites, bloody bowel discharge, and extreme abdominal fullness. Her body weight was 12 kg higher than her usual weight, her blood pressure was 104/72 mmHg, and her pulse rate was 128 beats per minute. Laboratory testing indicated that she had severe anemia with hemoglobin and hematocrit levels of 4.2 g/dL and 16.2%, respectively (Table 1). Although her liver enzyme levels were mildly elevated, coagulation tests yielded no abnormal findings (Table 2).

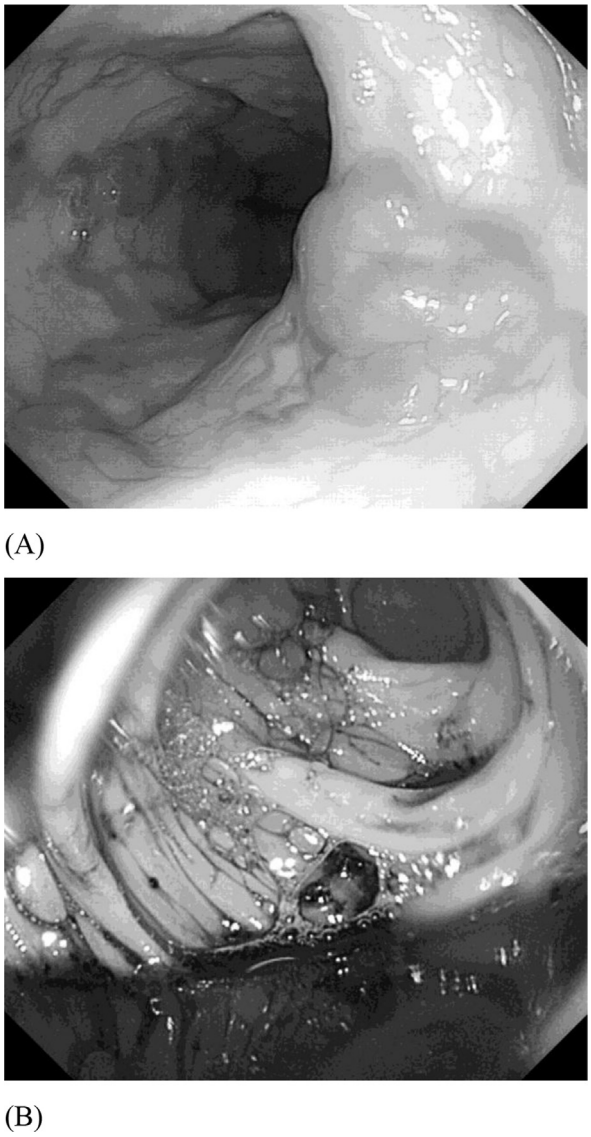

Fig. 1. (A) Urgent upper gastrointestinal tract endoscopy showing esophageal varices (Ls, F3, Cb, and RC-). (B) Massive oozing-like bleeding from a wide part of the colon.

Urgent upper-gastrointestinal tract endoscopy showed esophageal varices (Ls, F3, Cb, and RC-; Fig. 1A) and colonoscopy revealed oozing-like bleeding from a wide part of the colon (Fig. 1B). Abdominal ultrasonography and computed tomography (CT) scan (Fig. 2) revealed a large quantity of ascites, significant atrophy of the right lobe of the liver, and significant splenomegaly (spleen index 107.97 cm^2). A three-dimensional vascular image restructured

Table 2
Summary of liver function, ascites, endoscopic, and immunological findings.

Date (y/m)		AST (IU/L)	ALT (IU/L)	ALP (U/L)	Ascites	Endoscopic findings	CD4 count (Cells/mm^3)	HIV-RNA (Copies/mL)	ART regimen
2000/07	First visit	19	13	221	NP	NP	222	3800	d4T + ddI + NVP
2009/07	3 months before onset	50	70	226	Small	NP	140	<40	TDF+3 TC + NVP
2009/10	Onset of NCPH	83	82	268	Massive	Ls, F3, Cb, RC-	110	<40	TDF+3 TC + NVP
2010/10	One year after onset	59	65	277	Small	Ls, F2, Cb, RC-	110	<40	RAL + ETR
2014/04	4.5 years after onset	25	20	228	Small	Li, F1, Cb, RC-	177	<20	RAL + ETR

AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; ART: antiretroviral therapy; NP: not performed; Ls: locus superior; Li: locus inferior; F3: largest size varices; F2: enlarged tortuous varices; F1: small and straight varices; Cb: blue varices; RC: red color sign; d4T: stavudine; ddI: didanosine; NVP: nevirapine; TDF: tenofovir; 3 TC: lamivudine; RAL: raltegravir; ETR: etravirine.