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H. 知的財産権の出願・登録状況（予定を含む。）

1．特許取得
　なし
2．実用新案登録
　なし
3．その他
　なし

Ⅱ．研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

雑誌：

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
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Ⅲ. 研究成果の刊行物・別刷

LIVER TRANSPLANTATION 19:666, 2013

LETTER TO THE EDITORS

False Positivity for the Human Immunodeficiency Virus Antibody After Influenza Vaccination in a Living Donor for Liver Transplantation

Received February 13, 2013; accepted February 25, 2013.

TO THE EDITORS:

Because of increased productivity and availability, more people have had the chance to undergo prophylactic influenza vaccination. It has been reported that influenza vaccination has cross-reactivity with human immunodeficiency virus (HIV) antibody assays, but this information is not well known in the field of transplantation.[1] Recently, we experienced a case of living donor liver transplantation in which a healthy donor candidate was frightened and was further screened for the HIV antibody.

The patient was a 43-year-old female who was a candidate for partial liver donation for her husband, who was suffering from hepatocellular carcinoma associated with hepatitis B liver cirrhosis. She had never undergone a blood transfusion or abused drugs before her screening for living partial liver donation. According to her laboratory results, she was positive for the HIV antibody (1.7 cut off index). Otherwise, all data, including hepatitis B antibody results, were within normal limits. It was found that she had undergone vaccination for influenza 1 week before the screening. She was referred to a specialist in HIV infection, and western blotting for all antibodies (GP160, GP110/120, P68/66, P55, P52/51, GP41, P40, P34/31, P24/25, and P18/17) was negative. HIV RNA was undetectable in her blood (<40 copies/mL). Thus, she was considered to be HIV-negative with a high level of confidence and subsequently donated the left lobe of her liver. The recipient remained negative for the HIV antibody even after living donor liver transplantation.

With the prevalence of influenza vaccination and organ donation, physicians should keep in mind that recent inoculation with any brand of influenza vaccine is associated with a false-positive screening assay for HIV antibodies.[2]

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The protocol for our living donor liver transplantation received a priori approval by the institutional review committee.

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ELSEVIER

The Efficacy of the ImmuKnow Assay for Evaluating the Immune Status in Human Immunodeficiency Virus and Hepatitis C Virus–Coinfected Patients

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ABSTRACT

Background. The survival of human immunodeficiency virus (HIV)-infected patients has significantly improved since the introduction of antiretroviral therapy (ART). However, the mortality due to hepatitis C virus (HCV)-related liver disease has not been reduced in HIV/HCV-coinfected patients, and HCV has recently become the most significant cause of death in HIV/HCV-coinfected patients. Liver transplantation might be one of the treatments of choice in such cases, but it is very difficult to evaluate the immune status of these patients due to ART, anti-HCV treatment, and HIV-related immunocompromised state.

Aim. The aim of this study was to evaluate the immune status in HIV/HCV-coinfected patients using the Cylex ImmuKnow assay, which was designed to monitor the global immune status by measuring the adenosine triphosphate (ATP) levels produced by activated CD4+ T cells.

Methods. Twenty-eight HIV/HCV-coinfected patients were included in this study. We evaluated their immune activity using the ImmuKnow assay, and compared the data with those of HCV mono-infected patients indicated for liver transplantation as well as healthy controls.

Results. The ATP levels of HIV/HCV-coinfected patients were significantly higher than those of HCV mono-infected liver transplant recipients ($P < .001$), and were significantly lower than those of healthy controls ($P = .001$).

Conclusion. The ImmuKnow assay was considered to be a useful tool to evaluate the immune status of HIV/HCV-coinfected patients.

IN THE LATE 1980s in Japan, the use of contaminated blood products for hemophilia patients led to coinfections with human immunodeficiency virus (HIV) and hepatitis C virus (HCV). In fact, more than 90% of hemophiliacs infected with HIV by contaminated blood products also have HCV [1,2]. After the introduction of anti-retroviral therapy (ART) in the late 1990s, the survival of HIV-infected patients has significantly improved, largely due to the reduction in opportunistic infections related to acquired immunodeficiency syndrome (AIDS). However, the mortality due to HCV-related liver disease has not been reduced in HIV/HCV-coinfected patients [1,3]. In these patients, liver failure due to hepatitis C is enhanced by ART-related hepatotoxicity, especially noncirrhotic portal hypertension (NCPH) [4,5]. Accordingly, not only in cases with deteriorated liver function, but also in Child-Pugh classification class A cases, the patients can suddenly develop severe liver dysfunction [6,7]. Liver transplantation might be one of the treatments of choice in such cases, but the indications for transplantation in HIV/HCV-coinfected patients are not established.

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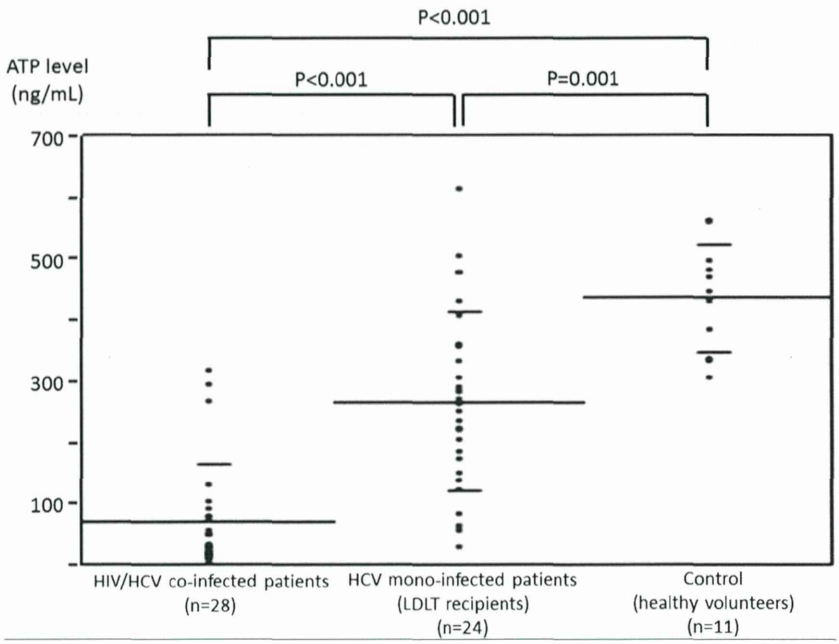

Fig 1. A comparison of the ATP levels among HIV/HCV–coinfected patients, HCV mono-infected patients indicated for LDLT, and healthy volunteers.

The ImmuKnow assay (Cylex, Columbia, MD, United States) was designed to monitor the global immune status by measuring the adenosine triphosphate (ATP) levels produced by activated CD4+ T cells. The assay uses only a small amount of whole blood and requires overnight incubation [8]. In the field of liver transplantation, several authors reported that recipients with lower ATP levels were more likely to develop infectious diseases than recipients with stronger immune responses. On the other hand, recipients with higher ATP levels were more likely to develop rejection than recipients with lower immune responses [9–13].

The aim of this study was to clarify the efficacy of the ImmuKnow assay for assessing the immune function of HIV/HCV-coinfected patients.

PATIENTS AND METHODS

Thirty HIV/HCV-coinfected patients underwent a comprehensive evaluation of their liver function between September 2009 and April 2012 at our hospital. They were all receiving ART, and, in most cases (26 of the 30 patients), their HIV viral load was undetectable. The 28 patients in this group were classified as Child-Pugh Class A and were enrolled in this study.

We conducted 2 analyses: (1) a comparison of the ATP levels among HIV/HCV-coinfected patients, HCV mono-infected patients who were indicated for living donor liver transplantation (LDLT), and healthy volunteers by Mann-Whitney U test, and (2) the correlation between the ATP levels and the CD4+ cell counts and the CD4/CD8 ratio in HIV/HCV-coinfected patients by Spearman rank correlation analysis. The statistical software programs used were JMP version 10.0.2 (SAS Institute Japan, Tokyo, Japan).

RESULTS

The median ATP levels in the HIV/HCV-coinfected patients, HCV-infected transplant recipients, and healthy controls were 259.5 (range, 30–613), 33 (range, 6–320), and 446 (range, 309–565) ng/mL, respectively (Fig 1). The ATP levels of HIV/HCV-coinfected patients were significantly higher than those of HCV recipients ($P < .001$), and significantly lower than those of healthy controls ($P = .001$).

In the HIV/HCV-coinfected patients, the ATP levels were significantly correlated with the CD4+ cell counts ($P = .03$), but not correlated with the CD4/CD8 ratio ($P = .76$; Fig 2).

DISCUSSION

In this study, the ATP levels of HIV/HCV-coinfected patients were higher than those of HCV recipients. Infectious diseases remain an important source of morbidity and mortality in the field of organ transplantation. Because of their immunocompromised state due to HIV, HIV-infected patients are considered to be more likely to develop infectious diseases peritransplantation than are HIV-negative patients. However, we found that the immune status of HIV/HCV-coinfected patients was maintained compared with that of HCV transplant recipients suffering from decompensated cirrhosis. Therefore, if HIV can be controlled by ART, the same strategy can be used to prevent infectious diseases as is used in patients with decompensated cirrhosis due to hepatitis C. Several studies have shown that patients who had low ATP levels measured by the ImmuKnow assay were more likely to develop an infection [11,13]. Monitoring the functional immunity using

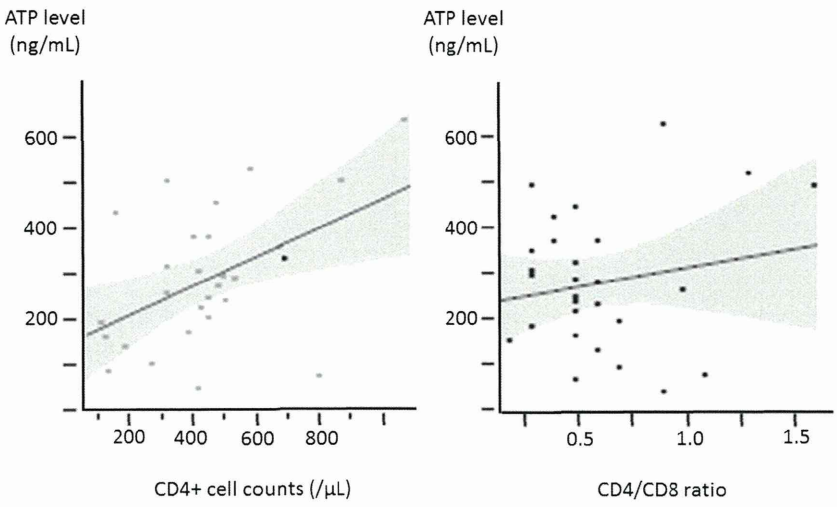

Fig 2. Correlation between the ATP levels and the CD4+ cell counts and the CD4/CD8 ratio in HIV/HCV–coinfected patients.

the ImmuKnow assay can help predict the risk of infection after liver transplantation.

In conclusion, the ImmuKnow assay is considered to be a useful tool to evaluate the immune status of HIV/HCV-coinfected patients.

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Hepatology Research

Hepatology Research 2013 doi: 10.1111/hepr.12132

Review Article

Liver transplantation for HIV/hepatitis C virus co-infected patients

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Since the introduction of antiretroviral therapy (ART) in the mid-1990s, AIDS-related death has been dramatically reduced, and hepatitis-C-virus (HCV)-related liver failure or hepatocellular carcinoma has currently become the leading cause of death in HIV/HCV co-infected patients. Liver transplantation may be one of the treatments of choices in such cases, but the indications for transplantation, perioperative management including both HIV and HCV treatments, immunosuppression and the prevention/treatment of infectious complications are all still topics of debate. With the improved understanding of the viral behaviors of both HIV and HCV and the development of novel strategies, especially to avoid drug interactions between ART and immunosuppression, liver transplantation has become a realistic treatment for HIV/HCV co-infected patients.

Key words: hepatitis C virus, HIV, liver transplantation

INTRODUCTION

IN JAPAN, IN the late 1980s, contaminated blood production of coagulation factor for hemophilia caused co-infection of HIV and hepatitis C virus (HCV). Actually, greater than 90% of HIV-infected patients have HCV as well.[1]

After antiretroviral therapy (ART) was introduced in the late 1990s, successful control of HIV was achieved in most cases and death due to AIDS was dramatically reduced, but HCV-related death due to liver failure or hepatocellular carcinoma became a serious problem, not only in Japan, but all over the world.[2–6] In such cases, liver transplantation (LT) is the only treatment option to achieve long-term survival, but several modifications of perioperative management are required. In this review, the outcome and the points of management of LT for HIV/HCV co-infected patients were reviewed.

REPORTED OUTCOME OF LT FOR HIV/HCV PATIENTS

THE REPORTED OUTCOMES of LT for HIV and HIV/HCV co-infected patients from Western countries after the introduction of ART are summarized in Table 1.[7–11] In general, most reports concluded that the results were worse than in the cases with HCV mono-infection, with a 3-year survival of approximately 60–70%. In Japan, the Tokyo group reported six cases of living donor liver transplantation (LDLT) between 2001 and 2004, of whom four died.[12] These unfavorable outcomes are likely related to the difficulties of determining the indications for LT and of perioperative management, including HIV/HCV treatment and the prevention and treatment of infectious complications. Terrault *et al.* reported that older donor age, combined kidney–liver transplantation, an anti-HCV positive donor and a body mass index of less than 21 kg/m^2 were independent predictors of graft loss.[10] After transplantation, several studies showed that acute cellular rejection was more frequent and severer in HIV/HCV co-infected patients than that in HCV mono-infected patients, possibly due to the difficulties in achieving optimal immunosuppression because of interactions between antiretroviral agents and immunosuppression.[10,11]

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Table 1 Outcome of liver transplantation for HIV/hepatitis C virus co-infection

Authors	Publication year	Country	*n*	Patient survival (%)		
				1 year	3 years	5 years
de Vera *et al.*[7]	2006	USA	27	67	56	33
Schreibman *et al.*[8]	2007	USA	15	73	73	–
Duclos-Vallee *et al.*[9]	2008	France	35	–	73	51
Terrault *et al.*[10]	2012	USA	89	76	60	–
Miro *et al.*[11]	2012	Spain	84	88	62	54

SPECIAL ISSUES REGARDING LT INDICATIONS FOR HIV/HCV CO-INFECTION

ART-related non-cirrhotic portal hypertension

IN HCV MONO-INFECTED patients, LT should be considered when the patients develop deteriorated liver function as indicated by a Child–Pugh classification of B or C. In HIV/HCV co-infected patients, liver failure due to HCV hepatitis was generally enhanced by ART-related hepatotoxicity, especially non-cirrhotic portal hypertension.[13–15] Accordingly, not only in cases with deteriorated liver function but also in class A cases, the patients can easily develop severe liver dysfunction suddenly,[16,17] so that all HIV/HCV co-infected patients should be carefully followed up so as not to miss the chance for LT. Also, Murillas *et al.* reported that Model for End-Stage Liver Disease (MELD) score is the best prognostic factor in HIV-infected patients,[18] so that HIV/HCV co-infected patients may be considered for LT before MELD score increase to achieve comparable results with HCV mono-infected patients. Several studies showed the aggressive fibrosis in HIV/HCV co-infected patients compared with HCV mono-infected patients,[19,20] but the mechanism of this aggressive fibrosis remains unclear. Recently, transient elastography or acoustic radiation force impulse imaging to check for liver stiffness has been introduced as an effective and non-invasive modality to determine patients' candidacy for LT.[21–23]

Count of $CD4^+$ T lymphocytes

Generally, the count of $CD4^+$ T lymphocytes has been required to be more than 200/μL to perform general elective surgeries in HIV-infected patients,[24] but in HIV/HCV co-infected patients, current studies show that a count of more than 100/μL is acceptable,[25,26] because patients generally have portal hypertension which can cause pancytopenia. In such patients, the ratio of CD4/CD8 is reported to be a feasible marker to predict postoperative complications including opportunistic infections. When the ratio is less than 0.15, the incidence of infectious complications is significantly higher.[27]

Preoperative infections

In regard to latent opportunistic infections that occur before LT, they are not absolute contraindications when they can be expected to be controlled.[28] Infections regarded as contraindications for LT included uncontrollable multidrug resistance HIV infection, chronic *Cryptosporidium enteritis*, progressive multifocal leukoencephalopathy and lymphoma.[29]

MANAGEMENT OF HIV/HCV IN LT

Management of HIV

THE NUMBER OF HIV RNA copies before LT is suggested as an independent risk factor of postoperative mortality, so that HIV should be controlled sufficiently before LT.[30] Accordingly, in the patients who are under consideration to receive LT, ART can be safely stopped before LT because HIV is generally well-controlled for a long period by ART. After LT, ART should be restarted as soon as possible because HIV RNA appears at 3–30 days after ART is stopped,[31] but the timing of restart of ART depends on the patient's condition, including liver function.[32] As long as the liver function has not fully recovered, or partial liver graft such as in LDLT has not sufficiently regenerated yet, ART cannot be started. Castells *et al.* reported in their case–control study that ART was started at a median of 8 days after LT (range, 4–28 days).[33] In principle, the ART administrated after LT should be the same as the pretransplant regimen, but the majority of ART drugs including protease inhibitor (PI) and non-nucleoside reverse transcriptase inhibitor (NNRTI) have interactions with calcineurin inhibitors

(CNI) or mammalian target of rapamycin (mTOR),[34] so that the monitoring of blood levels of immunosuppression is extremely important to avoid infectious complications or rejection. Currently, a novel HIV-1 integrase inhibitor, raltegravir (RAL), is expected to be a feasible drug because it has no interactions with CNI, unlike other drugs.[35,36]

Management of HCV

The treatment strategy for HCV in HIV/HCV co-infected patients is the same as in HCV mono-infected patients. Combination therapy of pegylated interferon (PEG IFN) and ribavirin is the standard treatment both before and after LT. The timing of the induction therapy after LT is controversial. A Tokyo group proposed early induction as a preemptive therapy before patients develop hepatitis,[37] while several other reports showed favorable results when the treatment was administrated only after the development of hepatitis was confirmed by liver biopsy.[38,39] Theoretically, the treatment should be started as soon as possible, because in HIV/HCV co-infected patients, HCV recurrence may be accelerated in an immunocompromised state.[30,40] The novel protease inhibitor, telaprevir, is currently introduced as an effective drug to achieve sustained viral response of 70%, even in genotype 1b, with PEG IFN/ribavirin in a non-transplant setting,[41] but this drug is metabolized via cytochrome P450 as a substrate, as are CNI and various protease inhibitors of ART for HIV. Close monitoring of the CNI trough level should be performed, and although triple therapy with telaprevir/PEG IFN/ribavirin is currently reported to be effective to prevent HCV recurrence after LT in HCV mono-infected cases, special attention should be paid when this regimen is adapted in HIV/HCV co-infected patients.

IMMUNOSUPPRESSION

AS PREVIOUSLY MENTIONED, many factors including ART, anti-HCV treatment and an HIV-related immunocompromised state make post-LT immunosuppressive treatment difficult. Many ART drugs, both PI and NNRTI, cause instability in the blood concentration of CNI through the cytochrome P3A4 (CYP3A4)-related metabolism. Most PI cause the overconcentration of CNI by inhibiting CYP3A4, while most NNRTI cause decreased levels of CNI by stimulating CYP3A4.[29,42] As mentioned earlier, RAL is introduced as a key drug in LT in HIV positive patients, because the metabolism of this drug is not related to CYP450, so it does not affect the blood concentration of CNI. Several reports have demonstrated both the *in vitro* and *in vivo* effectiveness of rapamycin in reducing HIV replication,[43-45] and Di Benedetto *et al.* found that rapamycin monotherapy was significantly beneficial in long-term immunosuppression maintenance and HIV control after LT.[46] Mycophenolate mofetil is expected to be an effective immunosuppressive drug because of its efficacy in reducing HIV infection by both virological and immunological mechanisms.[47-49] Using these drugs, a more effective regimen of immunosuppression with ART may be established.

In regard to the steroid, several studies proposed that a steroid-free regimen can be safely applied and effective in LT for HCV cirrhosis. Also, in HIV/HCV co-infected patients, steroid-free protocol may be beneficial to prevent both HIV and HCV recurrence after LT.[50,51]

CONCLUSIONS

LIVER TRANSPLANTATION FOR HIV/HCV co-infected patients remains challenging, but with recent developments in perioperative management and novel drugs for both HIV and HCV, the results are likely to be improved.

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ELSEVIER

Analysis of the Hepatic Functional Reserve, Portal Hypertension, and Prognosis of Patients With Human Immunodeficiency Virus/Hepatitis C Virus Coinfection Through Contaminated Blood Products in Japan

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ABSTRACT

Background. As the survival of human immunodeficiency virus (HIV)-infected individuals has improved due to the widespread use of antiretroviral therapy, the mortality rate due to hepatitis C virus (HCV)-related liver disease has increased in HIV/HCV-coinfected patients.

Aim. The aims of this study were to establish the appropriate therapeutic strategy for HIV/HCV-coinfected patients by evaluating the liver function, including the hepatic functional reserve and portal hypertension, and to investigate the prognosis of HIV/HCV-coinfected patients in Japan.

Patients and Methods. In addition to regular liver function tests, the hepatic functional reserve of 41 patients with HIV/HCV coinfection was evaluated using the indocyanine green retention rate and liver galactosyl serum albumin-scintigraphy. The data for 146 patients with HIV/HCV coinfection through blood products were extracted from 4 major HIV centers in Japan. In addition to liver function tests, the platelet counts (PLT) were evaluated as a marker of portal hypertension.

Results. In spite of the relatively preserved general liver function test results, approximately 40% of the HIV/HCV-coinfected patients had an impaired hepatic functional reserve. In addition, while the albumin and bilirubin levels were normal, the PLT was <150,000/μL in 17 patients. Compared with HCV mono-infected patients with a PLT <150,000/μL, the survival of HIV/HCV-coinfected patients was shorter (HCV, 5 years, 97%; 10 years, 86% and HIV/HCV, 5 years, 87%; 10 years, 73%; $P < .05$).

Conclusion. These results must be taken into account to establish an optimal therapeutic strategy, including the appropriate timing of liver transplantation in HIV/HCV-coinfected patients in Japan.

FROM 1970 until the early 1980s, blood products were imported to Japan, and contaminated blood products were unknowingly used to treat patients with hemophilia. It was later revealed that these patients were sometimes infected with both human immunodeficiency virus (HIV) and hepatitis C virus (HCV; HIV/HCV coinfection) [1].

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However, as the survival of HIV-infected people has improved due to the widespread use of antiretroviral therapy, the mortality due to HCV-related liver disease has increased in HIV/HCV-coinfected patients [2,3].

The main aims of this investigation were to investigate the status of portal hypertension and the prognosis in HIV/HCV-coinfected patients, and to establish an appropriate therapeutic strategy for HIV/HCV-coinfected patients, including the timing of liver transplantation, in Japan.

PATIENTS AND METHODS

Routine hematology and blood chemistry tests (general liver function), abdominal ultrasonography, and contrast-enhanced computed tomography (CT) were performed for 30 patients with HIV/HCV coinfection at Nagasaki University Hospital. To investigate the hepatic functional reserve, liver GSA-scintigraphy and the indocyamine green retention test at 15 minutes were performed. In addition, upper gastrointestinal tract endoscopy to diagnose gastroesophageal varices was performed.

The data of the 146 patients who had acquired HIV/HCV coinfection through blood products were extracted from 4 major HIV centers in Japan, including the AIDS Clinical Center, Osaka National Hospital, Yokohama Municipal Hospital, and Kyushu Medical Center. In addition to liver function tests, platelet counts (PLT) were evaluated as a marker of portal hypertension. As a control, HCV mono-infected patients from Nagasaki Medical Center were used for comparison.

RESULTS

In spite of the relatively well-maintained general liver functions, approximately 40% of the HIV/HCV-coinfected patients had an impaired hepatic functional reserve (Table 1). In addition, in spite of maintained albumin and bilirubin levels, the PLT was <150,000/μL in 17 coinfected patients, indicating the presence of ongoing portal hypertension.

Even with Child-Pugh A liver function, the HIV/HCV-coinfected patients showed a worse prognosis than the HCV mono-infected patients. The prognosis was especially poor in those with lower PLT than in the patients with a normal PLT (Table 2). When compared with HCV mono-infected patients with a PLT <150,000 μL, the survival of HIV/HCV-coinfected patients was much shorter (HCV, 5 years, 97%; 10 years, 86% and HIV/HCV, 5 years, 87%; 10 years, 73%; $P < .05$).

Table 1. Patient Characteristics

Child-Pugh A/B/C	38 (93%)/1 (2%)/2 (5%)
ICG R15 (%)	
<10/10–20/20–30/30<	24 (59%)/8 (20%)/3 (7%)/6 (14%)
GSA schincigram LHL15	
>0.9/0.8–0.9/0.8>	28 (69%)/6 (15%)/7 (16%)
Liver configuration on CT	
Normal/CH/LC	10 (24%)/17 (42%)/14 (34%)
Splenomegaly	
Yes/no	26 (63%)/15 (37%)
Esophageal varices	
Yes/no	13 (32%)/28 (68%)

CH, chromic hepatitics; LC, liver cirrhosis.

Table 2. Patient Survival after Diagnosis

	5Y OS	10Y OS	
HCV mono-infection (Child-Pugh A)	97%	86%	
HIV/HCV coinfection (Child-Pugh A)			
PLT > 150,000	94%	85%	
PLT < 150,000	87%	73%	$P < .05$ vs HCV mono-infection

5Y OS, 5 year patient survival; 10Y OS, 10 year patient survival.

DISCUSSION

In HIV/HCV-coinfected patients, liver failure due to HCV hepatitis was previously reported to be enhanced by antiretroviral therapy ART-related hepatotoxicity, especially manifesting as noncirrhotic portal hypertension (NCPH) [4,5]. One of the ART drugs, Didanosin (DDI), has been suspected to be related to the serious morbidity observed in coinfected patients [6]. Thus, not only in patients with deteriorated liver function, such as in Child-Pugh B or C cases, but also even in Class A cases, the patients' liver function can easily deteriorate abruptly [7]. The natural course of pure NCPH is unknown because it can be modulated by HCV or other causes, and has only been reported as case series. An important study of "NCPH in HIV Mono-Infected Patients Without HCV" was published in 2012 [8]. All 5 patients had portal hypertensive symptoms, such as ascites or variceal bleeding, after receiving antiretroviral therapy.

Therefore, all HIV/HCV-coinfected patients should be carefully followed up so as not to miss an opportunity for liver transplantation (LT) [9]. The prognosis for HIV/HCV-coinfected patients was reported to be worse than that for HCV mono-infected patients [10]. In the present study, coinfected patients with a PTL <150,000 μL had an especially poor prognosis, with a shorter survival than mono-infected patients. Our results should be taken into account to establish a therapeutic strategy, while also considering the appropriate timing of LT in HIV/HCV-coinfected patients.

In 2013, based on the evidence of rapid progression of the liver cirrhosis and portal hypertension in patients with HIV/HCV coinfection, a rank-up system for the waiting list for deceased donor LT was set up in Japan. Even HIV/HCV-coinfected liver cirrhotic patients with Child-Pugh class A can be listed for LT as "point 3" because of the NCPH (noncirrhotic portal hypertension) nature. Coinfected patients with Child-Pugh class B and C disease can be listed as "point 6" and "point 8," respectively, based on the data collected by the HIV/acquired immunodeficiency syndrome (AIDS) project team of the Ministry of Health, Labor, and Welfare of Japan, and the published literature [11]. This primarily covers victims who received contaminated blood products for hemophilia.

Future perspectives on LT for HIV/HCV coinfection include the following: new anti-HCV agents should be

developed to improve the control against HCV; new ART drugs, such as Raltegravir, should facilitate post-transplantation immunosuppressive therapy; noninvasive tests for portal hypertension, such as the fibroscan, should be performed for hemophilic patients; and the development of guidelines for the management hemophilia in the perioperative period should facilitate better outcomes.

In conclusion, the present results should be taken into account to establish an optimal therapeutic strategy, including the appropriate timing of LT in HIV/HCV-coinfected patients.

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＜原　著＞

血液製剤によるHIV-HCV重複感染者の予後—肝移植適応に関する考察—

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要旨：【背景】anti-retroviral therapyにより，HIV/HCV重複感染者の死亡の原因として，HCVによる肝疾患の割合増加に加え，非硬変性門脈圧亢進症の報告が増えている．【目的】本邦での血液製剤によるHIV/HCV重複感染者での門脈圧亢進症の実態を検証し，肝移植適応の再評価を考える．【方法】国内HIV診療主要4施設での血液製剤によるHIV/HCV重複感染者でChild分類Aの184例のデータを解析し，門脈圧亢進症の指標としての血小板数で生存率を比較した．【結果】HIV/HCV重複感染患者内では，血小板数数15万/μLの分類にて患者生存に有意差がみられた．同じChild分類Aで，HIV/HCV重複感染患者のなかで血小板数15万/μl未満の症例とHCV単独感染患者の症例と予後を比較したところ，HIV/HCV重複感染患者の予後は有意に不良であった．【考察】HIV/HCV重複感染患者はHCV単独感染患者よりも門脈亢進症進行例では予後不良で，Child分類Aでも肝移植待機リストへの登録を考慮しうると考えられた．

索引用語：HIV/HCV重複感染　非硬変性門脈圧亢進症　HAART　血友病　肝移植

はじめに

Anti-retroviral therapy(ART)によるHIVコントロールの改善により，HIV/HCV重複感染者の死亡の原因として，HCVによる肝疾患の割合が増加している[1)]．その原因として，C型慢性肝炎による非代償性肝不全に加えて，海外よりHIV感染者の非硬変性門脈圧亢進症の報告がなされてきている[2)3)]．究極的には，これらの患者は肝移植の適応となる可能性があり，その成績の報告もみられるが，HCV単独感染に対する移植成績と比較して芳しくない，とするものが多い[4)5)]．HIV/HCV重複感染者に対する肝移植の適応は，大きく2つの病態，1. 非代償性C型肝硬変，2. ARTなど薬剤性肝障害などによる非硬変性門脈圧亢進症，に分けられると考えられる．実際には，ほぼ全例がARTを施行されているため，これらの病態が混在するため，肝移植の適応とタイミングを困難なものにしている．

我々は以前，血液製剤によるHIV/HCV重複感染者の肝機能検査を施行し，見かけの肝機能検査ではChild Aの患者の中にも，門脈圧亢進症の患者が含まれていることを報告した[6)]．血液製剤によるHIV/HCV重複感染者には，Child Aであるにもかかわらず，内視鏡所見にてRed-Color sign陽性の食道静脈瘤が発見された患者もおり，通常のHCV肝硬変とは異なる病態が存在することが示唆されていたが，国内でのHCV単独感染者との予後の差異ははっきりとは報告されていない．

今回，HIV/HCV重複感染者の肝不全以外の門脈圧亢進症の状態にて，その生命予後を解析し，さらには，HCV単独感染者との予後を比較することにより，HIV/HCV重複感染者の肝移植適応についての再評価をすることを目的に本検討を行った．

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