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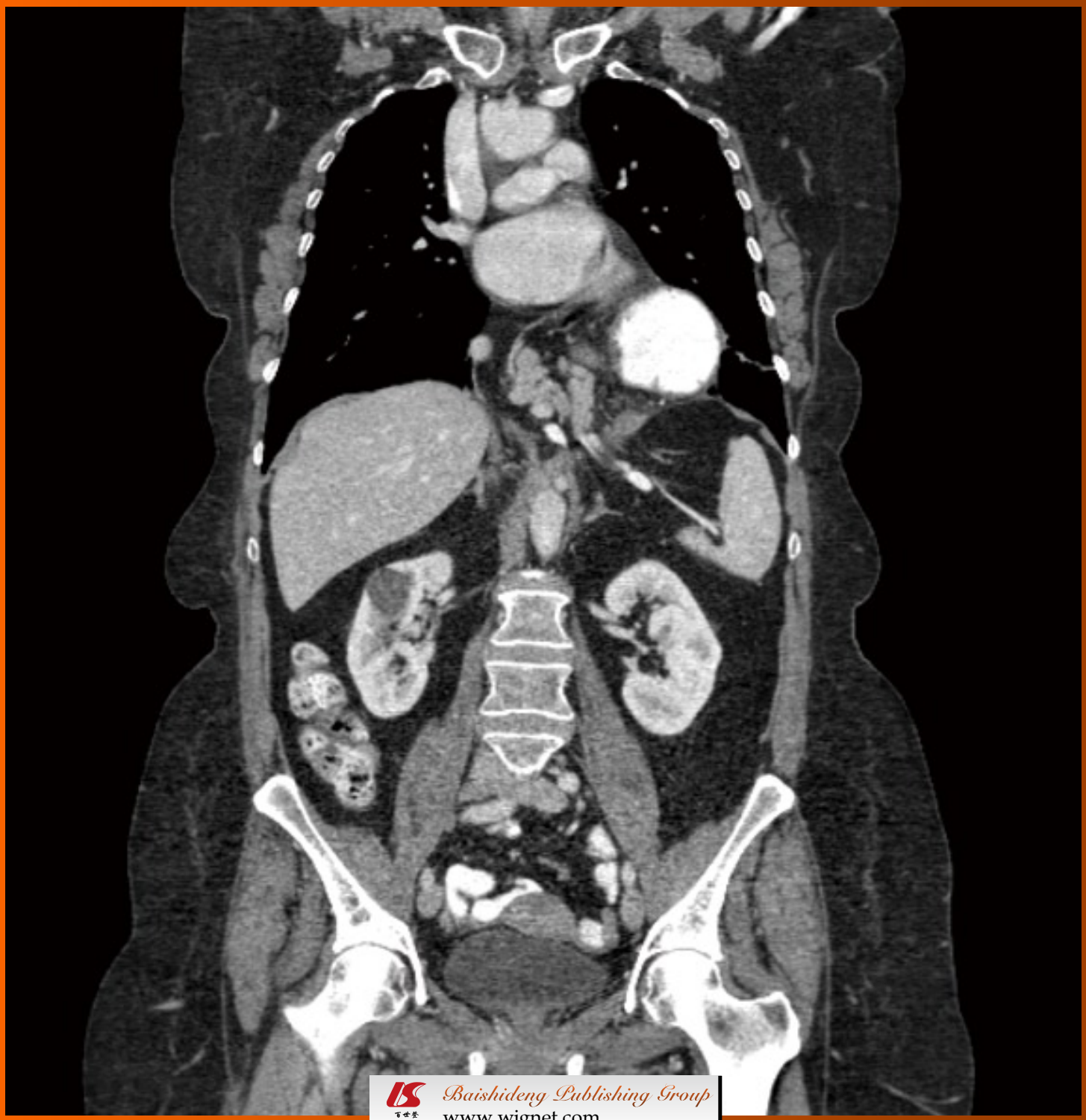

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EDITORIAL

Liver transplantation in HCV/HIV positive patients

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Abstract

Since the introduction of highly active antiretroviral therapy (HAART) in 1996 for human immunodeficiency virus (HIV)-infected patients, the incidence of liver diseases secondary to co-infection with hepatitis C has increased. Although data on the outcome of liver transplantation in HIV-infected recipients is limited, the overall results to date seem to be comparable to that in non-HIV-infected recipients. Liver transplant centers are now accepting HIV-infected individuals as organ recipients. Post-transplantation HIV replication is controlled by HAART. Hepatitis C re-infection of the liver graft, however, remains an important problem because cirrhotic changes of the liver graft may be more rapid in HIV-infected recipients. Interactions between the HAART components and immunosuppressive drugs influence drug metabolism and therefore meticulous monitoring of drug blood level concentrations is required. The risk of opportunistic infection in HIV-positive transplant patients seems to be similar to that in HIV-negative transplant recipients.

Key words: Hepatitis C virus; Human immunodeficiency virus; Living donor liver transplantation; Interferon; Rivabirin

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INTRODUCTION

Liver transplantation is an established standard therapeutic option for end-stage liver disease (ESLD) with a 1 year survival rate exceeding 80%[1]. Before the introduction of highly active antiretroviral therapy (HAART) in 1996, the results of transplantation for patients with human immunodeficiency virus (HIV) were poor[2-5] and HIV was considered a contraindication in most centers[6-8]. The 3 year survival rates were around 45% and the most frequent cause of death was acquired immune deficiency syndrome (AIDS)[2-5].

Since the introduction of HAART, HIV-related morbidity and mortality have dramatically decreased from 20-30 to 1.5-2.5 per 100 person-years[9,10]. In the setting of the improved prognosis in the HIV-infected population, the focus has turned to the morbidity and mortality associated with hepatitis C (HCV) and ESLD[11-15]. As HAART has changed HIV infection to a chronic condition, transplant centers around the world are slowly becoming less reluctant to accept HIV-positive patients as transplant recipients for both medical and ethical reasons[16-19] and liver transplantation is now considered a possible therapeutic option for these patients. The aim of the present review is to explore the new indications for liver transplantation in HIV/HCV co-infected patients.

EPIDEMIOLOGY OF HIV AND HAART

An estimated 33 million persons are currently living with HIV infection worldwide, including 16 million women and 2 million children less than 15 years of age[20]. In 2008, 2 million adults and 0.4 million children were newly infected and 2 million died from HIV infection. HIV infection is transmitted *via* heterosexual contact, intravenous drug use and homosexual contact.

Liver-related diseases among HIV-infected persons are caused by hepatitis B virus and/or HCV co-infection, hepatotoxic medication, alcohol and illegal drug use. Of these, co-infection with HCV is the most frequent cause of liver disease in HIV patients and substantially contributes to morbidity and mortality[21,22]. HIV and HCV usually share common routes of transmission. Approximately 4 to 5 million HIV-infected persons are co-infected with HCV. The prevalence of co-infection differs by geographical region and by patient demographical and behavioral characteristics ranging from 1%-5% in persons who acquired HIV infection by heterosexual or homosexual contact to 70%-95% in patients with current or former injecting drug use and transfused hemophiliac patients[23].

HCV MANAGEMENT BEFORE TRANSPLANTATION

There are several challenges in the management of HIV/HCV co-infected patients who require transplantation. The first is to minimize mortality while on the organ transplant waiting list because such patients frequently have a more rapid progression from the first decompensation to death. The interval between the first manifestation of liver decompensation and death is 16 mo for HIV/HVC co-infected versus 48 mo for HIV mono-infected patients. Prognostic factors after first decompensation include age, severity of liver disease [model for end-stage liver disease (MELD) score] and the nature of the decompensation event[24].

HCV/HIV co-infections adversely affect each other: HIV infection accelerates the progression of HCV disease by increasing HCV viremia, causing cellular immunodeficiency, increasing the risk of liver fibrosis and cirrhosis and leading to the rare fibrosing cholestatic hepatitis[25,26]. HCV may adversely affect the course of HIV infection[27,28] by reducing the efficacy of antiretroviral treatment and increasing the rate of antiretroviral medication-related hepatotoxicity[25,29]. The effect of antiretroviral therapy to reduce liver-related mortality in HCV co-infected persons is controversial[10,30]. Some co-infected persons are not eligible for HCV treatment due to somatic or psychosocial comorbidities, contraindications for HCV drugs and decompensated cirrhosis[31].

INDICATIONS FOR TRANSPLANTATION

Table 1 showed the inclusion criteria for liver transplantation. The acceptance criteria for liver transplantation in HIV-positive recipients continue to evolve with increased experience with the co-infected population. In deceased donor liver transplantation, there are ethical concerns regarding the use of a scarce resource for a group of recipients with unknown survival duration. The acceptance criteria have gradually expanded, however, based on acceptable initial results[32-34].

The best timing for liver transplantation from the point of view of liver damage (Child-Pugh or MELD) is unknown. Pre-transplant survival for liver candidates is reported to be poorer in HIV-infected individuals compared with others awaiting liver transplantation, despite equivalent MELD scores[24,35]. In one study, significantly fewer HIV patients (26% of 58) survived on a liver transplant waiting list compared to candidates without HIV (63% of 860)[36]. Although more rapid deterioration in HIV co-infected patients may be the cause[37], death in that study was not associated with MELD, viral load, CD4, ability to tolerate medications or HCV progression. Further studies are necessary to understand the risk factors for death in HIV-positive patients on the liver transplant waiting list[38].

The inclusion criteria of an NIH sponsored study in the USA[39] are AIDS-related opportunistic infections or cancers that are resolved by sufficient treatment prior to transplant. CD4 counts should be greater than 100/mL for those without a history of opportunistic infection and greater than 200/mL for those with a history of opportunistic infection completely treated before transplantation. These requirements may be applied 3 to 4 mo prior to transplantation. Opportunistic infections include chronic cryptosporidiosis, progressive multifocal leukoencephalopathy and multi-drug resistant systemic fungal infections. Patients with a history of AIDS-associated lymphoma should be excluded. Most clinical trials include individuals with a history of resolved cutaneous Kaposi's sarcoma if a recent high-resolution computed tomography scan reveals no evidence of pulmonary lesions[40].

In a Spanish consensus statement[41], the criteria are similar except for the requirement of CD4 cell counts greater than 350/mL in patients that do not fulfill the HAART criteria. Ragni *et al*[32] noted that cumulative survival among HIV-positive recipients is similar to that of age- and race-comparable HIV-negative recipients.

Another potential conflict regarding the absolute requirement for a CD4 cell count greater than 100/mL relates to the use of interferon therapy[42]. In a recent series at Paul Brousse Hospital[42], CD4 cell counts greater than 150/mL were observed in 7 patients and 6 of these 7 patients developed severe chronic HCV. The use of interferon can cause a transient decrease in CD4 cell counts. The absolute CD4 cell count prior to interferon therapy should be taken into account in the decision regarding liver transplantation.

HIV-RNA should be undetectable at transplantation. Unfortunately, however, most recipients cannot tolerate HAART therapy due to its hepatotoxicity. When an undetectable HIV viral load is not achievable, an experienced HIV clinician should predict the ability to

Table 1 Inclusion criteria for liver transplantation

NIH sponsored study in the USA[94]	1. No AIDS-related opportunistic infections 2. CD4 counts should be > 100/mL for those without a history of opportunistic infection and > 200/mL for those with a history of opportunistic infection. 3. HIV-RNA should be undetectable. In the event that an undetectable HIV viral load is not achievable as a result of drug-induced hepatotoxic, an HIV clinician should predict the ability to control the HIV virus post-transplantation.
Spanish criteria[41]	1. No opportunistic infections 2. CD4 counts > 100/mL 3. HIV-RNA should be undetectable or suppressible with antiretroviral therapy.
O'Grady[95]	1. Absence of AIDS-defining illness after immune reconstitution 2. CD4 counts should be > 200/mL or > 100/mL in the presence of portal hypertension. 3. Absence of HIV viremia 4. Antiretroviral therapeutic options available if the HIV disease reactivates

AIDS: acquired immunodeficiency syndrome; HIV: human immunodeficiency virus.

control HIV after the transplantation, based on a complete review of the antiretroviral history, HIV RNA history and resistance testing[43]. This issue is more controversial for patients with CD4 counts greater than 100/mL but who have detectable HIV that is multi-drug-resistant. Currently, most centers still consider this an exclusion criterion, although with more data demonstrating the safety of immunosuppression in the HIV-positive patient as well as an increasing number of antiretroviral agents, this exclusion criterion may be liberalized on a case by case basis[44].

SURGICAL RESULTS

Survival

Survival at 1 year post-transplantation ranges from 58% to 89% (Table 2). Ragni *et al*[32] reported 1, 2 and 3 year survival rates of 87%, 73% and 73% in 24 HIV-positive patients which were not statistically different from age and race-matched HIV-negative patients. Similar results[45] were reported based on an analysis of 15 HIV-positive recipients with a 3 year survival rate of 73% compared to 79% for HIV-negative recipients. Neff *et al*[33] reported that graft and patient survival rates in HIV-positive patients are similar to that of HIV-negative patients transplanted for the same indication. Studies that analyzed liver transplantation for a variety of reasons showed excellent outcome for ESLD irrespective of underlying HIV infection. Another report showed lower survival rates in 27 patients with 1, 3 and 5 year survival rates of 67%, 56% and 33% respectively[35]. A Spanish series found HIV-positive patient survival rates of 90% at 1 year and 67% at 3 years[46].

Two recently published studies comparing survival in HCV/HIV-co-infected and HCV-mono-infected transplant recipients reported a significantly lower survival rate in co-infected patients[35,42]. In a French study of 35 HCV/HIV-infected and 44 HCV-infected recipients, 2 and 5 year patient survival rates were statistically lower in co-infected patients, 73% *vs* 91% and 51% *vs* 81% respectively[42]. MELD was the only significant predictor for mortality and HIV infection did not predict survival. In a US study[35] of 27 HCV/HIV-infected and 41 HCV-infected recipients, the 3 and 5 year patient survival rates tended to be lower in co-infected patients, 56% *vs* 72% and 33% *vs* 72% respectively.

In a review of the United Network for Organ Sharing liver transplant database (between 1997 and 2006)[47], the 2 and 3 year survival rates in 138 HIV-positive recipients were 70% and 66% respectively. These outcomes were slightly worse than the 2 and 3 year survival rates of 81% and 77% respectively of the 30 520 HIV-negative recipients ($P < 0.05$). The overall results of liver transplantation in HIV-positive patients are favorable but large prospective clinical trials providing insight into survival and clinical management are required.

Complications

Rejection episode rates in HIV-positive recipients are not different from those of HIV-negative recipients[42]. HIV-associated opportunistic infections and AIDS-related diseases are uncommon. Only a single case of Kaposi's sarcoma and multicentric Castleman's disease has been reported[48]. Death from infectious complications, however, is reported to be more frequent in HIV-positive recipients[45]. Importantly, no HIV disease progression has been reported and HIV replication is efficiently controlled by HAART[32,35,42,49,50]. An exception, though, is the report by Schreibman *et al*[45] that HIV-infected patients experienced significantly higher mortality from infectious complications (4 of 15 recipients). The results of HCC cases within Milan-criteria are encouraging and there are no reports of recurrences[33,35,45,48,49,51-54].

Prognostic factors

A recent report[42] identified high MELD scores at the time of transplant as predictive of a poor outcome. Early and severe HCV graft re-infection is a major determinant influencing post-transplant outcome[32,34,48,51-53,55-58]. Another report[35] showed that HAART intolerance is a significant predictor. Other risk factors include low pre-transplant body mass index and African American race[59].

POSTOPERATIVE MANAGEMENT

Immunosuppression and HAART

Cyclosporine (CyA) inhibits CD4 cell apoptosis and

Table 2 Survival, hepatitis C virus recurrence, and therapy in hepatitis C virus/human immunodeficiency virus co-infected liver transplant patients

References	Institution	Years	*n*	Genotypes	Time to recurrence (mo)	IFN and RBV doses	Time to therapy (mo)	SVR (%)	FCH (*n*)	Death (*n*)	Follow up (mo)
Prachialis 2001[58], Norris 2004[56]	King's College	95-03	7	NA	5	From 2 wk: IFN, 3 MU tiw and RBV, after 3 wk: Peg- IFN 180 μg/wk	0.5 (*n* = 2), 6 m (*n* = 1)	0	2	5	12
Rafecas 2004[51]	Hospital Universitari de Bellvitge	02-03	4	4, 1b, 1b, 1a	7	NA	5 (*n* = 3)	0	0	0	17
Moreno 2005[55]	Hospital Ramon (Madrid)	02-03	4	NA	1-6	NA	1-6	0	1	1	14-18
Radecke 2005[57]	University Hospital Essen	98-01	4	NA	3-8	NA	NA	NA	1	2	10-61
Vogel 2005[48]	Bonn University	97-04	4	1a (*n* = 2), 2a/2c, 3a	1-8	NA	5-15	50	0	0	NA
Neff 2003[33], Fung 2004[71], de Vera 2006[35]	Thomas E Starzl Transplantation Institute	97-05	27	1 (*n* = 16), 2 (*n* = 2), 3 (*n* = 1)	6	IFN and Peg -IFN, RBV 800 mg/d	2-50	27	6	14	27+-5
Castells 2007[53]	Hospital Universitari Vall d'Hebro'n (Barcelona)	02-05	9	1 (*n* = 7), 3 (*n* = 2)	3+-3	Peg-IFN 1.5 μg/kg, RBV 800-1000 mg/d	NA	14	0	1	15+-13
Schreibman 2007[45]	University of Miami	99-06	8	NA	NA	NA	NA	25	0	2	6-74
Vennarecci 2007[52]	Regina Elena Cancer Institute (Rome)	02-06	10	NA	NA	NA	NA	10	3	6	5-46
Wojcik 2007[88]	Medical University of Lodz (Poland)	97-06	4	1a (*n* = 2), 2a, 3a	1-3	Peg-IFN 180 μg/wk, RBV 200-1000 mg/d	1-3	100	0	0	21-54
Duclos-Vallee 2005[50], 2008[42]	Paul Brousse	99-05	35	1 (*n* = 20), 2 (*n* = 1), 3 (*n* = 9), 4 (*n* = 4)	0-3	Peg-IFN 50-180 μg/wk, and RBV 400-800 mg/d	0-3	16	3	13	44+-83
Stock 2003[43], Roland 2008[96]	University of California, San Francisco	00-03	6	NA	1-11	NA	1-11	NA	2	4	NA
Testillano 2009[97]	Hospital de Cruces (Vizcaya)	01-07	12	1 (*n* = 8), 3 (*n* = 4)	NA	NA	NA	50	2	4	NA
Hughes 2010[98]	Emory University School of Medicine	NA	5	1	2-12	Peg-IFN 135-180 μg/wk, and RBV 600 mg/d	2-12	40	2	2	6-48
Di Benedetto 2008[54], 2010[99]	University of Modena and Reggio Emilia	03-	13	1 (*n* = 3), 3a (*n* = 7), 4 (*n* = 3)	2-16	Peg-IFN 50-180 μg/wk, and RBV 400-800 mg/d	NA	0	2	4	1-14

HCV: hepatitis C; IFN: interferon; Peg-IFN: pegylated interferon; RBV: ribavirin; SVR: sustained virological response; NA: not available; FCH: fibrosing cholestatic hepatitis.

p55Gag processing by binding to cyclophilin A[60-62]. Some beneficial effects of the combination of HAART and CyA have been demonstrated [63] but low-dose CyA exhibits no benefits in patients with stable early HIV disease[64].

Mycophenolate mofetil (MMF) inhibits inosine monophosphate dehydrogenase and depletes the pool of deoxyguanosine triphosphate. MMF is expected to reduce HIV infection by both virological and immunological mechanisms[65-70]. Antagonism due to the inhibition of thymidine kinase has been reported with MMF plus the thymidine analogues zidovudine and stavudine. Mitochondrial toxicity of nucleoside reverse transcriptase inhibitors (NRTI) is potentially augmented by the effect of MMF. Mitochondrial toxicity and lactic acidosis are linked to the use of didanosine, stavudine and zalcitabine and are attributed to damage to mitochondrial polymerase[71].

Sirolimus (SRL) downregulates the expression of chemokine receptor 5 on T-cells which is required for the propagation of macrophage tropic strains of HIV-1[72]. SRL inhibits the progression of Kaposi's sarcoma and primary effusion lymphoma[40,73].

Interactions between HAART drugs [protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs)] and calcineurin inhibitors or SRL are well described[74,75]. NNRTIs induce the expression of cytochrome P450, family A gene (CYP3A)[74]. PIs inhibit the production of cytochrome P450 enzymes or P-glycoprotein. CyA, tacrolimus and SRL are substrates of CYP3A4 and P-glycoprotein. PIs, therefore, increase

blood levels of CyA, tacrolimus and SRL, requiring dose reductions of 85 % to 99%[74-78] (Table 2). HAART without PIs may have fewer significant interactions with CyA, tacrolimus and SRL[79].

Efavirenz (NNRTI) induces the production cytochrome P450 enzymes[74] but when efavirenz or a nucleside analogue combination are added to the treatment regimen, little change in the dosing of tacrolimus is required. In contrast, nelfinavir and lopinavir/ritonavir inhibit the first pass metabolism of tacrolimus, resulting in an increase in its elimination half-life and a reduction in its oral clearance[75].

Monitoring for HAART-associated hepatotoxicity is important. The use of NRTIs is associated with hepatic steatosis, mitochondrial dyfunction and fulminant hepatic failure[80,81]. PI-related hepatitis occurs in 5 % to 9% of patients[82] and has an aggressive course in HCV-positive patients[83]. Liver dysfunction is observed in up to 30% of patients taking NNRTIs[84]. A French study[50] reported evidence of mitochondrial dysfunction in 5 patients with severe recurrent HCV, with most patients developing mitochondrial dysfunction while on stavudine or stavudine plus didanosine and in patients concurrently using ribavirin.

To maintain virological control of HIV infection, quantitative HIV RNA and CD4 cell counts should be measured with the first assays at 1 mo after transplant and subsequent studies every 2 to 3 mo thereafter. If patients have persistent HIV viremia, resistance testing should be performed to determine treatment options[59].

HCV management

HCV recurrence is a significant problem following transplantation[35,42,50] although there are reports of spontaneous clearance of HCV post-transplantation[85]. HCV recurrence appears earlier in HIV-infected HCV patients than in HIV-uninfected HCV patients (median time 2 mo) and the rate of the progression of fibrosis is enhanced. In one controlled study, the proportion of patients with bridging fibrosis or cirrhosis at 2 and 5 years post-transplantation was 28% and 48% respectively for HCV-HIV co-infected patients versus 10% and 18% respectively in HCV-mono-infected patients[42]. HCV recurrence is attributed to graft loss (Table 2). The prognosis for patients with fibrosing cholestatic hepatitis is poor[42,53].

Pegylated interferon and ribavirin combination therapy is the mainstay for the management of recurrent HCV disease. The mitochondrial toxicity of HAART, however, increases when used in conjunction with ribavirin[86,87]. The rates of a sustained virological response (SVR) are low in co-infected patients, apart from one recent study that showed 100% SVR[88]. SVR occurs in only 11% to 27% of treated patients[35,42,88,89] (Table 2). Biochemical responses are obtained in more than half of patients but histological stabilization or improvement is rare in virological non-responders. Tolerability of the full dose therapy is limited, contributing to the poor SVR rates.

In the HCV-mono-infected population, viral factors (a high viral load before and after transplantation) and host factors (donor age > 50 years) are associated with a more severe recurrence of HCV[90]. Corticosteroid boluses are also associated with a severe HCV recurrence and should be avoided. Rapid corticosteroid withdrawal after transplantation should be avoided and may be associated with a more rapid progression of fibrosis[91]. The effects of immunosuppressant agents, including tacrolimus, CyA, MMF, anti-interleukin 2 receptor antibodies, SRL and azathioprine, on the severity of HCV recurrence are controversial[90].

Prophylaxis for opportunistic infections[59]

The risk of opportunistic infection in HIV-positive transplant patients seems to be similar to that of HIV-negative transplants. The ability to suppress HIV viral loads in patients on HAART is associated with the stabilization of, or improvement in, CD4 counts, which decreases opportunistic infection in HIV-positive patients[92].

Prophylactic regimens for preventing opportunistic infection include those against *Pneumocystis jirovecii* with trimethoprim-sulfamethoxazole, toxoplasmosis (for CD4 counts < 100), Mycobacterium avium complex (for CD4 counts < 50) and histoplasmosis and coccidioidomycosis. For patients at risk for primary toxoplasmosis due to donor infection, trimethoprim-sulfamethoxazole should be considered for primary prevention; dapsone or atovaquone in combination with pyrimethamine can be considered for patients intolerant to trimethoprim-sulfamethoxazole[71].

CONCLUSION

Clinical trials[35,41,48,56,71,88] suggest that liver transplantation in HIV/HCV co-infected patients is safe and that HIV infection does not influence the outcome. The United Network for Organ Sharing no longer considers HIV an absolute contraindication for transplantation. The French agency for Organ Distribution[93] has also concluded that there is no reason to consider HIV a contraindication. Spain has published a national policy[41] advocating liver transplantation for patients with HIV infection within defined criteria.

To improve the results of liver transplantation in HIV-infected individuals, better selection of candidates at an earlier stage of liver disease and optimization of donor and perioperative factors are needed. The natural history of HCV re-infection and treatment algorithms must also be determined as HCV recurrence is the most important concern. Better management of HAART after transplantation is also required.

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CASE REPORT

Herniated pancreatic body within a paraesophageal hernia

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Abstract

A hiatal hernia can be classified as one of four types according to the position of the gastroesophageal (GE) junction and the extent of herniated stomach. Type Ⅰ, or sliding hernias, account for up to 95% of all hiatal hernias and occur when the GE junction migrates into the posterior mediastinum through the hiatus. Type Ⅱ occurs when the fundus herniates through the hiatus alongside a normally positioned GE junction. Type Ⅲ is a combination of types Ⅰ and Ⅱ hernias with a displaced GE junction as well as stomach protruding through the hiatus. Type Ⅳ paraesophageal hernias are the rarest of the hiatal hernias. Usually, colon or small bowel is herniated within the mediastinum along with the stomach. We present a case of a paraesophageal hernia with the mid-body of the pancreas as part of the hernia contents.

Key words: Paraesophageal; Hernias; Pancreas

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INTRODUCTION

A hiatal hernia can be classified as one of four types according to the position of the gastroesophageal (GE) junction and the extent of herniated stomach[1,2]. Type Ⅰ, or sliding hernias, account for up to 95% of all hiatal hernias[3] and occur when the GE junction migrates into the posterior mediastinum through the hiatus. Types Ⅱ-Ⅳ, paraesophageal hernias (PEH), together account for 5% of hiatal hernias[3]. Type Ⅱ occurs when the fundus herniates through the hiatus alongside a normally positioned GE junction. Type Ⅲ is a combination of types Ⅰ and Ⅱ hernias with a displaced GE junction as well as stomach protruding through the hiatus. Type Ⅳ is characterized by displacement of the stomach along with other organs into the chest.

We present an unusual case of a PEH containing the mid-body of the pancreas within the hernia sac.

CASE REPORT

The patient is a 61-year old female with a past medical history of gastroesophageal reflux disease, peptic ulcer disease, breast cancer, and hyperthyroidism, who was referred to our clinic for elective repair of a paraesophageal hernia. She had symptoms of chest pressure and discomfort associated with occasional dysphagia, especially to solid foods, and occasional heartburn and regurgitation. This led to an initial evaluation with an upper endoscopy, which demonstrated a large paraesophageal hernia. A computed tomography scan showed an almost completely intrathoracic stomach with the mid-body of the pancreas herniated up through the hiatus (Figure 1A and B). The

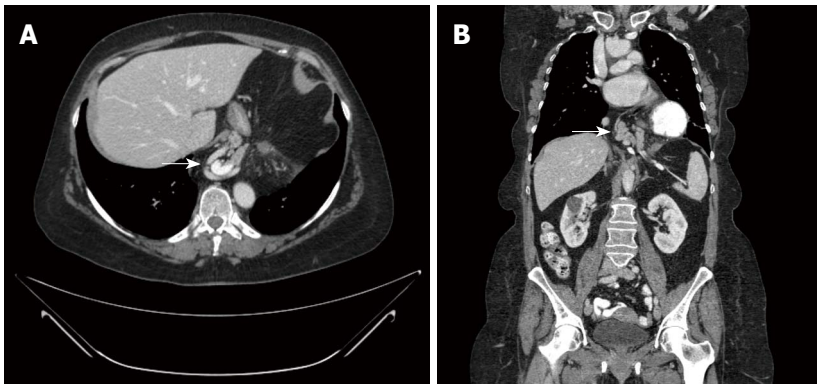

Figure 1 An almost completely intrathoracic stomach with the mid-body of the pancreas herniated up through the hiatus (arrows).

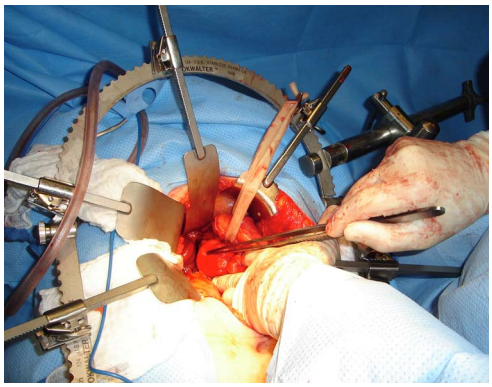

Figure 2 Posterior to the herniated stomach was the herniated pancreas.

patient otherwise had no signs of gastric volvulus. Aside from mild epigastric tenderness on abdominal examination, her physical examination was normal.

The patient was taken to the operating room for an elective paraesophageal hernia repair with Alloderm mesh and Nissen fundoplication. Upon exploration of the abdomen, a large paraesophageal hernia was found with the entire stomach rotated into the mediastinum in an organo-axial fashion. Posterior to the herniated stomach was the herniated pancreas (Figure 2). The hernia sac was dissected from the mediastinum and with this the stomach and pancreas were reduced into the abdomen and the hernia sac excised. The hiatal hernia was closed and the wrap performed.

The patient tolerated the procedure well. Her hospital course was uncomplicated. An esophagram on post-op day three was negative for leakage and the patient was put on a diet, which she tolerated. She was discharged home on post-op day four in good condition.

DISCUSSION

Type IV paraesophageal hernias are very rare, representing 5%-7% of all PEH[4]. The most cost common organ to accompany the stomach into the chest is the colon, most often the splenic flexure. Other more common organs include loops of the small bowel and omentum. It is extraordinarily rare for the pancreas to herniate in paraesophageal hernias, there being only five reported cases in the English literature. Most cases included the body and tail of the pancreas, with one case of the head of the pancreas herniating into the thorax. The majority were symptomatic[5-7]. Our case is unusual in that only the mid-body of the pancreas was herniated, not the tail and spleen.

It is controversial whether or not surgery is necessary for asymptomatic hiatal hernias, although it is agreed that surgery is the best choice for symptomatic PEH[3,8]. In asymptomatic patients, the potential risk of incarceration and strangulation is used by some as an indication for surgery[9]. Others claim that progression of symptoms is slow and seldom leads to emergency surgery, and therefore advocate a watchful approach for patients with large but asymptomatic PEH[10]. There is debate as to whether a transthoracic, transabdominal, or laparoscopic approach is best, but the underlying surgical principles for successful repair include reduction of hernia contents, removal of the hernia sac, closure of the hiatal defect, and an antireflux procedure.

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Events Calendar 2011

January 15-19, 2011
EAES Advanced Laparoscopic GI Surgery Course, Cairo, Egypt

January 20-22, 2011
Gastrointestinal Cancers Symposium (ASCO GI), San Francisco, CA, United States

January 26-30, 2011
5th UK Alpine Liver and Pancreatic Surgery Meeting, Carlo Magno Zeledria Hotel, Madonna di Campiglio, Italy

February 01-03, 2011
6th Annual Academic Surgical Congress, Huntington Beach, CA, United States

February 21-26, 2011
Minimally Invasive Surgery Symposium 2011, The Grand America Hotel, Salt Lake City, Utah, United States

March 03-06, 2011
The Society of Surgical Oncology 63rd Annual Meeting, San Antonio, TX, United States

March 10-13, 2011
The American Hepato-Pancreato-Biliary Association Annual Meeting, Miami Beach, FL, United States

March 14-17, 2011
British Society for Gastroenterology Annual Meeting, International Convention Centre, Birmingham, United Kingdom

March 25-27, 2011
NZAGS Conference 2011 GI Surgery, New Plymouth, New Zealand

March 30-April 02, 2011
The Society of American Gastrointestinal and Endoscopic Surgeons 2011 Annual Meeting, San Antonio Convention Center, San Antonio, TX, United States

April 02-06, 2011
The American Association for Cancer Research 102nd Annual Meeting, Orlando, FL, United States

April 10-12, 2011
The American Association of Endocrine Surgeons 32nd Annual Meeting, Houston, TX, United States

April 14-16, 2011
The American Surgical Association 131st Annual Meeting, Boca Raton, FL, United States

May 07-10, 2011
Digestive Disease Week, Chicago, IL, United States

May 07-10, 2011
45th Annual Meeting of the Pancreas Club, Chicago, IL, United States

June 15-18, 2011
19th International Congress of the European Association for Endoscopic Surgery, in collaboration with and incorporating the 15th National Congress of the Italian Society of Endoscopic Surgery, Torino, Italy

September 10-14, 2011
International Congress of Endoscopy, Los Angeles, CA, United States

September 22-24, 2011
5th joint EAES and ESGE, European Workshop on NOTES, Frankfurt, Germany

September 23-25, 2011
The New England Surgical Society 92nd Annual Meeting, Breton Woods, NH, United States

September 23-27, 2011
ECCO-European Society for Medical Oncology Congress, Stockholm, Sweden

October 23-27, 2011
The American College of Surgeons 97th Annual Clinical Congress, San Francisco, CA, United States

November 02-05, 2011
American Pancreatic Association 42nd Annual Meeting, Chicago, IL, United States

November 13-16, 2011
The Western Surgical Association 119th Scientific Session, Tucson, AZ, United States

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5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

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6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

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9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

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10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

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11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

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12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

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15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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