Coronary artery bypass graft combined with liver transplantation in patients with advanced alcoholic liver cirrhosis: A case report

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Abstract. Performing cardiothoracic surgery on patients with advanced liver failure and liver cirrhosis is high-risk for patients. Coronary artery bypass grafting is the most effective treatment for patients with liver failure that is complicated with severe coronary heart disease, and who cannot be treated using coronary stent intervention. In the current study, one case of coronary artery bypass grafting combined with liver transplantation was assessed, with the patient exhibiting advanced alcoholic liver cirrhosis. A coronary artery bypass graft was performed to relieve angina pectoris. Following surgery, wound exudation, secondary infection, liver failure, pleuroperitoneal fluid leakage, hypoproteinemia and other adverse treatment results occurred, and the chest wound did not heal. Allograft liver transplantation was subsequently performed and, following surgery, the chest wound healed gradually after debridement, and the patient recovered.

Introduction

Alcohol consumption accounts for 3.8% of global mortality and 4.6% of disability-adjusted life-years lost due to premature death (1). Among the various harmful effects of alcohol, alcoholic liver disease induces a wide spectrum of liver abnormalities, including simple steatosis, alcoholic hepatitis/steatohepatitis, progressive fibrosis and ultimately alcoholic cirrhosis and/or hepatocellular carcinoma (2).

The latest worldwide survey of coronary revascularization shows that 583,000 coronary-artery bypass operations were performed in 1995 (3). According to European statistics, the annual rate of use of balloon angioplasty is approximately 739 procedures per million population (4). Approximately 60 percent of patients treated with balloon angioplasty or bypass surgery have multivessel disease that could be treated by either procedure. Coronary artery bypass grafting is the most effective treatment for patients with liver failure that is complicated with severe coronary heart disease, and who cannot be treated using coronary stent intervention (5). However, coronary artery bypass grafting is contraindicated for patients with liver failure. Recently, a case of severe coronary heart disease with liver failure was successfully treated.

Case report

A 62-year old man was admitted to the Tianjin First Central hospital following 4 years of xanthochromia and 4 years of liver cirrhosis. The patient was admitted to the Department of Liver Transplantation in September 2017 with alcoholic liver cirrhosis and end-stage liver disease. A period of 5 years previously, the patient had exhibited skin and scleral xanthochromia with no obvious cause. This was accompanied by anorexia, nausea and intermittent fever, although the patient exhibited no signs of abdominal pain, diarrhea, hematemesis, unconsciousness or other symptoms, and no specific treatment was provided.

A period of 4 years previously (January 2014-December 2018), the patient had been hospitalized in the Tianjin First Central Hospital for anorexia and nausea. Abdominal ultrasonography indicated liver cirrhosis, and the patient received discontinuous hepatoprotective treatment.

A period of 2 years previously, the patient had exhibited abdominal distention and edema of the lower extremities. The effect of conservative treatment was poor, leading to the patient being admitted to the Department of Liver Transplantation for surgical treatment.

Considering that the patient had liver failure, a long-term smoking history, poor lung function and poor overall health, non-cardiopulmonary bypass treatment was selected, which exerts a small effect on lung function and circulation, and can be performed via an opening in the middle of the chest under routine anesthesia. The left internal mammary artery was bridged to the left anterior descending artery (LAD), and the great saphenous vein was bridged from the ascending aorta

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to the posterior descending branch. Conventional whole-liver allogeneic orthotopic liver transplantation was subsequently performed during the surgery. The donor liver was anastomosed to the superior vena cava, inferior vena cava and portal vein, and the hepatic artery and biliary tract were subsequently anastomosed. A T-shaped drainage tube was inserted. This treatment was approved by the Ethics Committee of Tianjin First Central Hospital and was in conformity with the guidelines of National Institute of Health. Preoperative written informed consent was obtained from the patient.

After hospitalization, a chest and abdominal CT was performed for bilateral pleural effusion, cirrhosis and ascites (Figs. 1 and 2). The blood routine results obtained on September 14th 2017 were as follows, normal ranges are displayed in brackets: White blood cell count (WBC), $2.72x10^9$ cells/l ($4\text{-}10x10^9$ cells/l); red blood cell count (RBC), $2.56x10^{12}$ cells/l ($3.5\text{-}5.5x10^{12}$ cells/l); hemoglobin count (HGB), 93.00 g/l (120-160 g/l); hematocrit count (HCT), 27.30% (40-48%); and platelet count, $50x10^9$ cells/l (100-300 cells/l). The biochemistry results obtained on the same day were as follows: Total protein, 53.0 g/l (60-80 g/l); albumin, 26.1 g/l (35-55 g/l); alanine aminotransferase, 15.3 U/l (10-64 U/l); aspartate aminotransferase, 25.5 U/l (8-40 U/l); bilirubin, 59.36 μmol/l (5.1-20.5 μmol/l); direct bilirubin, 34.49 μmol/l (0-8 μmol/l); indirect bilirubin, 24.87 μmol/l (0-13.6 μmol/l)); potassium, 3.81 mmol/l (3.5-5.3 mmol/l); sodium, 137.2 mmol/l (137-147 mmol/l); blood urea nitrogen, 2.61 mmol/l (3.1-8.0 mmol/l); chromium, 71.00 μmol/l (59-104 μmol/l); alkaline phosphatase, 101.1 U/l (45-125 U/l); γ-glutamyltransferase, 8.9 U/l (10-60 U/l); and Globulin, 26.9 g/l (20-40 g/l). The results of arterial blood gas analysis obtained on the same day were as follows: CO_2, 29.5 mmHg (35-48 mmHg); PO_2, 62.0 mmHg (83-108 mmHg); lactate, 3.03 mmol/l (0.5-1.6 mmol/l); and blood ammonia, 70 μmol/l (18-60 μmol/l).

On November 7, 2017, prior to surgery, the routine blood examination results were as follows: WBC, $2.54x10^9$ cells/l ($4\text{-}10x10^9$ cells/l); RBC, $2.46x10^{12}$ cells/l ($3.5\text{-}5.5x10^{12}$ cells/l); HGB, 88.00 g/l (120-160 g/l); HCT, 26.30% (40-48%); and HLT, $53x10^9$ cells/l (100-300/l). The results for preoperative coagulation function obtained on the same day were as follows: Kaolin partial thromboplastin time, 54.9 sec (26-42 sec); prothrombin time, 17.4 sec (8.8-13.8 sec); international normalized ratio, 1.54 (0.8-1.2); and prothrombin activity, 50% (80-120%). The results for preoperative pulmonary function obtained on the same day were as follows: Restriction of ventilation function, reduced slightly; obstruction, reduced slightly; small airway function, moderately reduced; and dispersion function, severely reduced. The results for pleural effusion obtained on the same day were as follows: 4.7 cm on the right side and 2.1 cm on the left side. The patient was in an alcoholic liver cirrhosis decompensation period, so symptomatic treatment was administered. Namely, magnesium isoglycyrrhizinate injections (200 mg/day) to improve liver function, human serum albumin (10-20 g/day) to treat hypoproteinemia and enteral nutrition emulsion (500 ml/day) to improve the nutritional status of patients. During hospitalization, the patient exhibited recurrent angina pectoris. On October 17th 2017, according to coronary angiography, the areas from the left main artery to the anterior descending artery were calcified, and left main artery stenosis was at 50%; the proximal to distal anterior descending artery exhibited diffuse lesions, and stenosis was at 70-90%. Aneurysms were also identified in the center of the anterior descending artery. The circumflex arteries were small and no obvious stenosis was observed. Distal right coronary artery stenosis was at 90% (Fig. 3).

The preoperative diagnosis was: i) Alcoholic cirrhosis and decompensated liver cirrhosis; ii) coronary heart disease and unstable angina; iii) chronic obstructive pulmonary disease; and iv) Grade C liver function (classified via the Child-Pugh classification) (4) with clear indications for liver transplantation. The patient exhibited angina pectoris and could not tolerate routine liver transplantation surgery, and no liver donor was available. Therefore, the patient was transferred to the Department of Cardiac Surgery, and an off-pump coronary artery bypass graft was performed on November 8, 2017. Three Bridging (5) was built during the surgery (left internal mammary artery-LAD; aorta-SVG-posterior descending branch; and aorta-SVG-diagonal branch). On day 4 following surgery, a hemorrhagic effusion occurred in the middle and lower segment of the anterior thoracotomy, and the daily exudate amount was ~600 ml. Exudate also effused from the xiphoid process when the wound was opened. Following bilateral chest drainage, there was still a large amount of exudation from the anterior chest wound. Debridement and bilateral pleural repair surgery were performed on November 21, 2017 (Figs. 4 and 5). Following surgery, the patient received appropriate correction of hypoproteinemia and anti-infection treatment (tigecycline, 50 mg/day, 21 days), however the wound did not heal. General anesthesia allograft liver transplantation was performed on December 8, 2017. Whole-liver orthotopic liver transplantation was performed intraoperatively. The donor liver was obtained from a brain-dead donor, and the cold ischemia period was 240 min. Intraoperatively, the superior vena cava, inferior vena cava and portal vein were routinely anastomosed. One steel sternum wire was removed, and the wound was fixed. Anti-rejection (methylprednisolone 8 mg/day, cyclosporine 170 mg/day and mycophenolate mofetil 2.0 g/day) and anti-infection treatments (Tigecycline, 50 mg/day) were provided after surgery, and the condition of the patient was stable following comprehensive nutritional treatment (enteral nutrition emulsion, 500 ml/day for 60 days). A purulent secretion was identified from the anterior chest wound at the level of the manubrium, and this was accompanied by a high fever. Culture following a wound swab indicated the presence of *Staphylococcus aureus*, and thus wound infection was considered. Anterior chest wound debridement was performed on January 8, 2018. Local necrotic bone was detected at the level of the manubrium. One steel sternum wire was removed at the second intercostal space. Recovery was good at the lower segment of sternum, and a curette was used to clean the necrotic bones. Necrotic bones were also identified at the right side of the manubrium, and debridement and gauze packing treatments were performed. The patient was transferred to a general ward to continue recovery. The sternum wound gradually healed, and there was intermittent purulent exudate near the xiphoid. Culturing indicated the presence of *S. aureus*, so chronic osteomyelitis was considered. Wound debridement was performed on February 5, 2018 due to the osteomyelitis. Sternal and costal cartilage necrosis was identified at the

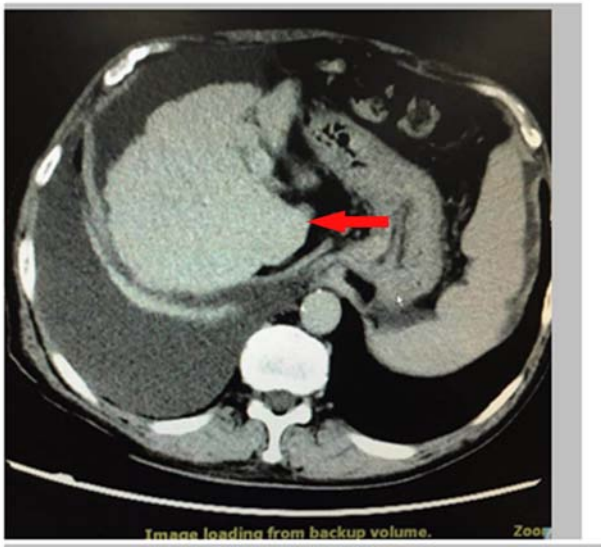

Figure 1. Abdominal CT prior to liver transplantation. After hospitalization, an abdominal CT indicated bilateral pleural effusion, cirrhosis and ascites, as shown by the red arrow.

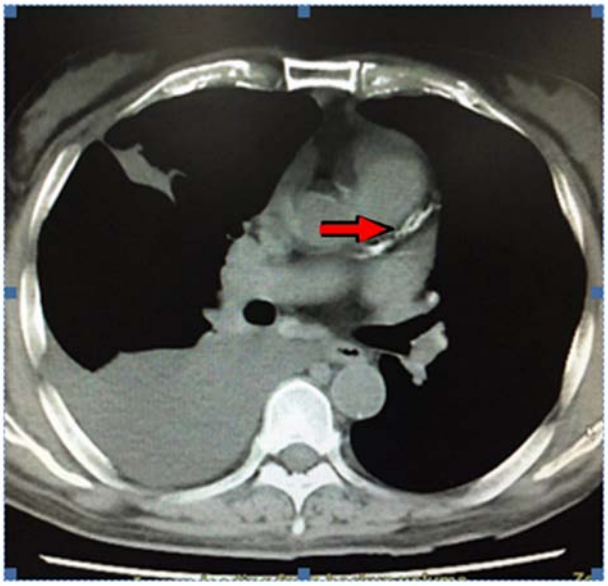

Figure 2. Chest CT prior to liver transplantation. After hospitalized, chest CT tested bilateral pleural effusion, cirrhosis and ascites as highlighted by the red arrow.

xiphoid process in the lower segment of the wound. One steel sternum wire was removed at the fourth intercostal space, and necrotic bone was scraped. A total of three costal cartilages on the left side and two costal cartilages were removed on the right side. Followings surgery, dressings were changed daily, the condition of the patient gradually stabilized and wound exudation gradually reduced. At 5 months after surgery, the wound had healed and the patient left hospital. The results of an abdominal CT (Fig. 6) and an ultrasound test were normal. The patient continued to receive methylprednisolone (8 mg/day), cyclosporine (170 mg/day), and mycophenolate mofetil (2.0 g/day) for anti-rejection therapy.

Discussion

Patients often exhibit coronary heart disease when waiting for liver transplantation and some patients cannot receive coronary stenting; therefore, coronary artery bypass grafting is the only effective treatment (6-9). Coronary artery bypass grafting is contraindicated in end-stage liver disease due to symptoms of coagulation dysfunction, refractory hypoalbuminemia, pleural effusion, edema of the lower extremities, hepatic encephalopathy, hypersplenism, leukopenia, thrombocytopenia and gastrointestinal bleeding (10,11). In 2004, a study performed at Northwestern University (Evanston, IL, USA) reported five cases of patients with severe coronary heart disease and hepatic failure who received simultaneous coronary artery bypass grafting and liver transplantation, with an average age of 57.8 years (6). No perioperative death was exhibited in the aforementioned patients, and at the 25-month follow-up the survival rate was 80% (12). In 1997, Pelosi *et al* (12) introduced 12 cases of liver transplantation following coronary artery bypass graft. To the best of our knowledge, no clinical literature report on coronary artery bypass graft surgery for alcoholic liver cirrhosis and hepatic failure exists. In the current case, the patient exhibited advanced alcoholic liver cirrhosis, and life-threatening angina pectoris occurred frequently while the patient waited for a donor liver. An emergency coronary artery bypass graft was performed subsequently, and wound infection (*S. aureus*) occurred following surgery. During wound treatment, orthotopic liver transplantation was performed, and the postoperative abdominal wound healed well. The chest wound also healed after multiple debridements.

End-stage liver disease is a contraindication for coronary artery bypass graft. If liver transplantation and CABG cannot be performed simultaneously, surgery should be selected carefully. End-stage liver disease leads to a number of complications (13,14), and blood loss is often high; heavy heparinization during coronary artery bypass grafting will exacerbate the risk of bleeding (15). Hypoproteinemia also causes poor nutritional status and poor tissue healing ability (16), and coronary artery bypass surgery wounds can easily become infected and lead to secondary sternal osteomyelitis (17). Systemic tissue edema and pleural effusion can cause a decrease in respiratory function, and pleural breakage may be difficult to repair due to thoracotomy and internal mammary artery incision (18). Postoperative decompensation of liver cirrhosis causes continuous production and outflow of pleural fluid, which can lead to slow wound recovery (19). Additionally, hypersplenism leads to severe leukopenia, anemia and other immune deficiencies, which can lead to secondary infections (20). Postoperative blood transfusion is also likely to induce hepatic encephalopathy and increase infection risk (21). Patients can also exhibit angina pectoris during the waiting period for liver transplantation, which may not be effectively alleviated using drug therapy. Coronary artery lesions can also develop into diffuse coronary calcification stenosis, and medical interventional therapy cannot be subsequently performed; in this case, salvage coronary artery bypass grafting should be performed (22).

During coronary artery bypass grafting, the damaged pleura should be completely closed to prevent pleural effusion, and to prevent interference with wound healing (23).

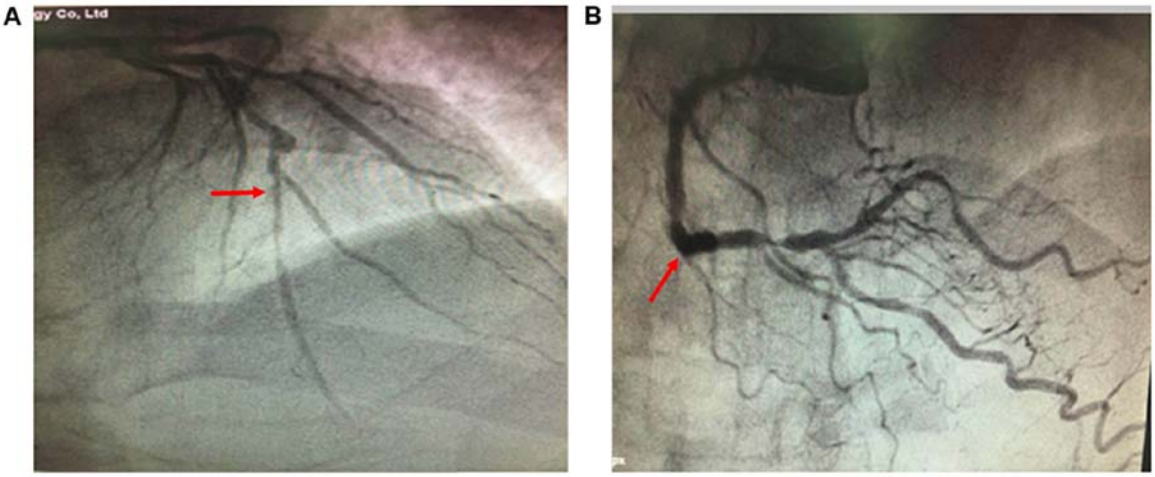

Figure 3. Coronary angiogram. (A) According to coronary angiography, the areas from the left main artery to the anterior descending artery were calcified, and left main artery stenosis was at 50% as indicated by the arrows. (B) According to coronary angiography, the proximal to distal anterior descending artery exhibited diffuse lesions, and stenosis was at 70-90%. Aneurysms were identified in the middle of anterior descending artery. The circumflex arteries were small and no obvious stenosis was indicated. Distal right coronary artery stenosis was at 90% as indicated by the arrows.

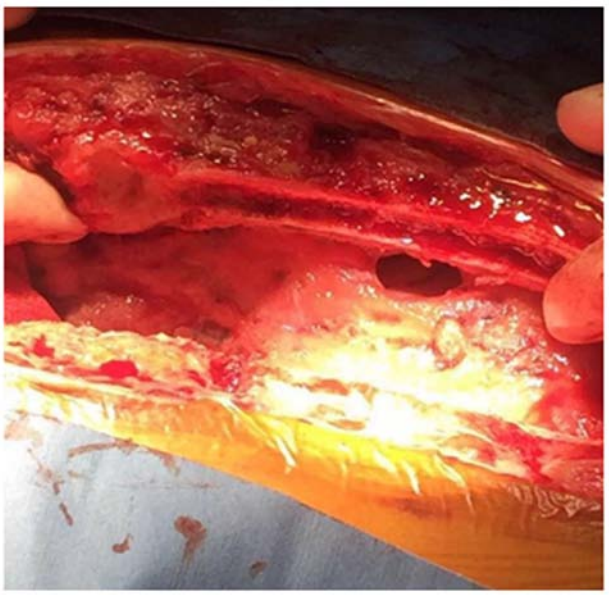

Figure 4. Visible right pleural breakage during debridement of the anterior chest wound. Exudate effused from the xiphoid process when the wound was opened. After bilateral chest drainage, there was still a large amount of exudate that effused from the anterior chest wound.

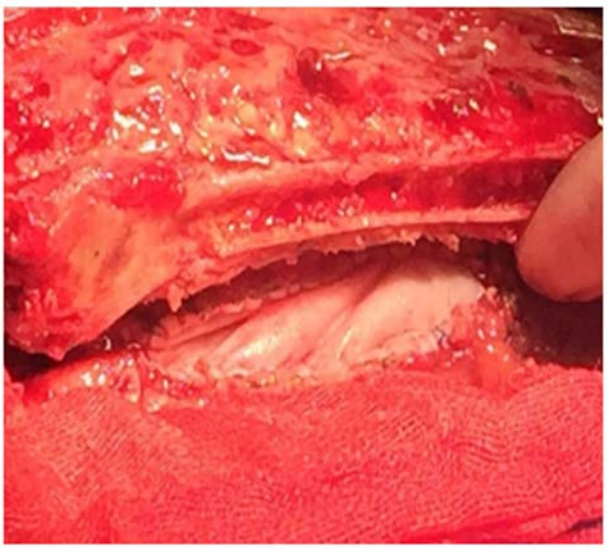

Figure 5. Repairing the right pleural breakage. After surgery, the patient was given appropriate low-protein and anti-infection treatment, but the wound still did not heal.

The majority of pleura in patients are thin, and it is difficult to repair these following pleural breakage (24). Pneumothorax occurred after opening the anterior thoracic wound, and pleural effusion continued. The anterior thoracic wound was opened and repaired, and the wound was sutured after pleural effusion catheterization. The middle and lower part of the wound was subsequently opened to change the dressing due to low protein, malnutrition, secondary infection, persistent exudation of pleural effusion, persistent reduction of protein and aggravated liver cirrhosis (25-28).

For patients with normal heart function and severe coronary artery disease, simultaneous liver transplantation during coronary artery bypass grafting can be selected, to avoid the risk of acute myocardial infarction during liver transplantation

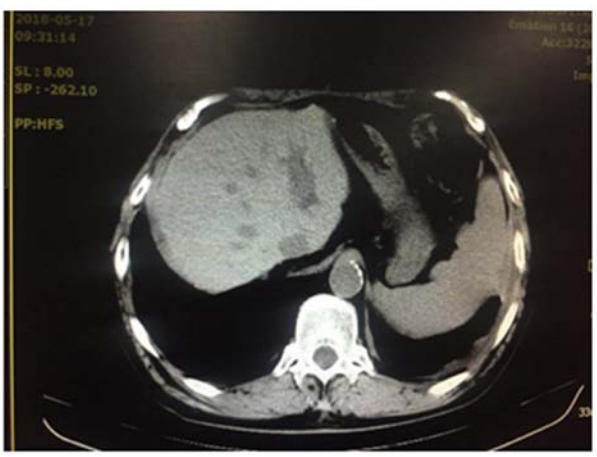

Figure 6. Abdominal CT after liver transplantation. All results of the abdominal CT were normal.

and reduce the impact of liver failure on patient recovery following the coronary artery bypass graft (12). In the present case, the angina pectoris was life-threatening and could not be alleviated, so an emergency coronary artery bypass graft was performed. As there was no suitable liver donor, liver transplantation and coronary artery bypass grafting could not be performed simultaneously. After coronary artery bypass grafting, the wound did not heal and liver function deteriorated, and a large quantity of pleural fluid leaked. Liver transplantation was performed when the anterior thoracic wound was unhealed. Immunosuppressive agents were used to decrease the risk of infection. Chronic osteomyelitis and *S. aureus* infection occurred in the anterior chest wound. The wound healed following two rounds of necrotic tissue debridement.

For patients with hepatic failure, when performing thoracotomy, the bilateral pleura should not be opened. If pleural damage and breakage is observed, an autologous or allogeneic pericardial patch should be used to close the breakage (29), and this is essential to prevent postoperative wound dehiscence, exudation and infection (30,31). A sternal incision, intercostal incision or a robot can be used to perform coronary artery bypass graft. In the current case, the bilateral pleural crevasses were not repaired, and pleural fluid continued to leak out after the operation. Then, tension pneumothorax occurred, and emergent pleural repair and wound suturing were performed. After suturing, the wounds could not heal due to low protein, anemia and hypersplenism caused by liver failure. During the operation, the superior and inferior vena cava were exposed, and an abdominal cavity expander was used, as the steel wire of the lower sternum was loosened, to avoid cutting the sternum. After liver transplantation, the wound was sutured after the sternum was fixed. Due to the use of immunosuppressive agents after transplantation, *S. aureus* infection was indicated in the upper sternum near the second costal cartilage at 1 month after transplantation, and debridement of the local sternum and costal cartilage was performed. During this period, the healed sternum should be protected to avoid cracking. A period of 2 months after transplantation, local infection in the lower segment of the sternum occurred, and healed after debridement.

Multidisciplinary collaboration and comprehensive supportive treatment after liver transplantation is the key to successful postoperative recovery. Performing liver transplantation during the period when the anterior chest wound is unhealed, combined with the use of immunosuppressive agents, can increase the risk of wound infection. After 5 days of intensive care treatment, the liver function of the patient gradually recovered, and the patient was transferred to an intensive care unit. The patient was given adequate nutritional support through a naso-intestinal tube; the recovery of gastrointestinal function accelerated, and the liver function became normal with treatment. The secretions of the anterior chest wound tested positive for *S. aureus* infection. The wounds healed gradually after two rounds of debridement. The patient recovered and was discharged 5 months after the coronary artery bypass graft and 4 months after liver transplantation. During the long course of treatment in the current case, lessons can be learnt regarding the surgical choice, wound management, postoperative liver function recovery, heart and kidney function maintenance, and nutritional support, and the present report may provide a reference for the use of thoracotomy in liver failure.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

JC and ZS contributed to make substantial contributions to the study conception and design, the acquisition of data and the analysis and interpretation of data. JC and ZS contributed to drafting the manuscript and critically revising the manuscript for important intellectual content. ZS gave final approval of the version to be published. ZS, KW and XK contributed to data collection and data entry. WJ and LZ contributed to the data analysis. CP and FX contributed to data interpretation. JC prepared the manuscript, and WZ and HC performed the literature analysis search. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study has been approved by the Ethics Committee of Tianjin First Central Hospital and was in conformity with the guidelines of National Institute of Health (permit no. 81004). All study participants provided written consent to be involved in the present study. All study participants had given their written informed consent for publication before participating in the current study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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