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ORIGINAL ARTICLE

Living Liver Donor Death Related to Complications of Myeloma

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We report a donor death after right hepatectomy for living donor transplantation due to an undiagnosed myeloma. The 47-year-old donor, who was the 147th case performed in our department, was in excellent health without any abnormalities in the preoperative investigations. Despite an uneventful right hepatectomy without transfusion, the patient developed a partial thrombus of the inferior vena cava with a right proximal pulmonary trunk embolism on postoperative day 6. Subsequently, he developed multiorgan dysfunction leading to a coagulopathy, respiratory distress, and renal failure requiring hemodialysis and mechanical ventilation. This clinical scenario led us to suspect a hematological disorder. Immune electrophoresis showed a monoclonal peak of immunoglobulin G (8.7 g/L), a myelogram revealed an abnormally high level of dystrophic plasmocytes (more than 7%), and biopsies of salivary glands confirmed the diagnosis of immunoglobulin G kappa myeloma. The patient progressively deteriorated because of simultaneous hemorrhagic and infectious pulmonary complications resulting in septic shock. Despite an adequate combination of antimicrobial therapy and pleural drainage, the donor died on postoperative day 57 from multiple organ failure. This unusual cause of donor death after right hepatectomy reinforces the need for an extensive preoperative assessment. We advocate the addition of urinary protein loss and electrophoresis to the standard donor assessment protocol. ***Liver Transpl 15:326-329, 2009.*** © **2009 AASLD.**

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The main concern pertaining to living donor liver transplantation is the risk to the donor, with reports of severe morbidity in the literature ranging from 0% to 67% and the mortality rate ranging from 0.2% to 0.8%.[1-4] This risk is often underestimated and rarely reported through prospective studies.[1] Strict criteria for the safety of liver resection have been well established and include stringent assessment recommendations and the requirement of high surgical expertise in order to ensure that the donor has an adequate residual liver parenchyma.[5] Postoperative morbidity and mortality remain high, especially in donors who undergo right hepatectomy.[6] Published cases of postoperative donor deaths are often considered uncommon and/or unusual.[3,7] Donor deaths should be reported for 2 reasons: first in order to have a more accurate estimate of the donor risk and second to have a better analysis of complications with the aim of understanding and preventing such catastrophic outcomes.

We report a postoperative death of a donor after right hepatectomy for living donor transplantation due to an unsuspected myeloma.

CASE REPORT

The donor was a 47-year-old man who volunteered as a candidate for liver donation for his 50-year-old brother. The recipient (blood group B) suffered from severe alcoholic cirrhosis and obesity (Model for End-Stage Liver Disease score = 26) requiring repeated hospitalizations for refractory ascites and encephalopathy. According to the cadaveric graft allocation rules at that time in France, the mean expected time on the waiting list was more than 6 months. This led us to consider the option

Abbreviations: ALAT, alanine aminotransferase; ASA, American Society of Anesthesiologists; ASAT, aspartate aminotransferase; CT, computed tomography; GGT, gamma glutamyl transpeptidase; ICU, intensive care unit; INR, international normalized ratio; POD, postoperative day.

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TABLE 1. Preoperative Biological Values of the Donor

Variable	Preoperative	Normal Range
ASAT/ALAT (UI/L)	16/32	10–34
GGT (UI/L)	22	10–38
Serum total bilirubin (mg/dL)	0.7	0.2–1
Hemoglobin (g/L)	15.8	12–17
White blood cell count (10^9/L)	5.8	4–10
Platelet count ($\times 10^9$/L)	223	150–450
Serum creatinine (mg/dL)	1.4	0.6–1.5
Total serum protein (g/L)	73	65–80
Serum albumin (g/L)	42	35–50

Abbreviations: ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; GGT, gamma glutamyl transpeptidase.

TABLE 2. Evolution of ASAT, ALAT, Total Bilirubin, Prothrombin Time, and Serum Creatinine After Hepatectomy in the Donor

		Postoperative Day			
Variable	Preoperative	1	3	5	7
ASAT (UI/L)	16	234	105	65	85
ALAT (UI/L)	32	272	141	100	78
Total bilirubin (mg/dL)	0.7	5.1	6.8	7	7.8
INR	0.9	1.5	1.6	1.3	1.2
Serum creatinine (mg/dL)	1.4	1.2	1	0.9	1.4

Abbreviations: ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; INR, international normalized ratio.

of living donor LT. The donor evaluation started on October 2006, and he was the 377th donor evaluated in our program. Physical examination revealed a tall, fit man of 80 kg with a height of 175 cm. His past medical history was uneventful, except for pyloric stenosis that was surgically treated at birth and an appendicectomy at the age of 14. He smoked 10 cigarettes a day for 10 years and stopped at the age of 27. He had no history of alcoholism, hypertension, or diabetes. According to the American Society of Anesthesiologists (ASA) score, he was classified as ASA1. There was no abnormality in his hemogram, renal function tests, or liver profile. Preoperative biochemical data are reported in Table 1.

The coagulation profile, routinely performed preoperatively according to our local protocol, did not detect any disorder (prothrombin time, 111%; factor II, 128%; factor V, 111%; factor VII, 127%; factor X, 130%; factor VIII, 125%; fibrinogen, 2.9 g/L; and von Willebrand factor, 97%). An extensive search for thrombophilic factors did not reveal any abnormality. Antiphospholipid antibodies were negative, antithrombin III was 118%, protein C was 157%, protein S was 97%, factor V Leiden mutation was negative, and factor II 20210 mutation was negative.

The liver anatomy, assessed by multiphase helical computed tomography (CT) scan and magnetic resonance cholangiography, was normal. The volumetric measurement of the liver showed a total liver volume of 1512 cc, a right liver volume of 1077 cc, and a left liver volume of 435 cc. The estimated graft/donor and remnant liver/donor weight ratios were 0.8 and 0.54, respectively. The estimated future remnant liver of the donor was 28.7%.

Prophylaxis against thromboembolic disease was started on the night before hepatectomy and was continued postoperatively with nadroparin (2850 IU/day subcutaneously), along with early mobilization and compression sleeves in the intraoperative and postoperative periods.

The right hepatectomy was performed through a bilateral subcostal incision with preservation of the middle hepatic vein and without vascular clamping. The duration of the procedure was 390 minutes. The estimated operative blood loss was 450 mL. The donor did not receive any homologous blood products. The donor was extubated in stable condition in the operating room and then transferred to the intensive care unit (ICU) for observation during the first night according to our institutional protocol. The postoperative evolution of the biochemical parameters is displayed in Table 2.

A major asthenia, combined with progressive ankle edema and tachycardia (100 bpm), led us to look for venous thrombotic complications. The thoraco-abdominal, contrast-enhanced CT scan performed on postoperative day (POD) 6 showed a right proximal pulmonary trunk embolism associated with a partial thrombus of the inferior vena cava arising from the right iliac veins up to the ostium of the right renal vein. The remnant liver displayed an estimated volume of 822 cc versus 435 cc preoperatively. The portal vein and the hepatic veins were normal. Cardiac echography and liver ultrasound eliminated the presence of right congestive heart failure. Intravenous unfractionated heparin therapy was immediately started. The donor was monitored in ICU. The physical examination revealed tachycardia (123 bpm), normal blood pressure, and normal respiratory rate (15 per minute) with oxygen saturation at 96% under 3 L/minute oxygen.

On POD 7, progressive renal failure with oliguria developed despite adequate volume replacement. Continuous venovenous hemofiltration was required on POD 10. This renal failure was thought to be related to intravenous administration of iodine containing contrast for the CT scan. However, an extensive hematological workup revealed a peak in the gamma-globulin spectrum of the serum protein electrophoresis. Immune electrophoresis displayed a monoclonal peak of immunoglobulin G (8.7 g/L), suggesting a myeloma. Finally, a myelogram revealed an abnormally high level of dystrophic plasmocytes (more than 7%). Several biopsies of the salivary glands were then performed to search for free light chains. These biopsies confirmed the diagnosis of immunoglobulin G kappa myeloma with probable renal involvement.

Simultaneously with the renal failure, the patient presented with progressive respiratory failure with a temporary response to noninvasive ventilation. However, mechanical ventilation became mandatory on day 10. Reasons for respiratory deterioration were numerous, including a massive right pleural effusion and diffuse atelectasis. An initial pulmonary bacteriological sample was sterile.

During the following PODs, the patient developed simultaneous hemorrhagic and infectious pulmonary complications. Three episodes of massive hemoptysis occurred without any biological overdosage of heparin. Three bronchoscopies were normal. Finally, it was concluded that the hemoptysis was due to hemorrhage related to the pulmonary infarcts. Curative anticoagulation was stopped, and a temporary inferior vena cava filter was placed by the interventional radiologist on POD 21. The donor developed ventilation-acquired pneumonia due to a methicillin-sensitive *Staphylococcus aureus* infection 3 days after mechanical ventilation. He then developed a superadded pulmonary infection with *Escherichia coli* and *Acinetobacter baumannii* responsible for septic shock. Despite aggressive antimicrobial therapy, the infection persisted because of a right pulmonary infected necrosis combined with pleural empyema. During the ICU stay, he had persistent oliguria and renal failure requiring daily hemodialysis.

Despite multiple pleural drainages and a combination of antibiotics, the donor died on POD 57 from multiple organ failure.

Incidentally, the recipient had an uneventful postoperative course leaving ICU on POD 7. One year later, he is physically well with normal liver function. No stigmata of myeloma were found on liver graft biopsy performed 6 months after.

DISCUSSION

The death of a donor is a catastrophic issue, whatever the circumstances are. We have performed 147 living liver transplants since 1996, and we had never previously faced such severe complications in a donor after this procedure. Living donor related morbidity, which ranges in the literature from 20% to 67%,[2,8-11] was 20% in our experience.[12] Although the estimated remnant right liver was slightly below 30%, which resulted in mild liver dysfunction that manifested as a persistently high level of bilirubin, the multiple complications in this donor, including hematological, renal, and immune dysfunctions, were most likely an exacerbation of the myeloma. In the current literature, the morbidity and mortality risks of surgery in patients with myeloma have never been described, but this disease is associated with several systemic complications, particularly thromboembolic episodes, hemorrhage, renal failure, and uncontrolled severe infections.[13]

Patients with myeloma are at high risk for spontaneous venous thromboembolism, with a reported incidence of 30%.[14] This is a known hypercoagulable state, and it has been demonstrated that prothrombotic abnormalities such as increases in the von Willebrand factor and factor VIII are commonly present.[15] We have shown in our earlier studies that liver living donors and particularly right lobe donors are at high risk for the development of postoperative thromboembolic complications attributed to an imbalance in the hemostasis profile of the donor with the release of procoagulant factor from the liver parenchyma during and after liver resection.[16,17] In the present case, the combination of myeloma and major liver resection likely produced a procoagulant state in the donor resulting in the extended thrombosis of the inferior vena cava complicated by a bilateral pulmonary embolism.

Renal impairment from tubular light chain damage is present in up to 20% at the time of diagnosis of myeloma.[18,19] Renal failure is an important adverse prognostic factor for early mortality.[20-23] However, in 25% of patients with myeloma, renal function is normal, as we observed in the preoperative assessment of our patient. At this time, a search for proteinuria could have been the only way to detect the disease. This test, which is not presently recommended in the preoperative evaluation for liver donation, should be systematically added for detecting this hematological disease.[5,10] During the early postoperative course, immune electrophoresis of urinary protein had not been performed because of an absence of diuresis at the time of suspicion of myeloma. The adjunctive toxic factor of iodine-based contrast during the CT scan in conjunction with a hypovolemic state was most likely responsible for the definitive renal failure. Although kidney biopsy was not performed in our case because of the high hemorrhagic risk, the persistence of severe hypoalbuminemia with nephrotic syndrome was in favor of renal involvement by the myeloma.

The particular susceptibility of myeloma patients to infectious disease is of major concern[24] because most of them present an impairment of lymphocyte function and, according to a recent series, 45% of myeloma deaths are caused by infection.[13] In the 7 deaths following right liver lobe donation reported by the European Liver Transplant Registry working group, there were 2 septic shocks with multiple organ failure described.[2,3] Our group in a series of 127 living liver donors revealed that the most frequent adverse events after living donor liver transplantation were pulmonary complications, with an incidence of 12%.[16] Thus, the susceptibility to infection associated with an impairment of the immune function induced by the myeloma promoted the uncontrolled pulmonary sepsis that led to the multiple organ failure of our donor.

The prevalence of myeloma in the population more than 50 years old is about 1%.[25] The actual preoperative assessment program of liver living donors does not include plasma protein electrophoresis or protein urinary loss detection, which are part of the myeloma diagnosis tests. This case report could lead to an enhancement in the liver living donor assessment protocol with plasma protein electrophoresis and urine detection of proteinuria. However, because of this prevalence, it remains to be determined why there is no similar report in the field of liver resections for hepatic

disease. Finally, as the myeloma prevalence increases with age, it could be judicious to propose these tests for patients who are awaiting major liver resection for other indications.

In conclusion, we advocate the addition of protein urinary loss detection and plasma protein electrophoresis to the donor assessment protocol. This first reported death from the complication of an unsuspected myeloma is another uncommon and/or unusual event responsible for a donor death. The vulnerability of healthy donors to such events after major hepatic resection should be explored in future studies. Nevertheless, this death has led us to suspend our living liver transplantation program for the following reasons: (1) the persistent high risk of donor right hepatectomy; (2) the progressive reduction of this procedure in Western countries, which does not allow us to reach a sufficient number of procedures per year; and (3) the Model for End-Stage Liver Disease allocation newly implemented in France, which prioritizes patients with a high risk of death on the waiting list.

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