Case Report

Orthotopic Liver Transplantation as a Rescue Therapy for Bleeding Giant Hepatic Hemangioma: The First Case Report in Thailand and Literature Review

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Hepatic hemangioma is one of the most common benign liver tumors. Hemangiomas can occur in people of all ages but are more commonly found in young women. Most patients have only one hemangioma, but multiple lesions are possible. The natural history of hemangiomas is usually benign, and bleeding or rupture is very rare. The treatment for bleeding or ruptured hemangioma includes embolization or surgery. The authors reported a case of a young female with giant bilateral hepatic hemangioma with bleeding. The size of the hemangioma precluded resection or enucleation. Transarterial embolization of her hepatic arteries was done but failed. She received orthotopic liver transplantation and had an uneventful post-operative course. Currently, she is doing well. This report is the first case in Thailand of liver transplantation as the rescue therapy for a patient with bleeding giant hepatic hemangioma.

Keywords: Giant hepatic hemangioma, Liver transplantation, Bleeding

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Hepatic hemangioma is one of the most common benign liver tumors detected by abdominal ultrasound in Thais[1]. The natural history of hemangiomas is usually benign. Bleeding or rupture is very rare. The first step in the management of bleeding or rupture hemangioma is stabilization of the patient by supportive transfusion or obtaining hemostasis with transarterial embolization of the tumor. The definitive treatment is surgical resection or enucleation. Liver transplantation can be used as a rescue therapy for patients with giant hepatic hemangioma who fail embolization and are not candidates for surgical treatment. The authors reported the case of a female patient who underwent liver transplantation as the rescue therapy for her bleeding giant hepatic hemangioma.

Case Report

A 33-year-old Thai female patient presented with abdominal pain and abdominal distension. She was diagnosed with a large hepatic hemangioma six months ago. She had an exploratory laparotomy, but the hemangioma was deemed too large for resection. The histopathology from a liver biopsy was consistent with a cavernous hemangioma. She was discharged from the hospital. She presented again with acute severe abdominal pain. An abdominal computed tomography (CT) scan revealed intralesional bleeding within the hemangioma. She received blood transfusion and embolization. However, the transarterial embolization of her both right and left hepatic arteries failed to stop the bleeding. Subsequently, she was referred to our hospital for liver transplantation assessment in February 2012.

Her physical examination revealed mild pale conjunctiva and no jaundice. Chest examination revealed decreased breath sound at right lung base. Cardiovascular examination was unremarkable. Her abdominal examination revealed marked abdominal distension with large abdominal mass extended from right upper quadrant to just above her pelvis. There was no stigmata of chronic liver disease. Extremities

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showed no peripheral edema.

The laboratory investigation revealed Hb 11.0 g/dL, WBC 7,400 cells/mm³, and platelet 129,000 cell/mm³. Serum aspartate aminotransferase 21 U/L (normal range: 5 to 34 U/L), serum alanine aminotransferase 28 U/L (normal range: 0 to 55 U/L), alkaline phosphatase 290 U/L (normal range 40 to 150 U/), direct/total bilirubin 0.3/0.6 mg/dL, (normal range: <0.5/1.2 mg/dL), international normalized ration (INR) 1.1, and creatinine 0.91 mg/dL.

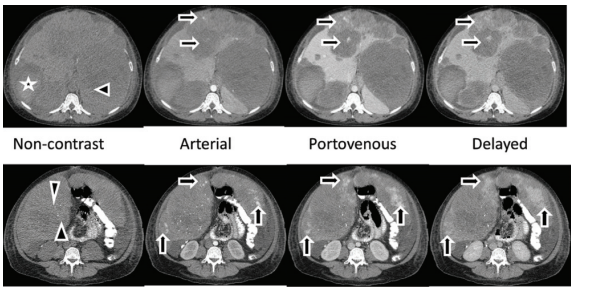
Her blood tests revealed HBsAg negative, anti-HBc negative, and anti-HBs positive. The anti-HCV and anti-HIV were negative. The VDRL and TPHA were all non-reactive.

CT chest and abdomen revealed a huge 30 cm conglomerulated low density mass involving almost the entire liver. The mass showed intralesional bleeding, containing calcification and puddles of enhancement. Several small lesions were also noted scattered within the liver (Figure 1).

She was put on the waiting list for liver transplantation after completion of the assessment process. She was admitted for bed rest at the hospital and periodically received blood transfusion. She underwent cadaveric liver transplantation in August 2012.

At the operation, she was found to have a large hepatic mass size 30×30 cm. The common bile duct, hepatic arteries, and portal vein were identified, and the liver was dissected from sub diaphragmatic region. The cadaveric liver transplantation was done with end-to-side IVC anastomosis, end-to-end anastomoses of portal vein, hepatic artery, and bile duct (Figure 2, 3). The entire liver weight was 6.1 kg.

She received corticosteroid, mycophenolate mofetil, and tacrolimus for her immunosuppression. Her postoperative course was uneventful, and she was discharged from the hospital two weeks after her liver transplantation. She remains well after almost five years post liver transplantation.



Markedly enlarged liver containing multiple large conglomerated masses in both lobes liver, which show intralesional bleeding (star), calcifications (arrow head), puddles of arterial enhancing portion and progressive enhancement (arrow)

Figure 1. Triphasic CT scan of her abdomen.

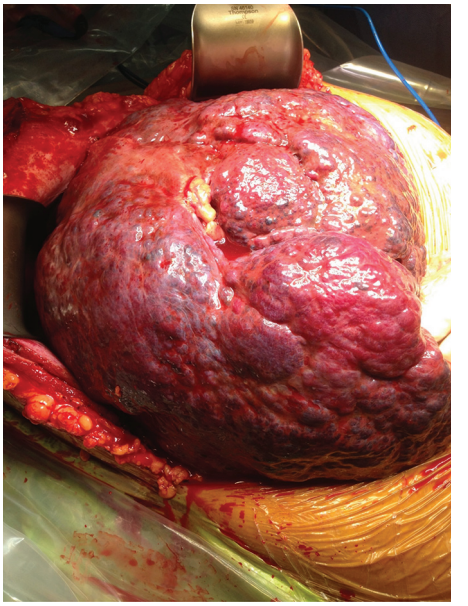


Figure 2. Intraoperative view of the giant hepatic hemangioma. The liver which showed the appearance of hemangioma occupied the entire upper part of her abdomen.

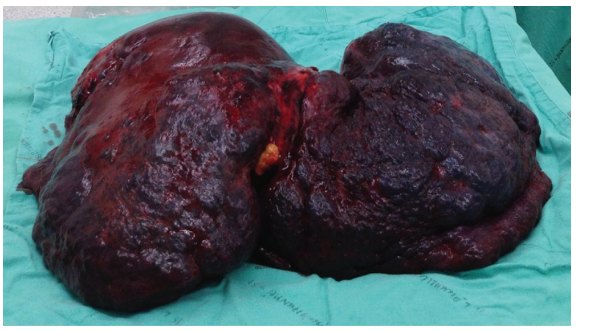
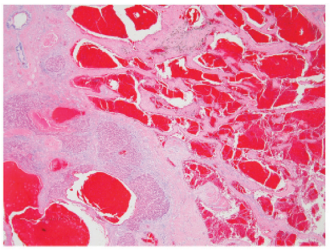


Figure 3. Giant hepatic hemangioma and the entire liver after being removed.

Discussion

Hepatic hemangioma is one the most common benign liver tumors. Most hepatic hemangiomas are asymptomatic and are found incidentally. They can be found in 1% to 2% of screening abdominal ultrasound in general population. Hepatic hemangiomas can occur in all ages but are commonly found in young females. The histopathology of hepatic hemangioma consists of blood-filled sinusoidal spaces and vascular lakes lined by endothelial cells. Most patients have only one

Gross description: A large spongy, red-brown lesion with focal fibrosis in the normal liver



Microscopic description: Large, dilated, blood-filled channels with bland endothelial lining (H&E, 20x)

Figure 4. Gross and microscopic description of the giant hemangioma.

tumor, but multiple lesions are possible. Most authors define giant hemangioma as being greater than 5 cm, however some define it as greater than 10 cm[2]. Most of hemangiomas are asymptomatic, however larger size and certain locations such as in left lobe are more likely to cause symptoms. The most common symptoms for large hemangioma (greater than 10 cm) are upper abdominal discomfort and indigestion, right or left quadrant pain, and abdominal mass[3]. Other uncommon presentations include hemolysis with consumption coagulopathy (Kasabach-Merritt syndrome) and spontaneous bleeding or rupture. The risk of spontaneous rupture is still unclear. In a retrospective case series of 97 cases of spontaneous rupture or bleeding hepatic hemangiomas, compared with patients who had non-spontaneous bleeding (defined as blunt trauma, pregnancy and delivery, biopsy, surgical intervention, and anticoagulation therapy), the difference of location and the size of hemangiomas were not statistically significant between the spontaneous and non-spontaneous rupture group. The non-spontaneous rupture was significantly more frequent in patients age less than 40 years than those older (p=0.0099). In addition, reports of mortality from hepatic hemangioma over the past 20 years were significantly lower than before (p<0.001)[4]. Another retrospective cross-sectional radiology database reviewed from one regional university hospital collected 2,071 patients with hepatic hemangioma over a seven-year period[5]. The spontaneous bleeding only occurred in 0.47%. The five patients with bleeding hemangioma had giant hepatic hemangioma defined as size greater than 4 cm. Exophytic lesions were found in four patients who presented with intraperitoneal bleeding. One patient with a centrally located tumor presented with intrahepatic bleeding.

The size or number of hemangiomas are not indicative for surgical treatment. The indications for the surgical treatment of hemangioma relate to tumor complications such as bleeding, rupture, Kasabach-Merritt syndrome, and organ or vessel compression[6]. The first management of bleeding and/or rupture hemangioma is to obtain hemostasis, then followed by the definitive treatment. Conservative therapy includes resuscitation and replacement with blood products. For those who continue to bleed, transarterial embolization of the tumor by an intervention radiologist is usually effective in controlling the bleeding. Transarterial embolization has been reported to successfully convert an inoperable hemangioma to an operable one[7] and embolization alone can be used as the sole treatment for giant hepatic hemangioma[8].The definitive surgical management for hemangiomas are resection, enucleation, or liver transplantation. Surgical resection or enucleation is often reserved for symptomatic and single-lobe lesion. Patients with symptomatic unresectable lesions, multiple lobar, or hilar involvement are considered for liver transplantation[9]. There are few successful case reports of liver transplantation (Table 1) for bleeding hepatic hemangioma[9], giant hepatic hemangioma involving both lobes with Kasabach-Merritt syndrome[10-12], and hepatic hemangioma mimicking hepatocellular carcinoma[13]. Our patient had bleeding from a giant hemangioma involving the entire liver that had failed embolization. The only available treatment was liver transplantation. Liver transplantation requires a multidisciplinary team and is not widely available in Thailand. The first patient who received liver transplantation was in 1990. The number of patients who had liver transplantations and the institutions that can perform the procedure has been increasing over the last two decades. Most patients on the waitlist for liver transplantation are patients with cirrhosis and its complications including hepatocellular carcinoma. Liver allocation and distribution are decided by the patient's medical urgency and blood group. Their medical urgency is guided in Thailand by the Model

Table 1. Review of the reported cases of liver transplantation for adult with giant hepatic hemangioma

Authors	Year of publication	Sex	Age	Indication for transplantation	Prior treatment	Type of donor	Waiting time
Klompmaker, et al.[11]	1989	M	27	Kasabach-Merritt syndrome	None	Deceased	NA
Russo, et al.[14]	1997	F	43	Abdominal distension, unable to resection	None	Deceased	3 months
Longeville, et al.[10]	1997	M	47	Kasabach-Merritt	Resection	Deceased	20 days
Keegan, et al.[15]	2001	M	34	Abdominal discomfort, dyspnea	Embolization	Deceased	NA
Kumashiro, et al.[16]	2002	F	48	Abdominal discomfort, Kasabach-Merritt	None	Living related	NA
Ferraz, et al.[12]	2004	F	28	Respiratory distress, Kasabach-Merritt	Embolization	Deceased	NA
Meguro, et al.[17]	2008	F	45	Abdominal discomfort, Kasabach-Merritt	Embolization	Living related	NA
Vagefi, et al.[9]	2011	F	39	Bleeding, abdominal compartment syndrome	None	Deceased	14 days
Zhong, et al.[18]	2014	F	27	Abdominal discomfort	None	Living related	NA

M = male; F = female; NA = not applicable

of End-stage Liver Disease (MELD). The MELD exemption allowed our patient who did not have cirrhosis or hepatocellular carcinoma to received liver transplantation. Most of the reported cases of transplant in hepatic hemangioma required deceased-donor liver transplantation with MELD exemption and a short waiting time. Three cases had living related donor transplantation. Our patient had to wait for almost six months in the hospital for her deceased-donor liver transplantation. The shortage of organ donation and the costs of the procedure and aftercare limits the numbers of liver transplantation in Thailand.

Conclusion

The treatment for bleeding or rupture of giant hepatic hemangioma usually include angiographic embolization and surgery. However, liver transplantation is an effective treatment and should be considered after the patient has failed or not a candidate for the other treatment modalities.

What is already known on this topic?

Hepatic hemangioma is one of the most common benign liver tumors. Most of them are asymptomatic. Asymptomatic hemangiomas usually do not require any treatment. The complications of bleeding or rupture hemangiomas are rare.

What this study adds?

Liver transplantation could be offered as the rescue therapy for bleeding or ruptured hepatic hemangioma in patients who are not candidate for surgery or have failed embolization.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Rungsinaporn K, Phaisakamas T. Frequency of abnormalities detected by upper abdominal ultrasound. J Med Assoc Thai 2008;91:1072-5.
2. Di Carlo I, Koshy R, Al Mudares S, Ardiri A, Bertino G, Toro A. Giant cavernous liver hemangiomas: is it the time to change the size categories? Hepatobiliary Pancreat Dis Int 2016; 15:21-9.
3. Zhang W, Huang ZY, Ke CS, Wu C, Zhang ZW, Zhang BX, et al. Surgical treatment of giant liver hemangioma larger than 10 cm: A single center's experience with 86 patients. Medicine (Baltimore) 2015;94:e1420.
4. Donati M, Stavrou GA, Donati A, Oldhafer KJ. The risk of spontaneous rupture of liver hemangiomas: a critical review of the literature. J Hepatobiliary Pancreat Sci 2011;18:797-805.
5. Mocchegiani F, Vincenzi P, Coletta M, Agostini A, Marzioni M, Baroni GS, et al. Prevalence and clinical outcome of hepatic haemangioma with specific reference to the risk of rupture: A large retrospective cross-sectional study. Dig Liver Dis 2016;48:309-14.
6. Toro A, Mahfouz AE, Ardiri A, Malaguarnera M, Malaguarnera G, Loria F, et al. What is changing in indications and treatment of hepatic hemangiomas. A review. Ann Hepatol 2014;13:327-39.
7. Lupinacci RM, Szejnfeld D, Farah JF. Spontaneous rupture of a giant hepatic hemangioma. Sequential treatment with preoperative transcatheter arterial embolization and conservative hepatectomy. G Chir 2011;32:469-72.
8. Sun JH, Nie CH, Zhang YL, Zhou GH, Ai J, Zhou TY, et al. Transcatheter arterial embolization alone for giant hepatic hemangioma. PLoS One 2015;

10:e0135158.
9. Vagefi PA, Klein I, Gelb B, Hameed B, Moff SL, Simko JP, et al. Emergent orthotopic liver transplantation for hemorrhage from a giant cavernous hepatic hemangioma: case report and review. J Gastrointest Surg 2011;15:209-14.
10. Longeville JH, de la Hall P, Dolan P, Holt AW, Lillie PE, Williams JA, et al. Treatment of a giant haemangioma of the liver with Kasabach-Merritt syndrome by orthotopic liver transplant a case report. HPB Surg 1997;10:159-62.
11. Klompmaker IJ, Sloof MJ, van der Meer J, de Jong GM, de Bruijn KM, Bams JL. Orthotopic liver transplantation in a patient with a giant cavernous hemangioma of the liver and Kasabach-Merritt syndrome. Transplantation 1989;48:149-51.
12. Ferraz AA, Sette MJ, Maia M, Lopes EP, Godoy MM, Petribu AT, et al. Liver transplant for the treatment of giant hepatic hemangioma. Liver Transpl 2004;10:1436-7.
13. Unal E, Francis F, Aquino A, Xu R, Morgan G, Teperman L. Liver transplant for mixed capillary-cavernous hemangioma masquerading as hepatocellular carcinoma in a patient with hepatocellular carcinoma. Exp Clin Transplant 2011;9:344-8.
14. Russo MW, Johnson MW, Fair JH, Brown RS Jr. Orthotopic liver transplantation for giant hepatic hemangioma. Am J Gastroenterol 1997;92:1940-1.
15. Keegan MT, Kamath GS, Vasdev GM, Findlay JY, Gores GJ, Steers JL, et al. Liver transplantation for massive hepatic haemangiomatosis causing restrictive lung disease. Br J Anaesth 2001;86: 431-4.
16. Kumashiro Y, Kasahara M, Nomoto K, Kawai M, Sasaki K, Kiuchi T, et al. Living donor liver transplantation for giant hepatic hemangioma with Kasabach-Merritt syndrome with a posterior segment graft. Liver Transpl 2002;8:721-4.
17. Meguro M, Soejima Y, Taketomi A, Ikegami T, Yamashita Y, Harada N, et al. Living donor liver transplantation in a patient with giant hepatic hemangioma complicated by Kasabach-Merritt syndrome: report of a case. Surg Today 2008;38:463-8.
18. Zhong L, Men TY, Yang GD, Gu Y, Chen G, Xing TH, et al. Case report: living donor liver transplantation for giant hepatic hemangioma using a right lobe graft without the middle hepatic vein. World J Surg Oncol 2014;12:83.