Hepatic Artery Vasospasm Masquerading as Hepatic Artery Thrombosis in a Case of Deceased Donor Liver Transplant

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Title: Hepatic Artery Vasospasm Masquerading as Hepatic Artery Thrombosis in a Case of Deceased Donor Liver Transplant

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Abstract
Hepatic arterial vasospasm can be a potential vascular complication after liver transplantation and can manifest as hepatic artery thrombosis. Due to scarcity of the literature on this pathology, its incidence, mechanism, relevance, diagnosis, and prognosis remain to be investigated. Our index case, a 64 year man with decompensated alcohol related cirrhosis underwent cadaveric orthotropic liver transplant and was having a normal post-operative course. On post-operative day 12, liver enzymes were elevated and Doppler ultrasound performed showed hepatic arterial occlusion. In view of hepatic artery thrombosis digital subtraction angiography (DSA) was done, which showed string bead appearance of graft hepatic artery, with no thrombosis or stenosis of hepatic artery anastomosis. It was managed by oral administration of vasodilator as well as intra-arterial administration of vasodilators through DSA catheter tip placed in hepatic artery. He responded well to the management and was discharged on post-operative day 24 with normal liver enzymes.

Keywords- hepatic artery, vasospasm, liver transplant, doppler ultrasound
Introduction

Hepatic artery (HA) vasospasm has not been well recognized as a post-operative vascular complication after liver transplant due to lack of sufficient data. Literature cites incidence of hepatic artery thrombosis (HAT) occurring in 2-5% of liver transplant recipients but there is no well documented incidence of HA spasm being treated with intervention.

Case Report

A 64 year-old male having decompensated alcohol related liver cirrhosis along with portal hypertension and jaundice and treatment history of cytomegalovirus, classified as Child-Pugh C and MELD score of 19 was subjected to a cadaveric orthotopic liver transplantation. Surgical procedure was performed with a piggy back technique used for hepatic outflow and veno-venous bypass was not required. Graft liver had single HA with right and left arterial branches and recipient had normal arterial anatomy with anomalous non HA confluence. Donor HA and recipient HA was anastomosed end to end using 8/0 prolene after spatulating. Total cold ischemia time was 270 minutes and calculated blood loss was around 2 litres.

Post operatively patient was being monitored with series of liver function tests along with other blood parameters and 12 hourly doppler ultrasound (DUS). The value of Aspartate Aminotransferase (AST) improved from 3547 U/L on day 0 to 57 U/L on post operative day 9, similarly value of Alanine Aminotransferase (ALT) improved from 956 U/L to 39 U/L respectively on day 9 and Alkaline Phosphatase (ALP) improved from 421 U/L to 291 U/L (Table 1). Normal waveform was seen on DUS done on day 1 to day 10 with normal waveform in hepatic veins (HV) and Inferior vena cava with peak systolic velocity (PSV) of 11cm/s. Hepatic artery showed normal pattern with PSV = 50cm/seconds and Resistive index (RI) of 0.65 and portal vein (PV) also showed normal wave form. Standard immunosuppression including tacrolimus, Mycophenolate mofetil and oral steroids were given.

An elevation of liver enzymes was observed on day 11. On day 12 with AST level increased from 420 U/L to 4793 U/L and ALT from 535 U/L to 1145 U/L (Table 1) while bilirubin on day 12 was 5.6mg/dL. Doppler ultrasound done on intervening night of post-operative day 11-12 demonstrated reduced doppler signal and flow in the graft hepatic artery. A diagnosis of possible HAT was kept and patient was then taken for an emergency contrast tomography angiography prior to re-exploration which showed visualisation of hepatic artery only in the proximal part. Distal part was not visualized. PV, HV and biliary system were normal. Possibility of hepatic artery thrombosis or stenosis was made.

We immediately conducted digital subtraction angiography (DSA) for intervention and urokinase thrombolysis for probable (HAT). A 5 Fr SIM 1 catheter was introduced under aseptic condition
through right femoral artery; diagnostic run of celiac trunk was obtained which showed short stump of dilated anastomotic site along with string of beads appearance was visualized subsequently over the graft portion of HA. Suspecting a spasm there, intra-catheter papaverine 3ml/minute (300mg in 100 ml normal saline) was injected. It was noticed that the graft HA opens up to show contrast flow immediately. However after 15 minutes the HA again collapsed to give string of bead appearance. There was no narrowing at the anastomosis and thrombosis. Again papaverine was given along with injection urokinase 25,000 IU and it responded well. We kept the catheter tip distal to HA anastomosis for 48 hours and slow urokinase was administered. Check DSA done after 24 hours showed both right and left hepatic artery. Similar findings were noted in DSA done after 48 hours and the catheter was removed. Simultaneously nicorandil was started intravenously at a dose of 48 mg diluted in 50 ml of normal saline and infused at 0.5 ml/hr which was increased to 1.5ml/hr. Gradual improvement in liver enzymes was noted and he was discharged on day 24 with AST level of 58 U/L and ALT of 40 U/L and normal total bilirubin level (1mg/dL). DUS on the day of discharge showed normal continuous hepatic arterial flow with PSV 45cm/sec and RI 0.60 with normal HV and PV colorflow.
Discussion

Arterial vasospasm is a state of arterial vessel constriction, affected segmental or entire vessel becomes rigid and lumen narrows or even gets occluded. Hepatic arterial flow follows Poiseuille’s law, when hepatic artery is contracted, its diameter reduces and as a result, the resistance of the hepatic arterial flow increases. Wei Chen et al in a retrospective study elaborated the findings of hepatic arterial vasospasm on DUS done in patients of early after liver transplantation. They conducted routine DUS on nine patients’ post-orthotopic liver transplant within 24 hours of surgery. Each of the 9 patients was given a single 10 mg dose of nifedipine sublingually and monitored by ultrasonography when vasospasm was suspected on the basis of the DUS results. They observed antegrade diastolic flow along the course of the main hepatic artery and its intrahepatic branches with the decrease in resistive indices on average from 1.0 to 0.76 ten to 45 minutes after administration of the vasodilator. Along with increase in PSV from 57 cm/s before nifedipine administration to 77 cm/s after administration. They concluded that high-resistance hepatic arterial flow (resistive index = 1) early after liver transplantation is indicative of hepatic arterial vasospasm if it responds to vasodilators and considered DUS as a useful tool for the diagnosis of hepatic artery vasospasm.

The reason behind hepatic arterial vasospasm is not well understood because its concept has not been established clinically. A study done highlighted the effect of university of Wisconsin (UW) solution on hepatic artery and showed that UW solution impairs the endothelium dependent relaxation of hepatic arteries. In our case we have used Histidine-tryptophan-ketoglutarate (HTK) solution as an organ preservation solution. Various studies suggested elevated level of plasma norepinephrine due to surgical stress, removal of donor liver might have an important effect on agonal arterial spasm.

Donor age and prolonged cold ischemia time can also be contributor for the vasospasm in post-operative period. In a study done by Garcia-Criado A et al. older donor age (>50 years) and extended cold ischemia time (410 minutes ) were related to high resistant hepatic arterial flow immediately after transplantation. Cold ischemia time calculated in our case was 270 minutes, which have favourable prognosis, but the donor age was 68 year, which can be a contributor to the above hospital course and hepatic artery vasospasm. Prolonged cold storage and reperfusion can cause sinusoidal endothelial cell injury leading to microcirculatory disturbances. Hepatic microcirculation alteration might result in increased resistance to hepatic arterial flow.

Hepatic arterial vasospasm can involve both the MHA and the intraparenchymal branches in varying degrees. Sakamoto et al. reported segmental MHA vasospasm during re-exploration surgery in two patients after liver transplantation. We encountered vasospasm of graft hepatic artery, on DSA short stump of MHA was opacified.
The impact of hepatic artery vasospasm in transplants is still not determined; it may cause reduction of arterial flow to the graft and may induce thrombosis. Vasospasm in a revascularized tissue could impair tissue perfusion even when the anastomises is patent was demonstrated in a study by Richard et al13. The impact of vasospasm in our patient was in the form of deranged liver function test on day 11; with increase in liver enzymes and increased bilirubin levels, which were significantly improved after intra-venous administration of nicorandil as well as intra-arterial papaverine and urokinase infusion. Though, it was demonstrated at the time of DSA that vasospasm was relieved with the use of papaverine and sustained with nicorandil, it is unclear whether use of urokinase over next 48 hours did ameliorate the prevention of its recurrence. Post one year follow up his DUS findings are normal.

**Conclusion**

Hepatic artery vasospasm can be another entity of vascular complication in liver transplant patients. This can be a rare possibility when early HAT is suspected. Only diagnostic DSA done prior to a decision about re-exploration, which may carry higher mortality or morbidity, can help in distinguishing this rare occurrence. If therapeutically managed in this situation through catheter based antispasmodic as well as augmentation of oral vasodilators, it can be treated successfully preventing a re-exploration in a transplanted patient. Further research is needed to completely understand the aetiology of Hepatic artery spasm, its relationship with HAT if any, and the prognoses of vasospasm with and without vasodilatation.
References


Figure legends

Figure1(a)- Digital subtraction angiography (DSA) images of the hepatic artery (HA) showing short string of beads appearance of graft portion of HA due to vasospasm (black arrow).

Figure1 (b)- Dilated HA anastomosis (white arrow) and string of beads appearance of graft portion of HA (black arrow) visualised after intra-arterial papaverine and urokinase and intravenous nicorandil administration
Table 1. Variations in liver enzymes value

<table>
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<th>Liver function test</th>
<th>Post-operative Day-0</th>
<th>Post-operative Day-09</th>
<th>Post-operative Day 11</th>
<th>Post-operative Day 12</th>
<th>Post-operative day 24</th>
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<td>Aspartate Aminotransferase (U/L)</td>
<td>3547</td>
<td>57</td>
<td>420</td>
<td>4793</td>
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<td>Alanine Aminotransferase (U/L)</td>
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<td>39</td>
<td>535</td>
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<td>Alkaline Phosphatase (U/L)</td>
<td>421</td>
<td>291</td>
<td>343</td>
<td>350</td>
<td>145</td>
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</tbody>
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Conception and design of the study- AB, LK

Analysis and interpretation of data- CT

Drafting the article- CT, AB

Critical Revision- AB, LK, DD, NK

Final approval- AB, LK
Abbreviations

AST- Aspartate Aminotransferase
ALT- Alanine Aminotransferase
ALP- Alkaline Phosphatase
DSA- Digital Subtraction Angiography
DUS- Doppler Ultrasound
HA- Hepatic Artery
HAT- Hepatic Artery Thrombosis
HTK- Histidine-Tryptophan-Ketoglutarate
MELD – Model for End Stage Liver Diseases
MHA- Main Hepatic Artery
MMF- Mycophenolate mofetil
PSV- Peak Systolic Velocity
RI- Resistive Index
UW- University of Wisconsin