

Modified Rapid Deployment Hemostat Terminates Bleeding From Hepatic Rupture in Third Trimester

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J Trauma. 2006;61:739–742.

Severe atraumatic intraperitoneal hemorrhage is uncommon during the third trimester of pregnancy. Within this small population of patients, ruptured hepatic adenoma, ruptured splenic artery aneurysm, and uterine rupture represent three common causes of antepartum third trimester intraperitoneal bleeding. Other less common causes include spontaneous bleeding because of the HELLP Syndrome (Hemolysis, Elevated Liver enzymes, Low Platelets) and intraperitoneal rupture of a placenta previa with percreta, among others. This case report describes the use of the Modified Rapid Deployment Hemostat (MRDH, Marine Polymer Technologies, Inc., Danvers, Mass.) to control exsanguinating hemorrhage in a patient with severe pre-eclampsia that was found to have a large spontaneous liver injury. With the scope of trauma surgery evolving into a more generalized trauma and emergency general surgery specialty, this report is also intended to provide insight into an uncommon but life-threatening cause of hemorrhage that may confront the emergency general surgeon.

CASE REPORT

A 32-year-old woman with a 28-week gestation presented to our facility with a 4-hour history of severe right upper quadrant pain of increasing severity. She was found to have a blood pressure of 220/110 mm Hg, heart rate of 100 bpm, and evidence of proteinuria on dipstick examination. Laboratory investigation revealed elevated liver function tests (serum glutamic oxaloacetic transaminase [SGOT] 1856 U/L,

serum glutamic pyruvic transaminase [SGPT] 1111 U/L), alkaline phosphatase 410 U/L, total bilirubin 1.8 mg/dL), a hematocrit of 33%, base excess of 0 mmol/L, and a platelet count of $126 \times 10^3 \mu\text{L}$. Over the next 3 hours, the hematocrit dropped to 22%, base excess dropped to -9 mmol/L , and platelets dropped to $89 \times 10^3 \mu\text{L}$. Based on these findings, the obstetrics service diagnosed this patient with severe pre-eclampsia and took her to the operating room for an emergent Cesarean section.

Upon opening the abdomen via a Pfannenstiel incision, approximately a liter of free intraperitoneal blood was evacuated. The obstetrics team quickly delivered the baby and called an intraoperative trauma surgery consultation. The trauma team found the patient tachycardic, but normotensive, with bleeding originating from the right upper quadrant. A midline incision was made to facilitate exposure, and this area was quickly packed with good control of hemorrhage. The lesser sac was opened and a normal splenic artery was appreciated without aneurysm. Exploration of the remainder of the abdomen was without obvious bleeding. All hemorrhage appeared to be from the liver.

The packs were slowly removed to reveal a large capsular rupture with deep extension involving segments five, six, and seven. There was significant congestive hepatomegaly, with focal areas of necrosis throughout the entire liver sparing the left lateral segments. Hemostasis was obtained with electrocautery and Surgicel (oxidized regenerated cellulose hemostat, absorbable, Johnson & Johnson Inc., N.J.). The abdomen was closed primarily and the patient was returned to the Intensive Care Unit (ICU) hemodynamically stable.

The liver transplantation team was consulted because of the worrisome intraoperative appearance of the liver. Multiple hepatic Doppler flow studies were conducted to rule out large vessel thrombosis. These studies revealed normal flow through the hepatic veins, hepatic arteries, vena-caval system, and the portal venous system. Over the next 24 hours, the patient became hemodynamically unstable, with a falling hematocrit, requiring significant fluid and blood product resuscitation, and developed a significant coagulopathy. She was returned to the operating room for re-exploration. Upon opening, a moderate amount of gross blood was noted. The liver appeared more congested with extension of the necrotic

Submitted for publication May 2, 2005.

Accepted for publication July 19, 2005.

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The manufacturer, Marine Polymer Technologies, Inc., did not participate in the design, data collection, analysis, or manuscript preparation regarding this investigation.

Supported by funds from Marine Polymer Technologies, Inc., Danvers, MA.

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DOI: 10.1097/01.ta.0000195491.92467.dd

areas to involve the surrounding previously normal liver parenchyma, with multiple punctate bleeding lacerations. Biopsies of these areas were taken and sent to pathology. A large subcapsular hematoma was also identified over the dome of the liver. Minimal manipulation of this area resulted in disruption of the hematoma, and exsanguinating bleeding ensued requiring massive transfusion. The liver was packed with reasonable control of bleeding. A temporary abdominal closure was placed and the patient was returned to the ICU for ongoing resuscitation. The liver transplantation team was again consulted for possible transplantation as a salvage maneuver. Review of the initial biopsies showed diffuse areas of microvascular necrosis with lymphocytic infiltrate and scattered areas of normal appearing parenchyma. Based upon these findings, the transplant team decided that enough functional liver remained, and all efforts should continue to salvage the native organ.

The next day, the patient marginally improved and was taken back to the operating room for re-exploration and pack removal. Additional biopsies were taken from multiple areas of the liver. When the packing was removed, there was diffuse severe bleeding from the exposed raw parenchyma, although no discrete large vascular injury was visible. The patient had become coagulopathic and was bleeding aggressively. Recombinant activated Factor VII was given intravenously twice (100 $\mu\text{g}/\text{kg}$) without any evidence of effect. Several deep suture ligatures were placed, however, these had no effect on hemorrhage control. Hemostasis was attempted with electrocautery as well as the argon beam coagulator without success. Over 2 hours had elapsed since the beginning of the re-exploration and the patient was becoming hypothermic. At this time, the liver transplant team contemplated salvage transplantation, and a potential donor was identified. As a final desperate measure to control hemorrhage, half of the bleeding surface of the liver was covered with Nu-Knit and cauterized with the argon beam over the Nu-Knit (oxidized regenerated cellulose hemostat, absorbable, in a stronger web that can hold suture, Johnson & Johnson Inc.). The other half was covered with a new hemostatic agent, the modified rapid deployment hemostat (MRDH). Both of these techniques have been used successfully as salvage maneuvers to control hemorrhage by our institution, although a direct comparison has never been made between these two techniques. Consequently, the decision was made to try both techniques on this life-threatening hemorrhage. Nu-Knit is routinely available at our institution, and the MRDH is available for compassionate use, based on our previous published experience with this hemostatic bandage,^{1,2} by contacting an on-call surgeon. Direct pressure was applied to both hemostatic agents for 5 minutes and standard packs rapidly placed over them. At the time the MRDH was placed, the patient was normothermic, pH was 7.29 units, base excess was -11 mmol/L, platelet count was $56 \times 10^3 \mu\text{L}$, PT was 25 seconds and PTT was greater than 120 seconds. The MRDH treated side appeared to have excellent hemostasis, while the Nu-Knit side had continued ongoing

bleeding, but not significant enough to remove the existing minimal clot and replace the Nu-Knit with MRDH. Bleeding had slowed enough that the transplant team decided to release the donor liver to another recipient and forgo transplantation of our patient at this time. A temporary abdominal closure was applied and the patient was returned to the ICU.

Review of the newest biopsies revealed worsening diffuse hepatic necrosis with no identifiable normal parenchyma remaining. Over the next day, hepatic function declined. The prothrombin time and partial thromboplastin time were grossly elevated to 22 and 117 seconds, respectively (and refractory to treatment), and the total bilirubin had increased to 12 mg/dL. Based on these findings, and the clinical picture of deterioration and fulminant hepatic failure, the trauma team and transplant team decided to proceed with salvage orthotopic liver transplantation. The patient was listed as Status One, a donor was quickly identified, and the patient was taken back to the operating room the next day (postoperative day 10 from the original exploration).

Upon inspecting the liver, complete hemostasis was noted in areas covered by the MRDH, while areas covered by Nu-Knit had continuous ongoing bleeding. At this point, the case was turned over to the transplant team. The patient underwent uncomplicated orthotopic liver transplantation. After a lengthy ICU stay, the patient recovered and was discharged home with excellent functional status. On follow-up, both the patient and the baby are in doing well.

DISCUSSION

This case report describes the use of a novel topical hemostatic agent, the MRDH, in a case of liver hemorrhage refractory to conventional interventions. Although this patient was eventually saved by a successful liver transplant, it is unclear if that could have been avoided by earlier control of hemorrhage with the MRDH. Certainly, one would agree that rapid control of life threatening hemorrhage could only improve outcome under any circumstance. It is not known if the extent of liver necrosis was predetermined by the natural history of the patient's disease, or if mild necrosis was worsened to complete necrosis and hepatic failure by ongoing hemorrhage, hemodynamic instability, and poor perfusion of the end organ.

The exact pathophysiology of the patient's diagnosis is still in question and remains a debate among obstetricians, surgeons, and pathologists at our institution, however, the diagnosis of this syndrome itself is agreed upon by all involved in the case. This presentation has been previously described³⁻⁷ as Spontaneous Hepatic Hemorrhage in Pregnancy (SHHP) and generally occurs in one in 15,000 births.³ Most experts feel this syndrome is related to the pre-eclampsia associated HELLP Syndrome, or one of several variants of this microangiopathic thrombosis syndrome.^{8,9} Pathologic examination of the recipient hepatectomy specimen revealed microangiopathic thrombosis consistent with SHHP and HELLP Syndrome. Some authors have proposed an association with the antiphospholipid syndrome;¹⁰

however, our patient tested negative for this. Successful treatment options previously described for SHHP include angiographic embolization,¹¹ laparotomy with packing,^{6,7} partial hepatectomy,¹¹ and liver transplantation.^{4,12} There are no reports of patients with disease this severe who were successfully managed conservatively.

The United States Food and Drug Administration recently cleared the MRDH for use as a class I medical device. The MRDH contains a purified chemical hemostat called fully acetylated poly-*N*-acetyl glucosamine.^{13,14} This device was found to be an effective hemostat in animals and humans after severe traumatic liver injury with acidosis, hypothermia, and coagulopathy.^{1,2} The device has also found success in controlling a variety of other types of bleeding, including arterial injuries, esophageal variceal bleeding, and splenic bleeding, among others.^{15–20} The exact hemostatic mechanisms of action of the MRDH remain incompletely elucidated; however, a summary of existing data has recently been published,¹ as well as several newer references describing specific molecular level platelet and red blood cell poly-*N*-acetyl glucosamine interactions.^{21–23} These interactions appear to be receptor mediated and are consequently high affinity and high specificity interactions. Other investigators have demonstrated efficacy of this polymer in fully anticoagulated animal models,^{24,25} suggesting a multi-faceted hemostatic mechanism independent of direct receptor-mediated platelet or red blood cell interactions. It has subsequently been shown to control puncture wound hemorrhage in isolated rat aortic rings in the absence of any formed elements of blood.²⁶ The mechanism of action was speculated to be via polymer-induced local endothelin release.²⁶ The data suggests multiple mechanisms of action of the MRDH, and additional work is necessary to completely understand the hemostatic mechanism.

SHHP is a devastating condition with hemorrhage not unlike the severe blunt hepatic injury familiar to the trauma surgeon. Understanding SHHP and the HELLP Syndrome, as well as the available hemostatic adjuncts, may better prepare the emergency general surgeon to deal with this particular intra-abdominal catastrophe. This is the first description of the use of the MRDH in a nontraumatized patient with significant hemorrhage. Our single experience with the MRDH under these circumstances was successful in controlling atraumatic hemorrhage and postponing liver transplantation. Additional research and experience is needed to characterize the properties of this new bandage under a variety of conditions.

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