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Hepatic hematoma after islet cell transplantation

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Allogeneic islet cell transplantation (ICT) is an alternative treatment in a selected group of subjects with type 1 diabetes mellitus (T1DM)(1). Percutaneous trans-hepatic portal access (PTHA) is a minimally invasive technique for ICT which avoids open or laparoscopic surgery, general anesthesia and prolonged hospitalization(2,3). Bleeding, portal vein thrombosis and portal hypertension are the most reported complications(5-7)(8). The potential risk of acute bleeding may be less with a controlled operative (laparoscopic) approach, however the feasibility of the percutaneous approach has made it preferable to date in most centers (9,10)

Improvements in islet purification, smaller infused volume, infusion by gravity, and addition of heparin are factors that have reduced the incidence of portal vein thrombosis(11,12). Bleeding complications are rare, but when they occur, typically originate from the parenchymal tract after removal of the infusion catheter. This may be exacerbated with heparin administration, however sealing of the intrahepatic tract using gelfoam slurry (collagen suspension); collagen-thrombin paste (D-statTM or AviteneTM-contrast paste), thrombostatic coils, and/or cautery has been shown to reduce risks of bleeding (13-15). We

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describe a case of a massive subcapsular hepatic hematoma after intra-portal ICT secondary to arterial bleeding (Case#1) and review procedure-related hemorrhages at DRI-Miami.

Case#1: a 50 year-old female with T1DM for 21 years who was on an insulin pump with severe hypoglycemia episodes, hypoglycemia unawareness and unstable glucose control received, her first allogeneic ICT under an immunosuppressive regimen consisting of induction thymoglobulin-etanercept (1st ICT), basiliximab-etanercept (2nd ICT) and maintenance with sirolimus/tacrolimus. Six months after the 1st ICT (7.281 IEQ/kg) insulin dose was reduced by 50%. A second ICT (11,748 IEQ/kg) was performed 241 days after initial infusion utilizing the PTHA approach (11). A packed cell volume of 6ml (total 303ml with diluents), mixed with 3871 units of heparin (70U/Kg) according to protocol was infused by gravity. There was no significant elevation in mean portal vein pressure, measuring 2,3 and 5mmHg before, during and after ICT respectively. The catheter tract was sealed with Gelfoam pledgets and D-STAT™ (15). a continuous heparin infusion was commenced according to protocol to achieve and maintain partial thromboplastin time (PTT) between 50-60 seconds which was substituted by enoxaparin 30mg BID at 48h after ICT. Abdominal ultrasound at 24 hours post procedure showed no significant abnormality, specifically no evidence of intra- or extra-hepatic bleeding (Hb:12.5g/dl; hematocrit (Hct): 37.5). The Subject was discharged at 48 hours post infusion. The subject was readmitted via the ER on POD 4, describing progressive dull abdominal pain that had started shortly after discharge, and culminated in severe right upper quadrant pain, a syncopal episode, nausea and vomiting on the day of admission. A CT scan showed a subcapsular hematoma with 15cm (cranio-caudad dimension) adjacent to the right hepatic lobe, active extravasation of contrast, and large amounts of free abdominal and pelvic fluid. Hb and Hct had fallen to 7.5g/dl and 21.5% respectively.

A hepatic angiogram was performed which demonstrated a pseudoaneurysm, concluded to be the cause of the bleeding. The pseudoaneurysm was successfully treated using coil embolization, the patient received a five unit blood transfusion and was discharged in stable condition (Hb:11.1g/dl-Htc:31.4%). The patient continued to suffer with right upper quadrant pain, percutaneous drainage was offered but the patient opted for non-operative management with opiate analgesics. Serial repeat cross-sectional CT at 1 and 6 months revealed a 14.6×14.4×5.8cm hepatic hematoma which shrunk to 5.0 × 2.5cm, by which time the subject had achieved insulin independence. Analgesics were weaned and discontinued. An MRI at 12 months showed a 3.7 × 1.8cm residual cyst, and the surrounding liver was normal with no periportal or generalized steatosis. The subject remains insulin free (>475 days) with HbA1c 5.1%.

On previous reports, the risk of bleeding after ICT varied from 0-3.6%, and originated from the liver parenchymal tract (2,3,13-15). At DRI-Miami, 52 subjects received 89 ICT from 100 donors (March, 2012). We retrospectively evaluated demographics and laboratory findings of ICT (Fig-1). The bleeding incidence (6.7%) is similar to other ICT centers (15). Overall, 3/6 required blood transfusions, 5/6 bleedings occurred on ICT procedures utilizing gelfoam only. There have been no further bleeding complications since D-stat was introduced (12) until the present case described. Case#1 had the highest hemoglobin drop after ICT at our center. The number of needle passes and heparin dose did not differ from Case#1 to former ICT cases.

Multiple needle passes to access the portal vein, elevated portal pressure, heparin dose (45U/kg), platelet <150,000/mm³ and aspirin use are associated with ICT bleedings. False-aneurysms of the hepatic artery and its branches are rare but well recognized potential complications after invasive transhepatic procedures (16,17). The complications described in this case report was a delayed event, not evident on ultrasound imaging at 24 hours. While

most ICT patients may have mild residual right upper quadrant pain when they are ready for discharge, usually the day after their procedure, the pain should not be severe as in this case. Pain which worsens after discharge should prompt an immediate careful investigation to detect rare but potentially life threatening complications such as this one.

Non-operative management of hepatic hematomas for hemodynamically stable patients without signs of infection include: blood transfusion, pain control, prophylactic antibiotics and bed rest. Subcapsular-hematomas/asymptomatic-intraperitoneal bleeds often resolve spontaneously, but may occasionally extend and cause hepatic compartment syndromes (14). Hemorrhage with hemodynamic instability, tachycardia and/or hypotension requiring blood transfusion may need urgent surgical or laparoscopic interventions(5,14). Pseudoaneurysms are rare complications occurring in less than 1% percutaneous transhepatic procedures, however when detected should be treated due to their risk of late bleeding. Depending on size and location, false-aneurysms are treated either by percutaneous embolization, or by direct thrombin injection(18,19).

A large hepatic hematoma caused by an arterial bleeding, might be controlled by angiographic embolization and managed non-operatively. We present this case to demonstrate a rare complication and its management, occurring as a result of ICT.

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Demographics and ICT Characteristics

Procedures	Presented procedure (n=1) (Case #1)	Other procedure related bleedings (n=5) (Case #2, 3, 4, 5)	Procedures with no complication (n=83) (47 subjects)
Patients' characteristics			
Gender	Female	3 Females, 1 Male	28 Females, 19 Males
Age	49.5	43.17 ± 9.8	44.4 ± 8.5
Duration of diabetes (years)	21.38	34.17 ± 10.9	29.5 ± 11.3
Microvascular complications	No	Yes (4) No (1)	Yes (60) No (23)
Macrovascular complications	No	Yes (4) No (1)	Yes (35) No (28)
(n) IA/LAK	1(IA)	4(IA), 1(LAK)	772 (IA), 11(LAK)
ICT	2 nd ICT	1 st ICT(2), 2 nd ICT(3)	1.8 ICT/subject
Weight (kg)	55	55.5 ± 5.1	66.1 ± 11.4
Hemoglobin (mg/dl)	12.1	11.8 ± 1.1	12.7 ± 1.5
Hematocrit	35	34.3 ± 3.4	37.2 ± 4.72
Platelet (mm3/1000)	198	237 ± 50.4	246 ± 64.5
INR	1.05	1.01 ± 0.13	1.006 ± 0.1
Islet mass (IE/kg)	11811	7105 ± 1536	7525 ± 2439
Packed cell volume (ml)	6	2.96 ± 1.1	3.5 ± 2.2
Total volume infused (ml)	303	272.6 ± 50.4	252.2 ± 70.6
Number of needles passes	2	3.25 ± 2.6	2.4 ± 1.6
Time to portal vein access (min)	32	22 ± 20	17.1 ± 11.6
Heparin dose (Uxkg)	3850	2694 ± 1849	2672 ± 1074
Pre-tx Portal Pressure (mmHg)	3	2.8 ± 1.1	4.4 ± 2.3
Peak portal pressure (mm/Hg)	5	5.6 ± 1.8	7.17 ± 2.9
Hemoglobin drop (pre-post)	27.2%	13.9% (± 12.8)	5.96% (± 5.36)

Case#1

Figure 1.

Demographics and ICT Characteristics. Case#1: CT-Scan image of hepatic hematoma at 1st month (14.6×5.8 cm) at 6th month (5.0×2.5 cm). MRI at 12th month (3.7 × 1.8cm).