

AMSER Case of the Month:

33-year-old male presents with abdominal pain, melena, pancytopenia, elevated liver enzymes and ferritin, status post haploidentical peripheral blood cell transplant (HIPBCT)

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Patient Presentation

- HPI: 33-year-old male with past medical history of Acute Myeloid Leukemia (AML) and Myeloproliferative Disorder (MPD) status post haploidentical peripheral blood cell transplant (HIPBCT). Patient presents from county jail with abdominal pain, melena, and hemoptysis for one week.
- PMHx: AML/MPD s/p HIPBCT, anxiety, asthma, BP I, depression
- PSHx: Left ear myringotomy, 4 GI endoscopies, colonoscopy
- Family Hx: non-contributory
- Social Hx: Drinks 750 ml cognac daily, smokes 1.5-2 ppd, smokes marijuana daily, currently incarcerated

Pertinent Labs

- CMP
 - AST/ALT 295/262
 - Alk phos 1,107
 - TB 1.8
- CBC
 - WBC 1.27 (ANC 0.53)
 - H/H 8.2/24.7
 - Platelets 32
- Iron 234, ferritin 16,294, transferrin 181, TIBC 259

What Imaging Should We Order?

Select the applicable ACR Appropriateness Criteria

Variant 3:

Acute nonlocalized abdominal pain. Neutropenic patient. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
CT abdomen and pelvis with IV contrast	Usually Appropriate	☢☢☢☢
CT abdomen and pelvis without IV contrast	May Be Appropriate	☢☢☢☢
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	○
US abdomen	May Be Appropriate	○
MRI abdomen and pelvis without IV contrast	May Be Appropriate	○
CT abdomen and pelvis without and with IV contrast	May Be Appropriate	☢☢☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢☢
WBC scan abdomen and pelvis	Usually Not Appropriate	☢☢☢☢☢
Radiography abdomen	Usually Not Appropriate	☢☢
Nuclear medicine scan gallbladder	Usually Not Appropriate	☢☢
Fluoroscopy contrast enema	Usually Not Appropriate	☢☢☢☢
Fluoroscopy upper GI series with small bowel follow-through	Usually Not Appropriate	☢☢☢☢

This imaging modality was ordered by the Hematology physician



CT Findings (unlabeled)

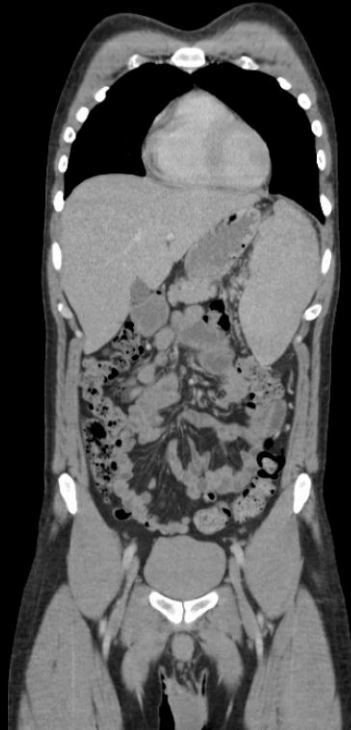


Fig. 1



Fig. 2

CT chest abdomen pelvis with IV contrast. Two coronal sections are shown.

CT Findings (labeled)

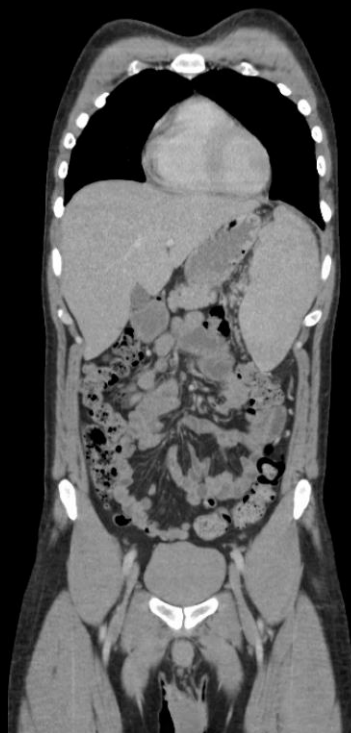


Fig. 1

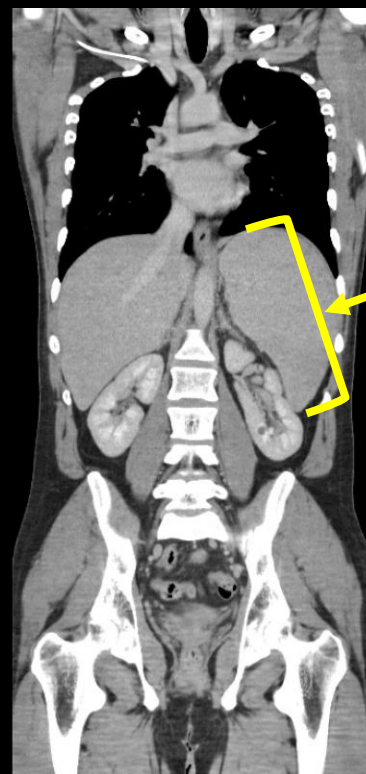


Fig. 2

Fig. 1 demonstrates normal liver Fig 2. demonstrates splenomegaly

US Findings



Fig. 1

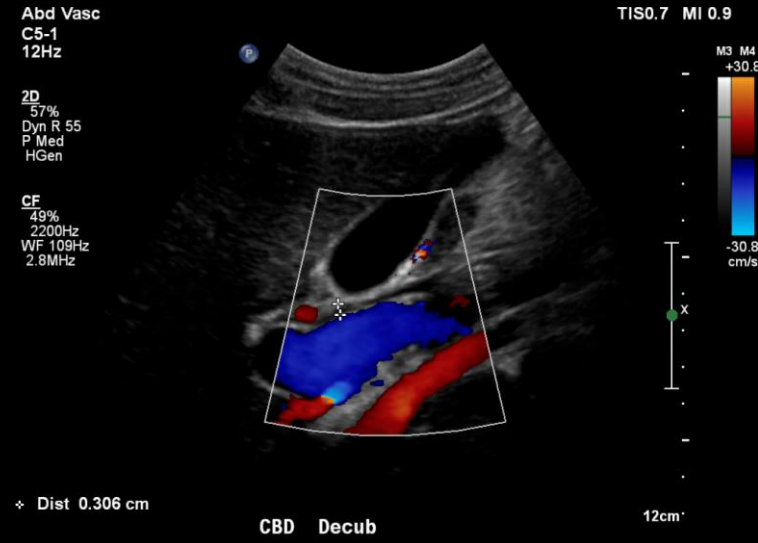


Fig. 2



Fig. 3

Fig. 1 shows a normal liver in the longitudinal plane. Fig. 2 demonstrates a normal 3 mm common bile duct. Fig. 3 demonstrates and enlarged spleen measuring 13.4 cm which correlates with CT findings

Differential Diagnosis

- GVHD
 - Drug toxicity
 - Cirrhosis
 - Hemochromatosis
 - Wilson's Disease
 - Viral hepatitis
 - Primary biliary cirrhosis
 - Veno-occlusive disorder
 - Enteritis
 - IBD
- Given the patient's history and lack of imaging findings, suspicion for GVHD is high and a liver biopsy is ordered.

Liver Biopsy²

- Transjugular liver biopsy (TJLB) is preferred over percutaneous liver biopsy (PLB) for the following indications:
 - Ascites
 - Coagulopathy (prolonged PT or PTT or a low platelet count) to the extent that PLB is contraindicated. A safe upper limit for deranged bleeding parameters has not been described in the literature. Some institutions use a Normalized Ratio (INR) >1.7 times the control or a platelet count <35,000. Our patient's platelets were 32,000.
 - Other reasons, e.g., a small shrunken liver, extreme obesity, or peliosis hepatis.

Transjugular Liver Biopsy



The right IJ is accessed using a 21 gauge needle under US guidance and dilated to accept a 9 Fr Ansel sheath

Transjugular Liver Biopsy



Fig. 1

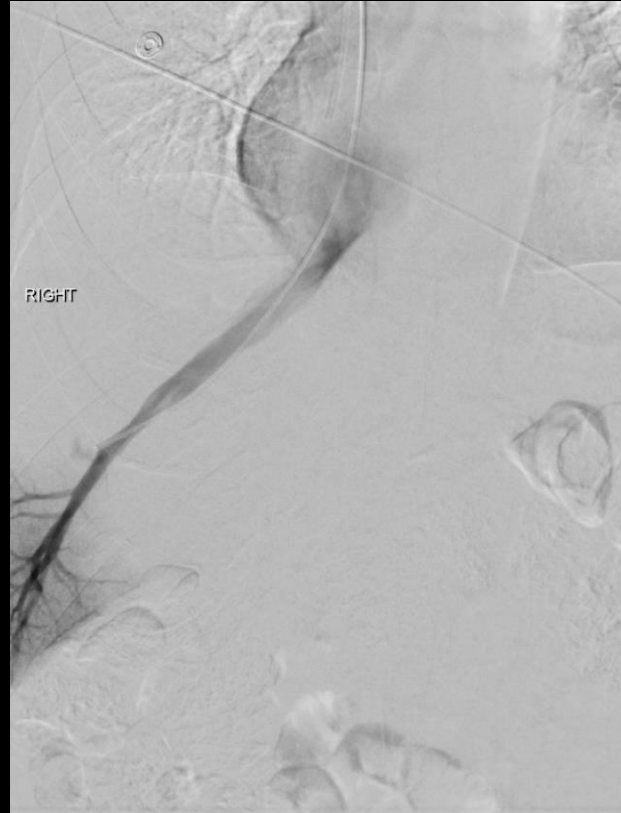


Fig. 2

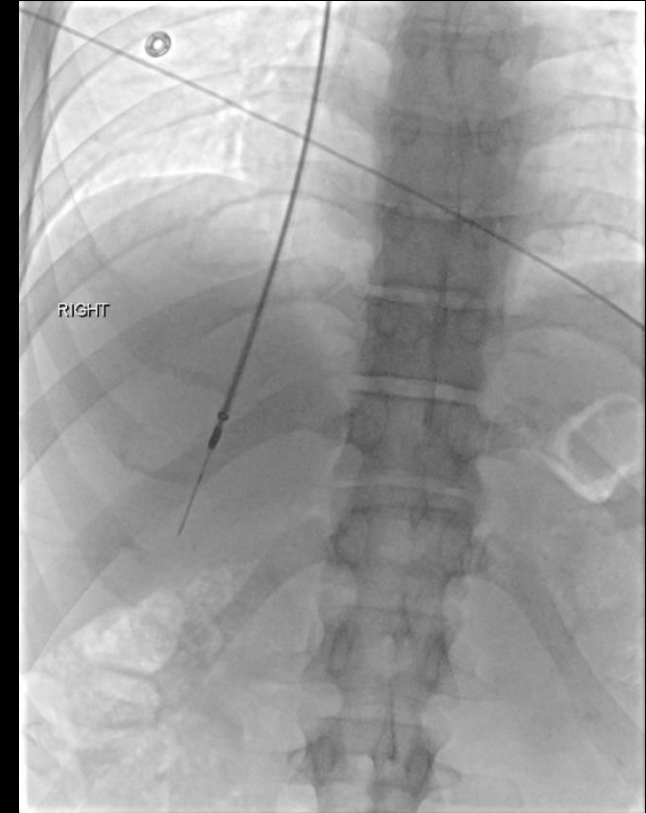


Fig. 3

Fig. 1 demonstrates the operator accessing the RHV with an MPB catheter. The RHV is confirmed using DSA imaging with a hand run of IV contrast (Fig. 2). An Amplatz wire was inserted into the RHV and the sheath of the T Lab TILB kit was advanced. The wire was removed, and the biopsy needle was advanced to the middle 1/3 of the RHV (Fig. 3) and angled anteriorly. 3 core specimens were acquired.

Biopsy Results

Fig. 1 – Normal portal triad with a branch of bile duct (green arrow), branch of portal vein (blue arrow), and branch of hepatic artery (red arrow).

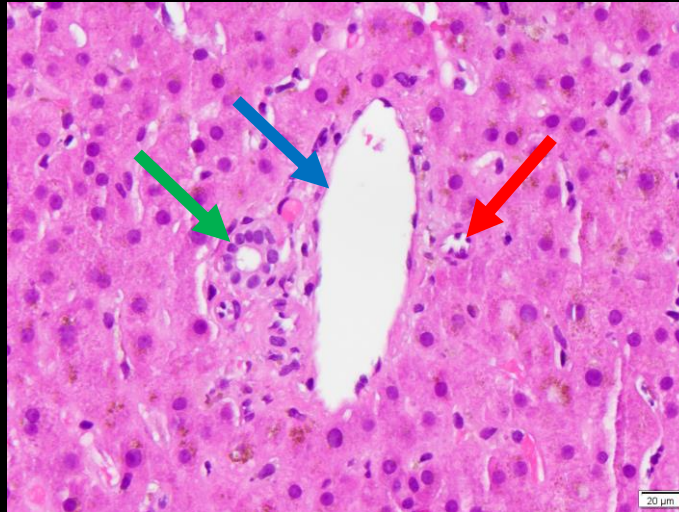


Fig. 1

Fig. 2 – Low cuboidal cells of bile duct branch staining positive for CK7 (green arrow) – normal result. Several CK7 positive staining hepatocytes (brown arrow) – abnormal result.

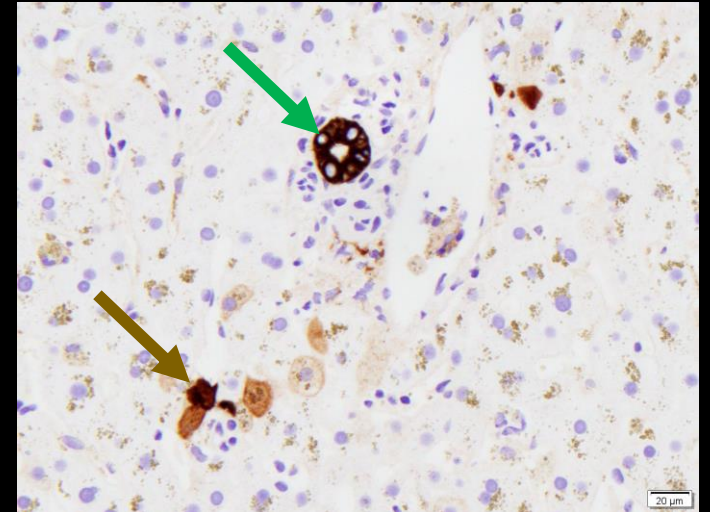


Fig. 2

Fig. 3 – Low-powered field showing multiple portal triads without evidence of bile ducts (blue arrows).

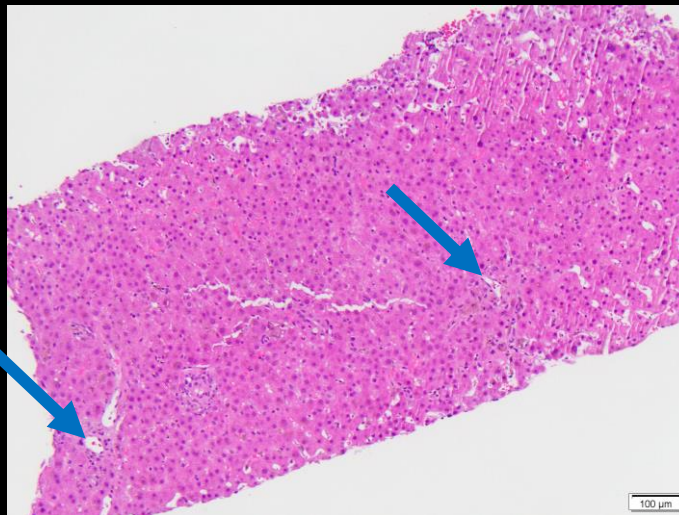


Fig. 3

Fig. 4 – Detail of branch of hepatic portal vein (blue arrow) with no associated bile duct

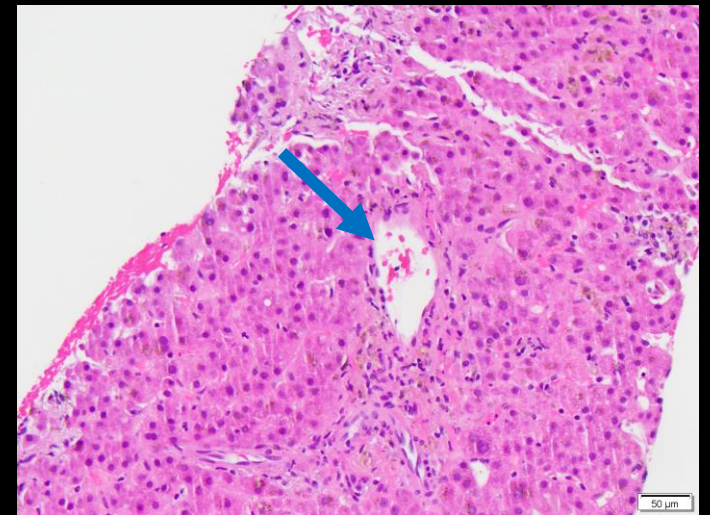


Fig. 4

Biopsy Results Pathology Report

- Ongoing cholangiopathic changes (ductal senescence, ductopenia, abundant cytokeratin positive intermediate hepatobiliary cells) consistent with hepatic graft versus host disease
- **Periportal fibrosis – no evidence of bile ducts in 7 of 11 visualized portal triads**
- Mixed mesenchymal-parenchymal iron overload (4/4)

Graft versus host disease diagnostic criteria³

- Early phase
 - Lymphoplasmacytic infiltration of portal tracts
 - Damage to bile duct epithelium
 - Cytoplasmic swelling and vacuolation
 - Enlarged and overlapping nuclei (reactive epithelial atypia)
 - Apoptosis
- Late phase
 - **Loss of bile ducts**
 - Increased fibrosis

Graft versus host disease diagnostic criteria³

- Acute vs. chronic GVHD: clinically 100 day cutoff
 - Poor correlation between pathologic features and clinical definition of acute vs. chronic
- Acute GVHD
 - Develops 2-6 weeks after allogeneic transplant
 - Primary targets
 - Skin 90%
 - Liver 40-60%
 - GI tract 30-50%
 - Early recognition of GVHD and prompt intervention improves outcome
 - Advanced GVHD easy to diagnose but mortality can be 50%
- Chronic GVHD
 - Resembles autoimmune connective tissue disorders
 - Mortality is high due to infections promoted by GVHD associated immunodeficiency
 - Target organs more widespread but skin, liver and GI tract play a major role
- In liver typically presents as obstructive jaundice due to destruction of small intrahepatic bile ducts, similar to primary biliary cirrhosis

Final Dx:

Late phase, acute graft versus host disease with
concomitant iron overload

GVHD⁵

- Acute and chronic graft-versus-host disease (GVHD) are multisystem disorders that are common complications of allogeneic hematopoietic cell transplant (HCT) which mostly affects the **skin** (maculopapular rash), **GI tract** (nausea, emesis, abdominal cramps, diarrhea), and **liver** (elevated bilirubin concentration).
- Immune cells transplanted from a non-identical donor (the graft) recognize the transplant recipient (the host) as foreign, thereby initiating an immune response

GVHD⁵

- Acute GVHD typically manifests as an inflammatory T cell infiltrate with tissue destruction, primarily driven by activation of donor T lymphocytes and release of pro-inflammatory cytokines.
- Chronic GVHD is relatively acellular with fibroproliferative findings, driven by complex and less well-understood syndrome that involves interactions of the innate immune system (macrophages, neutrophils, dendritic cells) with alloreactive and dysregulated B and T cells.

Case Discussion

- Given the patient's history of HIPBCT in the setting of AML/MDS, GVHD was high on the differential for this patient. GVHD can often present alongside iron overload for reasons that are not fully understood. It is believed that the liver may have a decreased ability to sense iron levels and release hepcidin, an inhibitory peptide hormone produced by hepatocytes. Additionally, patients with MDS often have pancytopenia treated with multiple RBC transfusions which may also contribute to the patient's abnormal iron studies.⁴

References:

1. ACR Appropriateness Criteria®. Acr.org. <https://www.acr.org/Clinical-Resources/ACRAppropriateness-Criteria>. Published 2016.
2. Keshava, S. N., Mammen, T., Surendrababu, N., & Moses, V. (2008). Transjugular liver biopsy: What to do and what not to do. *The Indian journal of radiology & imaging*, 18(3), 245–248. <https://doi.org/10.4103/0971-3026.41839>
3. <http://surpathcriteria.stanford.edu/transplant/livervhd/printable.html>
4. Deeg, H. J., Spaulding, E., & Shulman, H. M. (2009). Iron overload, hematopoietic cell transplantation, and graft-versus-host disease. *Leukemia & lymphoma*, 50(10), 1566–1572. <https://doi.org/10.1080/10428190903144659>
5. <https://www-uptodate-com/contents/clinical-manifestations-diagnosis-and-grading-of-acute-graft-versus-host-disease>