Hemochromatosis Discovered During Acute Infliximab Induced Liver Toxicity: A 2 for 1 Diagnosis

Alicia Shaikh DO O.D., Erik Raborn DO MPH, Bryce Parrish DO, Tenzin Tseky MD, Jennifer Jeng DO, Micheal Kochik DO, Edwin Golikov DO, Ami Patel DO, Thomas Taylor MD

Arnot Health
Graduate Medical Education

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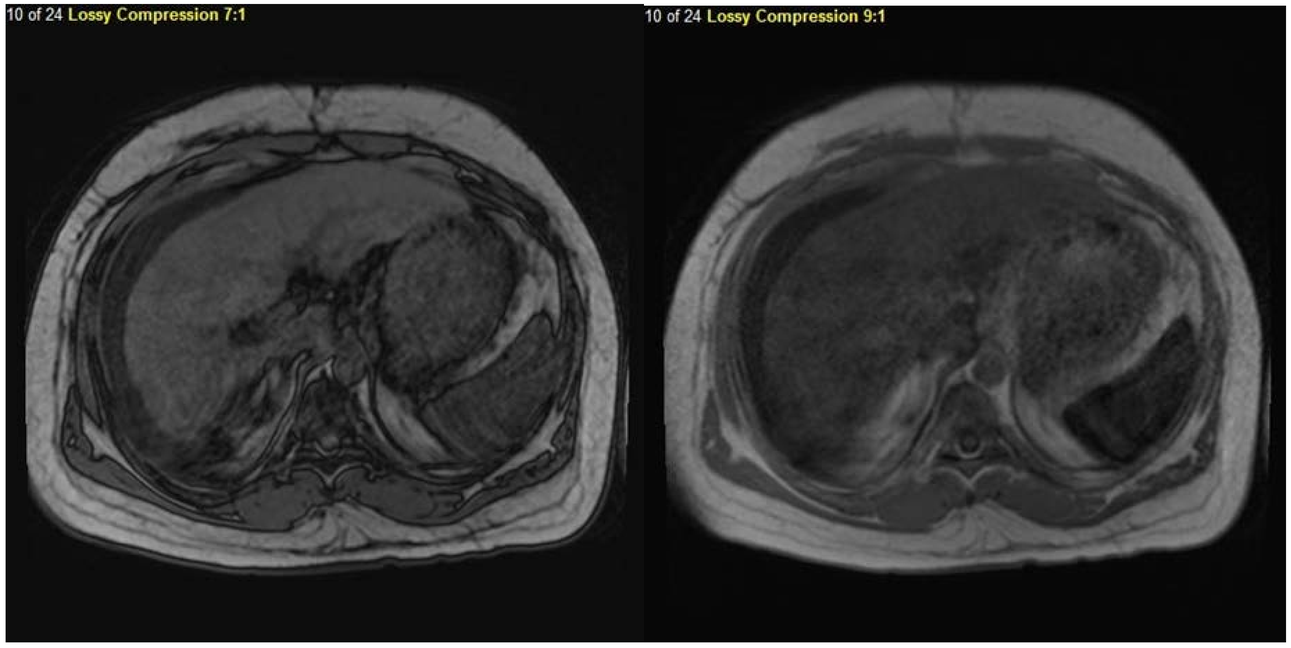
LAKE ERIE CONSORTIUM FOR OSTEOPATHIC MEDICAL TRAINING

CASE

We present an unusual case of Hemochromatosis discovered during acute hepatic injury from Infliximab. A 40 year old, African American male with PMH of Crohn's, diabetes, and developmental delay who had scleral icterus, elevated liver enzymes on blood work with ascites. His Crohn's disease was originally diagnosed with colonoscope with biopsies showing cryptitis with crypt abscesses in 2014. He has been well controlled on Infliximab infusion once every eight weeks, but he missed in office follow and lab work. Eventually he was followed with the discovery abnormal LFTS with AST/ALT at 880/720; TBili of 11.7 and Alk Phos of 172. Additional work up revealed A1c of 7.1 % ferritin immeasurably high (>1500), a total iron of 158 uG/dL, TIBC 182 UG/Dl, with a saturation of 88%. He underwent MRI imaging which revealed a diffuse dropout on in phase imaging throughout the liver, spleen, and areas of signal drop out along the edge of the pancreas which is with heavy metal deposition. Often when patients present with hepatic injury and Crohns, Infliximab is the culprit and drug induced hepatic injury should be strongly considered. However, the MRI imaging does not support this acute drug induced process as the sole diagnosis [1]. Therefore, a secondary process was suspected. He was referred to U of R for liver biopsy and the pathology report stated both acute and chronic hepatitis with parenchymal collapse with areas of bridging necrosis favoring drug induced liver injury secondary to infliximab. Additionally, there is an extensive 4+ iron deposition in hepatocytes, bile ducts, and Kupffer cells/ Periportal with pericellular fibrosis. Which is more consistent with a Hemochromatosis.



Axial and coronal out of phase (left) and in phase (right) MRI of the abdomen demonstrates loss of hepatic and splenic parenchymal signal on the in phase image.

•Axial fat-suppressed T2-weighted MRI image shows loss of signal in the hepatic and splenic parenchyma, as well as a small amount of ascites

•IMAGING

The imaging modality best for both diagnosis and follow up of hemochromatosis is MRI. Both T1 and T2-weighted sequences will show signal loss in the liver, as well as the other involved organs. This distribution may aid the clinician in differentiating between the primary and secondary forms. Another key part of the protocol is T2* GRE, where there will be loss of signal in the involved organs on in phase imaging. This sequence can also offer an estimation of the degree of hepatic iron concentration and therefore be used to evaluate the effectiveness of chelation therapy.

1. Daniel D Penrice, MD, Amrit K Kamboj, MD, Douglas A Simonetto, MD, Infliximab-induced Liver Injury: A Common Link Between Crohn's Disease and Acute Liver Injury, *Inflammatory Bowel Diseases*, Volume 27, Issue 1, January 2021, Pages e7–e8,

2. Federle MP. Hemochromatosis. *Statdx: Diagnostic Support for Radiology.* My.statdx.com Accessed 03/07/2021.

•3. Hepatic Iron Deposition in Patients With Liver Disease: Preliminary Experience With Breath-Hold Multiecho T2'-Weighted SequenceHersh Chandarana, Ruth P. Lim, Jens H. Jensen, Cristina H. Hajdu, Mariela Losada, James S. Babb, Steve Huffman, and Bachir Taouli American Journal of Roentgenology 2009 193:5, 1261-1267

•Knutson M, Wessling-Resnick M. Iron metabolism in the reticuloendothelial system. Crit Rev Biochem Mol Biol. 2003;38(1):61-88. doi: 10.1080/713609210. PMID: 12641343.

Discussion

Hemochromatosis is an iron overload disorder, which results in structural and functional impairment due to increased absorption of iron from the gut, effecting the cells within the liver, pancreas, and heart. If there is iron deposition without organ damage, the condition is referred to as hemosiderosis, and cannot be differentiated from hemochromatosis on the basis of imaging alone. However, this case had organ damage as described previously, with both laboratory and microscopic findings. The pathological process initially involves the reticuloendothelial system to capture and sequester iron from circulation. After, its picked up it collects intracellularly resulting in iron deposition in the liver, spleen, lymph nodes, and bone marrow[4]. Classic Hemochormatosis will typically present in the 4th-5th decades, while the secondary form presents earlier[1]. Males are effected 10x more frequently than females, as females are relatively protected by iron loss from menses and pregnancy. Potential complications include periportal fibrosis and eventual cirrhosis, hepatocellular carcinoma, impotence, insulin-dependent diabetes mellitus, and cardiac failure. In the setting of iron overload, fibrosis acts synergistically in the development of fibrosis[3]. At this time, there is considerable support for an underlying hemochromatosis revealed during the investigation of infliximab induced liver injury, which would have not been pursued had the evidence from the MRI shown a more classic hemochromatosis pattern. After discontinuing the infliximab the patient started to recover, with LFTs returning to a more normal range with a persistently elevated Ferritin, also consistent with Hemochromatosis.