Syncope with Too Much Iron-y

Hemochromatosis as a Possible Contributing Factor in Acute Liver Failure

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Background

- Acute Liver Failure (ALF) is defined by acute liver injury (<26 weeks), coagulopathy and hepatic encephalopathy in the absence of preexisting liver disease.[1]
- Typical Etiologies of ALF include Acetaminophen Toxicity, Viral Hepatitis but less common etiologies should be considered in the absence of risk factors.[2]
- Up to 15.5 % of cases of ALF, no etiology can be determined.[1]
- Hemochromatosis is defined as impaired iron storage resulting in inappropriate visceral iron deposition.
- Hemochromatosis workup should involve genetic testing for HFE mutations accounting for over 90% of presentations.[3]

Objective

Presenting the Treatment of Acute Liver Failure and the Difficulty of Establishing the Primary Cause.

Case Presentation

A 34-year-old male presented with syncopal episode at work. Patient's spouse had reported nausea and vomiting at home with new onset jaundice as well as increasing confusion. Patient had no prior history of heavy drinking, smoking, medications or herbal supplements. During this same time span, patient had reportedly stopped regularly urinating.

On arrival, patient was brought to the ICU for uremia, renal failure, hypotension and acute liver injury noted on admission. Patient quickly lost capability of airway protection and was subsequently intubated and started on Sustained Low Efficiency Dialysis (SLED). Patient renal function improved with Viral and Toxic workup of Acute Liver Failure resulting in negative findings. Gastroenterology was consulted for further workup of ALF with Ferritin and Transferrin Saturation Levels at 2060ng/mL and 65.4% respectively. Patient stay was complicated with blood transfusion required due to erosive esophagitis and Mallory Weiss Tearing presumed to be caused by both nasogastric tube irritation and multiple removals by patient. Patient was initially considered for liver transplant but further workup was unable to be performed inpatient due to financial circumstance.

The patient was discharged with follow up with Gastroenterology for endoscopic surveillance and further work-up of possible hemochromatosis.

Graphs and Imaging Findings

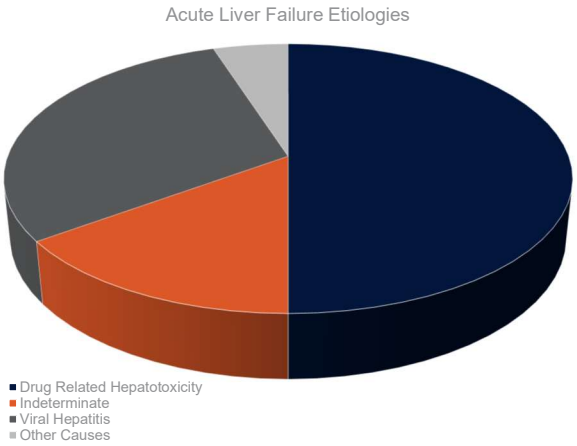

Figure 1: Etiologies of Acute Liver Failure: Drug Related Hepatotoxicity 50%; Indeterminate Causes up to 15%; Viral Hepatitis 30% with other causes (Wilson's Disease, Veno-Occulsive, Pregnancy related etc.) making up approximately 5%.[1,3] **Numbers subjective to country of origin**

Figure 2: Hepatomegaly noted on imaging with evidence of cardiomegaly commonly seen in hemochromatosis. Not pictured: Splenomegaly seen in further imaging.

Discussion

Although rare, hemochromatosis can lead to ALF. The pathophysiology of ALF often involves hepatocyte necrosis/ apoptosis, with cerebral edema being the most serious complication, attributed to disruption of the blood-brain barrier by inflammatory mediators.[2] Treatment necessitates early recognition and supportive measures to manage potential complications like hemodynamic instability, bleeding, fever, and malnutrition. Hyperosmolar therapy and renal replacement therapy are utilized to address cerebral edema and intracranial hypertension, with SLED employed in our case.[1] Liver transplant evaluation is warranted in severe cases.

Hemochromatosis, rarely implicated in ALF, results from pathological iron accumulation, either hereditary or secondary to conditions necessitating transfusions. Mutations in the HFE gene (C282Y; H63D) can augment iron absorption.[2] Clinical manifestations range from cirrhosis to arthropathy, heart failure, arrhythmias, "bronze diabetes," hypogonadism, and hypothyroidism. Elevated ferritin levels (>200ug/mL in women, >300ug/mL in men) and transferrin saturation (>40% in women, >50% in men) raise suspicion, with levels above 1000ug/mL warranting further evaluation.[2] Treatment involves repeated phlebotomy/chelation therapy based on the cause of iron deposition. End-stage liver disease transplantation survival rates tend to be lower compared to non-iron overloaded counterparts.[1] Regular monitoring for Hepatocellular Carcinoma via ultrasound and AFP levels every six months is crucial, as it contributes significantly to mortality in hemochromatosis.[3]

Conclusion

Treatment of Acute Liver Failure requires urgent recognition to react and to anticipate possible complications from sequential multiorgan disfunction. Early recognition of increased intracranial pressure with urgent CRRT and other measures has aided in increasing survival of ALF patients as high as 79% at one year.[2]

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