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GASTROENTEROLOGY & HEPATOLOGY

A Case Report of Acute Idiopathic Hepatitis Requiring Liver Transplant

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INTRODUCTION

Acute liver injury may be very difficult to treat, especially when the etiology is unknown. We describe a case of a patient who presented with signs and symptoms of acute liver injury and went through an extensive work-up that did not reveal a definitive cause. The lack of diagnosis can be distressing for the patient, so it is important to regularly communicate the current plan and potential future necessary steps (such as a transplant surgery) to facilitate smooth, informed decision-making throughout the whole process.

SUBJECTIVE

A 59-year-old male with a past medical history of mild asthma, eosinophilic esophagitis, and hyperlipidemia was transferred to Thomas Jefferson University Hospital for severe acute liver injury. The patient initially presented to an outside hospital emergency department the week prior after his primary care physician discovered elevated liver function tests (LFTs) on routine blood work, with an aspartate transaminase (AST) of 1347 U/L, alanine transaminase (ALT) of 954 U/L, alkaline phosphatase (ALP) of 326 U/L, and total bilirubin (Tbili) of 4.1mg/dL. The patient was told to stop taking his atorvastatin 20mg which was recently increased from 10mg around 6 months prior.

At the outside hospital, the patient reported to have generalized body aches, right upper quadrant pain, weakness, jaundice, and pale stools that started for nine days prior. The patient stated that the symptoms were originally mild but worsened over the past several days, and he could not identify any specific triggers. The patient reported that around two weeks earlier, he had gone camping for three days in the Poconos, where he and his companions cooked and ate food and water that they brought with them. He denied foraging or eating mushrooms and reported that the other members of the camping trip were healthy after the trip. The patient reports that since the camping trip, he has had an itchy rash on his right lower leg.

Upon review of systems, the patient denied any subjective fever or chills, chest pain, or shortness of breath. He denied any history of liver disease, smoking, alcohol usage, herbal supplements, or acetaminophen use. The patient had no recent new medication other than 1 dose of amoxicillin which he took for a dental procedure and stopped after noticing his LFTs. He had no pertinent past surgical history. He denied any family history of liver disease or autoimmune disorders.

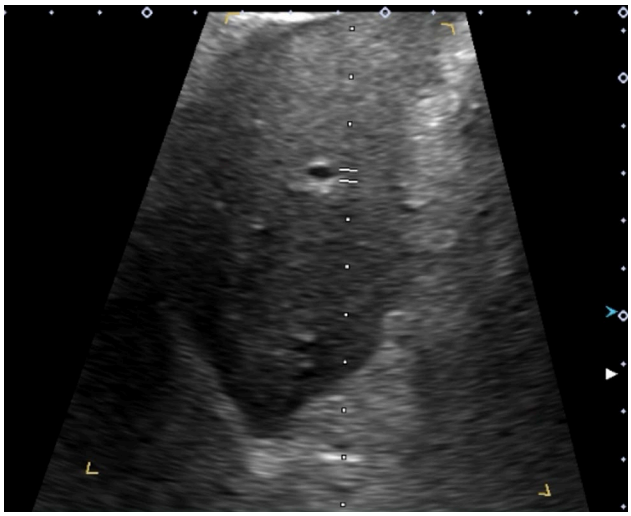

Figure 1: Gray scale ultrasound liver with coarsened echotexture and nodular surface.

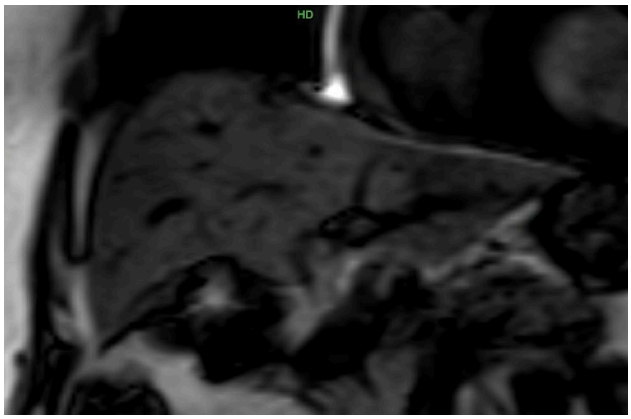

Figure 2: MRI Abdomen with contrast MRCP revealing hepatic steatosis and multiple subcentimeter hepatic cysts.

OBJECTIVE

On presentation, the patient's vital signs were stable with a blood pressure of 123/64, heart rate of 66. On physical exam, the patient was not in acute distress, resting comfortably and fully oriented. The patient had bilateral scleral icterus, jaundice of his face and upper body, as well as a small right lower leg rash. Abdominal exam revealed a mildly distended, non-tender abdomen with no masses, hepatomegaly, fluid wave, or flank tenderness. The remainder of his physical exam was within normal limits with no notable asterixis.

The patient's laboratory results revealed elevated LFTs, with an AST 1052 U/L, ALT 709 U/L AlkP 308 U/L, and Tbili 5.9 (direct 4.1) mg/dL. The patient's Prothrombin Time (PT) was 27.5 and his internationalized normalized ration (INR) was 2.4. On arrival the patient's model for end stage liver disease (MELD-Na) score was 30.

The patient's imaging was notable for an abdominal ultrasound showing a liver with a coarsened echotexture and nodular surface (**figure 1**). An abdominal MRI showed hepatic steatosis and innumerable subcentimeter hepatic cysts (**figure 2**).

The patient underwent liver biopsy, which revealed severe acute hepatitis with significant hepatocyte necrosis and diffuse lobular and portal inflammation with neutrophils, lymphocytes, and eosinophils. Special stains with adequate controls for trichrome and reticulin showed that the liver's nodularity was due to severe hepatocyte damage, with no signs of cirrhotic fibrosis. This severity of necrosis was interpreted as being unlikely caused by cholestasis/gallstones, and more likely from a toxic or infectious cause. Serology from the previous hospital showed negative results for autoimmune causes. The patient's continued with an extensive workup for acute hepatitis, in which all results were negative (**Table 1**).

The patient was treated intravenous vitamin K with continued monitoring of the patient's INR, mental status, and LFTs while holding his statin. Over the next week, the patient's LFTs, INR, and clinical symptoms such as ascites continued to worsen, and a subsequent paracentesis was performed which revealed a PMN count of 448 cells/mm^3 consistent with spontaneous bacterial peritonitis.

After completing a course of Zosyn, the patient's MELD score had reached 38, at which point he underwent successful liver transplantation for fulminant liver failure, recovered well postoperatively, and was discharged from the hospital five days after the surgery.

Table 1: Laboratory workup for acute hepatitis

Bacteria	
A. Phagocytophilium	IgG <1:64 IgM < 1:20
Ehrlichia chaffeensis	IgG <1:64 IgM < 1:20
R. Typhii	IgG and IgM not detected
Lyme	IgG/IgM: negative
RMSF	Rickettsia rickettsii IgG/IgM: not detected
TB/Mycobacter	QuantiFERON-TB negative Acid fast bacilli stain and culture (from liver biopsy) No AFB seen. QuantiFERON TB Gold, negative TB1-NIL and TB2-NIL ≤0, negative
Syphilis	Syphilis Ab: negative
Mycology	
Coccidioides	Ab CF: not detected IgG/IgM: negative
Parasites	
Microbiology blood parasite smear	No parasites detected
Toxoplasma	Ab IgG <7.2 (negative) IgM Ab <8 (negative)
Babesia microti DNA real-time PCR	Not detected
Viral	
Hep A	IgM nonreactive
Hep B	Surface Ab: reactive 56.04 mIU/mL Core IgM: non-reactive Surface antigen non-reactive Core Ab: non-reactive Virus DNA: not detected Quant PCR: no DNA detected
Hep C	Antibody: nonreactive Qnt PCR: RNA negative
Hep E	IgG detected IgM not detected
HIV	Ab/Ag negative
CMV	CMV Ab IgM: negative CMV Quant DNA PCR: not detected
EBV	EBV early antigen IgG: .44 (No detectable IgG antibody to ELISA methodology) EBV DNA, QN PCR: not detected
SARS COV-2	Negative
HSV-1	HSV-1 DNA, QN PCR: not detected HSV-1 IgG: Positive
HSV-2	HSV-2 DNA, QN PCR: not detected HSV-2 IgG: Negative
Mumps	Mumps IgG Ab: negative
Rubeola	Rubeola IgG Ab: positive
Respiratory Pathogen Panel **extracted nucleic acids amplified by reverse PCR testing for: Influenza A with subtype H1 or H2, Influenza B, RSV A, RSV B, Coronavirus 229E, Coronavirus OC43, Coronavirus NL63, Coronavirus HKU1, Human Metapneumovirus, Rhinovirus/enterovirus, Adenovirus, Parainfluenza virus 1-4, Human Bocavirus, Chlamydophila pneumoniae, and mycoplasma pneumoniae.*	Negative
Rubella	Rubella Ab: positive
Varicella zoster	IgG: Positive VZV QN PCR: not detected

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Post-operative explant liver pathology showed findings of submissive necrosis with of unclear etiology with a differential diagnosis including drug induced liver disease and infectious disease. The patient was seen regularly at outpatient visits and at his 6-month follow up was recovering well and was able to return to work.

DISCUSSION

Acute hepatitis is associated with fever, fatigue, abdominal pain, dark urine, light-colored stool, generalized pain, and jaundice. Etiology may include autoimmune, viral, bacterial, parasitic, herbal, or drug-induced causes. We presented the case of a middle-aged man with acute hepatitis symptoms who was monitored for several weeks while undergoing laboratory workup, biopsy, and imaging studies in hopes of finding any autoimmune, toxic, or infectious causes. The patient eventually received a liver transplant without receiving an answer as to what caused his disease.

In adults, it is suggested that up to 50% of acute hepatitis cases are caused by acetaminophen toxicity, while 11% are from unknown etiologies.[1] There is generally very scarce data or research on cases of cryptogenic acute hepatitis in the adult population, and consequentially, there is no standard treatment or work-up plan for these difficult scenarios. In the pediatric patient population however, there is data showing that up to 30-50% of acute liver injuries are cryptogenic.[2] Interestingly, between October 2021 and September 2022, there was a noticeable increase in cases of acute hepatitis of unknown etiology in the pediatric population, with at least 1296 cases reported; notably, most of these patients tested positive for adenovirus but had negative immunohistochemical staining for adenovirus on biopsy, making it difficult to definitively conclude virus's role in the disease progress.[3] Though this is an interesting finding, our patient was negative for adenovirus, and tested negative in a vast and thorough virology panel.

One can only guess if there was a toxic substance that the patient ingested in the Poconos but given that his other companions were all healthy after the camping trip, this seems unlikely. At one point our team suspected a potential drug-induced liver injury, as the patient had started taking atorvastatin around one year earlier (and increased the dosage six months after starting). Although cases are rare, recorded incidents of statin-induced liver injury have shown symptoms such as jaundice, generalized weakness, and abdominal pain like our patient. Such cases revealed that elevations in LFTs can occur as early as within hours of the first dose and up to months later, but the majority of the cases showed cholestatic injury patterns and self-resolved within a few months of stopping the statin.[4] Notably, atorvastatin and simvastatin were the most common culprits of drug-induced liver injury, with atorvastatin having the highest rate of inducing a cholestatic/mixed pattern of injury.[4] However, when considering statin-induced acute liver failure, there is no reported difference between the incidence in the general population and the incidence in patients taking statins.[5] Given these findings, it is hard to make a definitive connection between our patient's atorvastatin usage and the fulminant liver failure.

Given the lack of research on cryptogenic hepatitis, especially in the adult population, it remains difficult to manage and treat this disease. In these scenarios, it is important to maintain constant communication with pathology, infectious disease, and surgery while consistently keeping the patient aware of potential outcomes and future interventions. It became apparent to both the medical team and the patient that the liver's condition would only continue to worsen with each passing day amidst the investigation, so an early education and consent for a transplant operation was tantamount to the patient's care and peace of mind.

If future providers encounter acute liver injury of unknown origin, they should take note to keep a daily MELD score, as in our case, the patient's condition deteriorated rapidly over a short period which prompted the transplant surgery (when the patient had reached a score of 38). The MELD score is a useful tool for assessing both severity and mortality in liver cirrhosis patients, with high sensitivity and positive predictive value for patient mortality. Therefore, patients with a MELD score of at least 20 should be considered as having a high risk of death, which is important for prioritizing them as liver transplantation candidates as soon as possible.[6]

CONCLUSION

It can be difficult to do workup and treatment plan for cases of acute liver injury of unknown etiology in adult patients, especially as most of the current research and literature point to idiopathic acute liver injury in the pediatric population. With the lack of a definitive guideline for diagnosis and treatment, our team provided supportive care to the patient while conducting a lengthy and thorough investigation to

rule out potential infectious, toxic, or autoimmune causes. Our case showed that it is never guaranteed that a medical investigation, no matter how comprehensive, will elucidate a definitive diagnosis and treatment plan. Thus, it is important make early preparations for possible transplant and educate the patient through each step of the process. Throughout the patient's stay, he was informed on potential causes of his disease, the labs such as LFTs and INR that we were measuring daily and what they indicated, the medications that were being used to give him supportive treatment, and what our team's plan was with each passing day. This real-time patient education and communication gave the patient having ample time to process the situation and consent for a transplant.

REFERENCES

1. Argo CK, Caldwell SH. Editorial: Severe Acute Liver Injury: Cause Connects to Outcome. *Am J Gastroenterol*. 2017;112:1397–1399.
2. Centers for Disease Control and Prevention. Overview: Children with Hepatitis of Unknown Cause.
3. AlShurman, M., AlShurman, B.A., Sehar, H. *et al*. Uncovering the Underlying Causes of Severe Acute Hepatitis of Unknown Aetiology in Children: A Comprehensive Review. *Dr. Sulaiman Al Habib Med J* 5, 101–117 (2023). https://doi.org/10.1007/s44229-023-00043-0
4. Averbukh LD, Turshudzhyan A, Wu DC, Wu GY. Statin-induced Liver Injury Patterns: A Clinical Review. J Clin Transl Hepatol. 2022 Jun 28;10(3):543-552. doi: 10.14218/JCTH.2021.00271. Epub 2022 Jan 10. PMID: 35836753; PMCID: PMC9240239.
5. Russo MW, Scobey M, Bonkovsky HL. Drug-induced liver injury associated with statins. *Semin Liver Dis.* 2009;29(4):412–422.
6. Emenena I, Emenena B, Kweki AG, Aiwuyo HO, Osarenkhoe JO, Iloeje UN, Ilerhunmwuwa N, Torere BE, Akinti O, Akere A, Casimir OE. Model for End Stage Liver Disease (MELD) Score: A Tool for Prognosis and Prediction of Mortality in Patients With Decompensated Liver Cirrhosis. Cureus. 2023 May 20;15(5):e39267. doi: 10.7759/cureus.39267. PMID: 37342753; PMCID: PMC10278970.

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