



Case Report

Enterovirus Induced Severe Rhabdomyolysis and Acute Fulminant Liver Failure in an Adult Requiring Liver Transplantation-A Case Report

Santhalakshmi Angappan*, Abdul Kader Tabbara, Jacob Pawloski, Anoop Chhina, Dragos Galusca

Henry Ford Hospital, Detroit, Michigan, USA

***Corresponding author:** Santhalakshmi Angappan, Henry Ford Hospital, Detroit, Michigan, USA

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Abstract

The authors report a case of a young healthy adult with severe rhabdomyolysis and acute fulminant liver failure with Multiple Organ Dysfunction Syndromes (MODS), possibly from an enterovirus infection. To the best of our knowledge, this is the first-ever reported case of enterovirus-induced rhabdomyolysis and acute liver failure in an immunocompetent adult. The treating physician must be aware of the association between viral infections, viral myositis, and severe rhabdomyolysis with acute liver failure, which can facilitate the optimal management of such patients. Prompt recognition may provide an opportunity for early interventions including intravenous immunoglobulin and liver transplantation if warranted.

Introduction

Enteroviruses account for more than 10-15 million symptomatic cases per year in the United States [1]. The clinical presentation from human enterovirus infection can range from mild febrile illness to severe illness including myocarditis, meningoencephalitis, and more rarely, acute liver failure (ALF) with a fulminant course, especially in the pediatric and immunocompromised populations [2]. Most infections are self-limiting and require only symptomatic treatment. Enterovirus sepsis and severe hepatitis is more frequently seen in neonates [3], although there have been rare case reports of severe hepatitis in immunocompromised adults [4,5]. In addition, there have been rare instances of successful liver transplantation in neonates as a treatment for acute liver failure due to disseminated enterovirus infection [6,7].

Severe rhabdomyolysis from viral myositis most often is associated with mild elevations in liver enzymes. However, in rare circumstances, severe rhabdomyolysis can be associated with ALF leading to Multi-organ dysfunction in an immunocompetent

adult. The authors report a case of a young healthy adult with severe rhabdomyolysis and acute fulminant liver failure with multiple organ dysfunction syndromes (MODS), possibly from an enterovirus infection. To the best of our knowledge, there has been no reported literature on enterovirus-induced ALF and severe rhabdomyolysis in immunocompetent adults. Written consent was obtained from the patient's family.

Case Presentation

A 25-year-old male from the United Kingdom, with no known co-morbidities presented to an outside hospital in the United States with a 3-day history of flu-like symptoms. These symptoms included malaise, lethargy, and fever, which then progressed to altered mental status. The patient traveled to the US for a vacation. History was notable for a syncopal episode after a half marathon, 10 days before the travel, and herbal supplement (Thermopure) intake for bodybuilding. On evaluation at the outside hospital, laboratory work was remarkable for aspartate aminotransferase/alanine aminotransferase AST/ALT >7000, total bilirubin 8.5, creatine phosphokinase CPK 90,326, ammonia 127,

creatinine 4.8, potassium 8.5, and lactate 9.3. He was started on an N-acetylcysteine (NAC) infusion and hemodialysis and transferred to our hospital for escalation of care.

On arrival, the patient was encephalopathic and in severe respiratory distress. He was intubated for airway protection. Lab values were significant for AST 777 U/L, ALT 6039 U/L, total bilirubin 7.6 mg/dl, international normalized ratio (INR) 9.5, CPK 112,409 U/L, and ammonia of 142. Considering his hepatic encephalopathy and coagulopathy, a liver transplant workup was initiated. He was started on empirical antibiotics, coagulation correction, and sustained low-efficiency dialysis (SLED). Workup for all infectious causes both bacterial and viral was negative except for bio-fire from the nasopharyngeal swab, which was positive for Enterovirus. Both urine and stool polymerase chain reaction (PCR) for the enterovirus was negative. T2, urine legionella, streptococcus pneumonia, Epstein Barr virus (EBV) DNA, hepatitis serology, and (human immunodeficiency virus) HIV were negative. Eventually, the patient required an orthotopic liver transplant within the first 48 hours of presentation. The explant liver pathol microvesicular steatosis and coagulative necrosis. His post-operative course was complicated by persistently elevated CPK and severe ongoing rhabdomyolysis. The patient had to undergo multiple fasciotomies for bilateral lower extremity compartment syndrome. In view of his persistent rhabdomyolysis, he had a muscle biopsy, which revealed necrosis without viral inclusion particles. The patient had a lumbar puncture, which was negative. He also had an MRI imaging of his brain, in view of his persisting altered sensorium. Imaging revealed multiple small vessel ischemic changes, not correlating with his age. His liver function was returning to normal limits with immunosuppression on board.

The patient was started on IVIG for high suspicion of enterovirus induced severe rhabdomyolysis and acute liver failure, after a multidisciplinary discussion. Following this, the patient's clinical course improved significantly. The patient was transitioned from SLED to intermittent hemodialysis. The patient also had a tracheostomy and PEG tube insertion in view of anticipated prolonged recovery. He was treated with antibiotics for ventilator-associated pneumonia (VAP). Over the course of time, his sensorium improved marginally to obey simple commands and required minimal ventilator requirements. The patient continued to have persistent weakness and significant muscle wasting from the severe rhabdomyolysis.

In view of anticipated prolonged recovery and the need for prolonged rehabilitation, as per family request, he was transferred back to the UK in a hemodynamically stable condition. At discharge, the patient was on cyclosporine, Cellcept, prednisone, and antibiotics for VAP coverage.

Discussion

Enterovirus induced severe rhabdomyolysis and acute liver failure was high on our differentials since the patient had flu-like symptoms before the presentation and tested positive (bio fire) only for enterovirus in his entire infectious workup. However, we were not able to isolate the virus in the stool or urine. Although the precise pathophysiology underlying virus-induced rhabdomyolysis is unknown, two mechanisms have been postulated, direct viral invasion and toxin-mediated injury. [8] There are reports where the virus cannot be isolated if the patient is out of the active infectious period and the extensive muscle necrosis can be from the toxin-mediated injury from the viremia.

[8-10] Moreover, viral particles are occasionally difficult to differentiate from glycogen by EM; therefore, there is some doubt about these observations. Biopsies of clinically affected musculature that are essentially unremarkable raise the possibility of a circulating "toxin" or cytokine causing rhabdomyolysis. In addition, the fact that the patient showed significant clinical improvement after he was started on IV IgG favored enterovirus-induced illness to be high on our differentials. Though there are no case reports to date on enterovirus-induced severe rhabdomyolysis and acute liver failure in immunocompetent adults, there are case reports on enterovirus-induced rhabdomyolysis and acute liver failure in pediatric patients and on immunocompromised adults.

Acute liver failure is the deterioration of liver function that occurs rapidly in days or weeks, usually in a person who has no preexisting liver disease. ALF is most caused by a hepatitis virus or drugs, such as acetaminophen. Uncommon etiologies include enterovirus family, certain pesticide injection, and ayurvedic or herbal supplement intake. Also, never in literature has the dramatic CPK values have been associated with marathon running or heavy workouts. Our research on the herbal supplement thermopure, which contains green tea extract, did not reveal any association with severe rhabdomyolysis or acute liver failure.

The authors present this case here to highlight the possibility of viral myositis in severe rhabdomyolysis and fulminant liver failure. It is imperative that treating physicians are aware of the association between viral infections and severe rhabdomyolysis with acute liver failure, which facilitates the optimal management of such patients. Human Enterovirus polymerase chain reaction PCR testing in both stool and urine should be performed in cases of ALF and severe rhabdomyolysis with uncertain etiology.

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