Complete heart block associated with hepatitis A infection in a female child with fatal outcome

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Abstract

Hepatitis A virus infection can cause extra-hepatic manifestations like myocarditis. An 8-year-old female with HAV infection presented with fever, abdominal pain, vomiting, and icterus. She developed viral myocarditis with complete AV dissociation on ECG and was treated with a temporary pacemaker, but her condition worsened, and she died.

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Short title: Complete heart block associated with HAV infection

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Informed Consent

A written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Abstract

Hepatitis A virus infection can cause extra-hepatic manifestations like myocarditis. An 8-year-old female with HAV infection presented with fever, abdominal pain, vomiting, and icterus. She developed viral myocarditis with complete AV dissociation on ECG and was treated with a temporary pacemaker, but her condition worsened, and she died.

Keywords: Hepatitis A virus; hepatitis; myocarditis; pacemaker; pediatrics

Clinical Key Message:

Hepatitis A viral infection can be associated with viral myocarditis and complete heart block that can lead to cardiogenic shock and death eventually.

Introduction:

Hepatitis A virus (HAV) is a positive-strand RNA virus of the picornaviridae family. It may affect individuals at any age, from infancy to maturity. The majority of children afflicted are asymptomatic, with just 30% developing symptomatic hepatitis, whereas 80% of adults exposed have clinical signs and symptoms of hepatitis⁽¹⁾. Hepatitis A, unlike hepatitis B and C, does not cause chronic liver damage and normally cures in approximately two months ⁽²⁾. The majority of viral hepatitis A transmission occurs through the fecooral route. The most common form of transmission is food-borne transmission. Hepatitis A outbreaks have happened in the past across the world and are assumed to have a cyclical recurrence pattern ⁽³⁾. Most of the children infected are asymptomatic but symptoms can range from mild to severe. Most common symptoms are fever, diarrhea, anorexia, abdominal pain, jaundice. Adults are more often symptomatic than children and are more prone to develop complications.

Host immune response to HAV results in cellular death. An excessive immune response can lead to severe hepatitis and can rarely cause fulminant hepatitis ⁽⁴⁾. Complications include "cholestatic hepatitis, relapsing hepatitis, autoimmune hepatitis, Fulminant hepatic failure, acute kidney injury and other extrahepatic manifestations". Rare Extrahepatic manifestations include anemia, acute pancreatitis, neuritis, pleural and pericardial effusion, myocarditis. The infection can lead to fulminant hepatitis and death in some patients⁽⁵⁾. After recovery, it provides a lifelong immunity

There is no specific treatment for Hepatitis A. Supportive treatment is usually provided and the patient completely recovers from the disease most of the time within 2 months to 6 months. In some patients, it can lead to fulminant hepatic failure, severe extrahepatic manifestation and even death.

Hepatitis A leading to pericarditis, myocarditis, and pleural or pericardial effusion has been reported in the literature but is extremely rare $^{(6,7)}$. Cases of complete heart block following infectious hepatitis have been published $^{(8)}$ and myocarditis following viral infection can lead to complete heart block $^{(9,10)}$. Complete heart

block secondary to amoebic hepatitis and measles are also reported in the literature^(11,12) but we have not found any case report of complete heart block secondary to hepatitis A in the literature.

Case Report:

An 8 years old female child, presented to emergency with complaints of high-grade fever for seven days and yellow discoloration of the body and sclera for 3 days associated with vomiting and abdominal pain. On examination, she was pale, had a heart rate of 54 beats/min, a feeble pulse, respiratory rate of 35/min, and blood pressure was not recordable. Normal lung sounds and normal heart sounds with bradycardia. She was afebrile on presentation; blood glucose level was 122 mg/dl. She was immediately admitted to the High Dependency Unit of Pediatrics, and then to the Pediatric Intensive care Unit (PICU)

Lab investigations were ordered. Leukocytes were normal. The patient had raised ALT levels (995U/L), and raised bilirubin levels 6.6mg/dl. The patient had Sodium levels at 126mEq/L, potassium levels at 4.8 mEq/L and Calcium levels at 7.8mg/dl. The patient had raised hepatitis A (HAV) IgM levels. She was primarily diagnosed as a case of acute viral hepatitis due to the hepatitis A virus (HAV). Cardiac enzymes were found raised. CPK at 812 U/L, CKMB at 122 U/L and LDH at 1264U/L. (table 1) Supplemental oxygen was initiated. Electrolytes were corrected immediately and IV calcium was administered. She was clinically suspected to be a case of viral myocarditis secondary to acute viral hepatitis.

Abdominal ultrasound showed pericholecystic edema, normal-sized liver, mild abdominal and pelvic ascites and mild bilateral pleural effusion on chest USG. Chest X-ray was done which showed pleural effusion on the right side with a blunt costophrenic angle and cardiomegaly. (Figure 1). ECG was done, which showed complete AV dissociation with a fixed atrial rate of 13 bpm and fixed ventricular rate of 46 bpm and varying PR intervals. (Figure 2) The patient was managed in cardiology, and a temporary Pacemaker (TPM) was placed immediately. The patient was medically managed with atropine and dopamine.

On the third day of admission, oxygen saturation dropped further low to 77%. On examination, the patient was tachypneic, apprehensive, severely distressed, with nasal flaring, pulse was not palpable and there was generalized puffiness along with pedal edema. There were bilateral crepitations in the lower zone; the abdomen was distended and tendered along with the firm liver. ABGs were ordered, which showed a Blood pH of 7.49, HCO3 of 13.7 mEq/L, PCo2 of 17.9 mm Hg, and PO2 of 84 mm Hg. The Patient was shifted to CPAP and was considered at risk of cardiogenic shock. The patient was managed with inotropes. Dobutamine, rivaroxaban in lower doses and furosemide (0.5mg/kg) were added to the treatment regimen. The patient died on the fourth day of admission (DOA) due to cardiogenic shock. The case timeline is shown in figure 3

Discussion:

The patient had no history of any cardiovascular disease and was admitted to the pediatric ICU as a case of acute viral hepatitis with secondary or associated cardiac involvement, with clinically diagnosed myocarditis and complete heart block. The patient was strongly suspected of complete heart block due to viral myocarditis secondary to acute viral hepatitis due to HAV which is a very rare complication of HAV infection. The child had not been diagnosed with any congenital cardiac anomaly or congenital heart block. She had never been hospitalized before it. She never had any apparent cardiac risk and the family history was negative for any cardiomyopathy.

HAV infection is most of the time asymptomatic but can lead to fulminant hepatitis in some cases and some extra-hepatic manifestations like myocarditis ⁽¹³⁾. Mechanism leading to myocarditis in HAV infection is not known but it is believed that the immune response to infected cell play a central role in myocarditis⁽¹³⁾. WHO has reported that around 7134 people died from hepatitis A worldwide in 2016. USA (CDC) reported around 12474 cases of hepatitis A in 2018.

Myocarditis-induced heart block has been reported in the literature⁽¹⁴⁾. Viral pathogens are the leading cause of myocarditis. Myocarditis due to COVID-19 has been one of the dangerous complications of COVID-19 ^(15,16). Other infectious causes of myocarditis reported in the literature include measles, amoebic hepatitis, Lyme disease, herpes, coxsackie, adenovirus $etc^{(17,18)}$. Cases of viral myocarditis present with abnormal ECG and raised cardiac markers. Definite diagnostic investigations usually required in these cases are echocardiography, cardiac MRI, and endomyocardial biopsy but the critical condition, need of a pacemaker and limited resources often makes it difficult to properly investigate a case of myocarditis. One should be cautious of myocarditis secondary to HAV infection and the patient must be screened with the help of cardiac markers in case the patient develops hypotension. Clinically suspected cases should be investigated at the earliest, and cases should be managed with supplemental oxygen and inotrope therapy ⁽¹⁹⁾. Temporary Pacemaker and automatic implantable cardioverter-defibrillator (AICD) should be considered at the earliest. The use of a ventricular assist device is beneficial and should be offered considering the deteriorating condition of a patient and to those at risk of cardiogenic shock. Complete heart block due to myocarditis can be managed with pacemaker implantation but persistent low blood pressure even after installation of a pacemaker (as in this case) increases the risk of mortality in the child⁽²⁰⁾.

The cardiac MRI and myocardial biopsy are investigations of choice to diagnose myocarditis ⁽²¹⁾. Clinical picture of cardiomegaly and deranged cardiac enzymes without any ischemic manifestations raise clinical suspicion of myocarditis. We were not able to get a cardiac MRI of the patient because of the critical condition of the patient and the necessity of pacemaker; we had clinically diagnosed the patient as a case of viral myocarditis, leading to a complete heart block.

Conclusion:

Acute viral hepatitis caused by the hepatitis A virus can be complicated by complete heart block secondary to viral myocarditis and may necessitate the installation of a temporary pacemaker (TPM) and can also lead to death due to cardiogenic shock. Specialized pediatric cardiac care is necessary to timely diagnose the condition. Close monitoring of the deteriorating cardiac condition of the child is important to prevent death. It is important to timely consider cardiac complications of symptomatic HAV infections, and consider early shifting of patients to Mechanical Circulatory Support.

Abbreviations: Hepatitis A virus (HAV), Temporary pace-maker (TPM), Electrocardiograph (ECG), Atrioventricular dissociation (AV dissociation), Pediatric Intensive Care unit (PICU), Alanine Transaminase (ALT), Aspartate aminotransferase (AST), Creatine Phosphokinase (CPK), Creatine Kinase myocardial Band (CK-MB), Lactate dehydrogenase (LDH), Continuous positive airway pressure (CPAP), Day of Admission (DOA)

Declarations

Ethics approval and consent to participate

Not applicable.

Availability of data and material

Not applicable.

Competing interests

None.

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None.

Authors' contributions

Mansoor Ahmed, Haseena Naseer, Mohammad Ebad ur Rehman, Abdulqadir Nashwan, and Jawad Basit conceptualized the case report, drafted the initial manuscript, critically reviewed the manuscript, gave final approval and agreed to be held accountable for all aspects of the work

Mateen Arshad, *Afnan Ahmad* conceptualized the case report, collected the data and graphically presented the data, were involved in initial drafting of the manuscript, critically reviewed the manuscript, gave final approval and agreed to be held accountable for all aspects of the work

Dr. Muhammad Asad conceptualized, critically reviewed and revised the manuscript, gave final approval and agreed to be held accountable for all aspects of the work

All authors read and approved the final manuscript.

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Tables & Figures

Table 1. Clinical Presentation

Figure 1. Chest x-ray showing pleural effusion and cardiomegaly

Figure 2. ECG showing complete AV dissociation

Figure 3. Case timeline

Patient characteristics and clinical presentation on 1st DOA.

Clinical Examination Gender Age Fever Heart Rate **Respiratory Rate** Pulse Blood pressure Lab. investigations and findings on 1st DOA Typhidot (For Typhoid) HAV IgM ALT AST CPK CK-MB LDH Hepatitis A virus (HAV), Alanine Transaminase (ALT), Aspartate aminotransferase (AST), Creatine Phosphokinase (CPK)





Case Timeline

