

## An unusual complication of acute viral hepatitis A: Hemolytic anemia

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### Abstract

Acute viral hepatitis A usually presents with self-limited jaundice, abdominal pain, nausea and vomiting. Rarely, patients develop extrahepatic manifestations including hemolytic anemia. We present a patient recently diagnosed with hepatitis A that subsequently developed acute anemia with a hemoglobin of 3.6g/dL. Initial blood work was consistent with hemolysis, including haptoglobin <30mg/dL, lactate dehydrogenase 996U/L and reticulocyte count 9.3%. She was treated briefly with steroids then supportive care and responded to treatment. Patients that develop hemolytic anemia as a result of acute hepatitis A recover as acute illness resolves.

### Keywords

hepatitis A; anemia; hemolysis; complications of hepatitis A

### Introduction

Hepatitis A is one of the most prevalent causes of acute hepatitis worldwide. Given the availability and effectiveness of vaccination, rates of viral hepatitis A significantly decreased in the United States until recently with multiple areas across the United States experiencing outbreaks [1]. Disease presentation can be variable but the majority of patients present with self-limited abdominal pain, nausea, vomiting and jaundice. However, few patients present with fulminate liver failure and have required liver transplantation [2]. Other rare extrahepatic presentations of hepatitis A include acute kidney injury, neurologic complications and anemia [3]. We present a case of a patient recently diagnosed with hepatitis A that developed acute hemolytic anemia.

### Case Report

We present a case of a 38-year-old female with a past medical history of type 2 diabetes mellitus and hypertension that presented to our medical center for management of anemia. Patient was admitted

to an outside hospital two months prior with abnormal liver function tests. She has no family history of liver disease and denied any alcohol use. She was ultimately diagnosed with acute hepatitis A and treated supportively. After discharge, the patient developed worsening fatigue. Physical exam revealed jaundice, scleral icterus and diffuse abdominal tenderness. Blood work revealed minimal improvement in her liver function tests with a total bilirubin 49.6 mg/dL (reference range <1.5mg/dL), direct bilirubin 29.1 (reference range <0.3ml/dL), AST 212 U/L (reference range 14-40U/L), ALT 193 U/L (reference range 9-48U/L) and INR 1.4 (reference range 0.9-1.1). She was also found to have renal impairment with a creatinine of 1.87mg/dL (reference range 0.50-1.20mg/dL) and hemoglobin 3.6 g/dL (reference range 11.2-15.7g/dL). She had no active signs of bleeding. She was transfused 4 units of packed red blood cells and started on Prednisone 40mg daily given concern for hemolytic anemia prior to transfer. Initial blood work at our institution revealed appropriate response to transfusion with a hemoglobin of 9.5 g/dL. Hematologic workup revealed a platelet count 110 (reference range 182 - 369K/uL), lactate dehydrogenase 996 U/L (reference range 100-199U/L), haptoglobin <30mg/dL (reference range 44-215mg/dL), reticulocyte count 9.3% (reference range: 0.5 to 1.7%) and direct antiglobulin test negative. Steroids were held initially given side effects previously experienced with steroids and adequate respond to transfusion. The patient was treated supportively and required no additional transfusions during admission. Markers of hemolysis were improving by the time of discharge and she continues to receive weekly blood work showing stable hemoglobin and improving liver function tests.

## Discussion & conclusions

Rates of hepatitis A are rapidly increasing in the United States. Due to multistate outbreaks, more patients are seeking medical assistance and even requiring admission for symptom management, close monitoring of liver function tests and management of extrahepatic manifestations of acute hepatitis A [4]. Given the health care burden of acute viral hepatitis A, it is crucial to promptly diagnosis, monitor and recognize other associated presentations.

Rare extrahepatic presentations of acute hepatitis A including acute kidney injury, hematologic abnormalities such as hemolytic anemia and neurologic complications occur in less than 10% of affected patients [5]. Based on previous studies, the incidence of hemolytic anemia is less than 5% of patients diagnosed with acute hepatitis A [6]. Given the rarity of this association, previous studies have not been completed to determine factors that predispose specific patients with hepatitis A to develop hemolytic anemia but multiple case reports suggest an increase frequency in patients with underlying glucose-6-phosphate dehydrogenase deficiency [6,7].

Prompt recognition of hemolytic anemia is crucial given it can lead to life threatening anemia. Patients recently diagnosed with hepatitis A that develop acute anemia without overt signs of bleeding should be evaluated for hemolysis. Blood work including haptoglobin, lactate dehydrogenase, direct Coombs test, reticulocyte count and blood smear should be performed to confirm the diagnosis [8].

Multiple treatment options have been proposed for patients that have developed hemolytic anemia as an extrahepatic manifestation of hepatitis A. Based on previous case reports and hematology litera-

ture, many patients receive steroids at a dose of 1mg/kg/day [9,10]. One case report highlights the use of plasmapheresis in patients that do not respond to steroids, though the effectiveness of this intervention remains uncertain [7]. Our patient was initially started on steroids; however, these were stopped after two doses as she subsequently improved with supportive care with transfusions. No studies have been performed to determine which intervention is the most effective and appropriate length of treatment if steroids are initiated. Previous literature suggests that supportive care or a shorter course of steroids may be appropriate [7,11].

In summary, patients with acute hepatitis A typically present with self-limited abdominal pain, nausea, vomiting and jaundice. Less than 10% of patients present with extrahepatic manifestations including hemolytic anemia. Anemia is typically treated with supportive care, steroids and in some cases plasmapheresis. Anemia typically recovers as acute hepatitis A resolves.

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