

Transient Bone Marrow Suppression Secondary to Acute Hepatitis A: A Case Report

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Abstract

Background

Hepatitis A virus (HAV) infection is well known for its liver manifestations, ranging from asymptomatic to life-threatening fulminant hepatitis with death. However, HAV infection may additionally cause extrahepatic manifestations in the form of severe hematologic and renal complications. Even with such knowledge, prevalence and clinical significance of these manifestations, i.e., bicytopenia and acute kidney injury (AKI), are not well explored. This case report places these complications in the limelight and reports on their updated prevalence, providing valuable information for both specialists and general practitioners.

Case Presentation:

A 23-year-old male with a 2-week history of fever, jaundice, oliguria, and gastrointestinal symptoms presented after consuming street food. He was initially treated with fluids, transfusions, acetaminophen, and steroids but was referred to us due to a worsening condition. His lab tests were elevated liver enzymes, bicytopenia, and AKI. Hemodialysis, transfusions, and supportive care led to remission within 2 weeks.

Discussion

It is a case of hepatitis A with rare complications of bicytopenia and AKI. Bicytopenia, likely due to bone marrow suppression, and AKI, aggravated by dehydration and hyperbilirubinemia, were successfully managed with supportive treatment. Hemodialysis and transfusions restored the complications, demonstrating the importance of early diagnosis and supportive treatment in complicated hepatitis A.

Conclusion

This is a rare case in the literature that has the ability to make awareness about the diverse complications of hepatitis A, particularly its relation with bicytopenia and AKI.

Keywords

Transient bone marrow suppression; Acute hepatitis A; Case report.

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Introduction

Hepatitis A virus (HAV) infection presents clinically in a broad spectrum, ranging from asymptomatic infection, particularly in children, to fulminant hepatitis in adults, necessitating liver transplant in up to 80% of cases [1]. Fulminant hepatitis A is relatively rare and occurs in approximately 0.015% to 0.5% of infected patients [2]. Although chronic hepatitis and cirrhosis are not HAV infection complications,



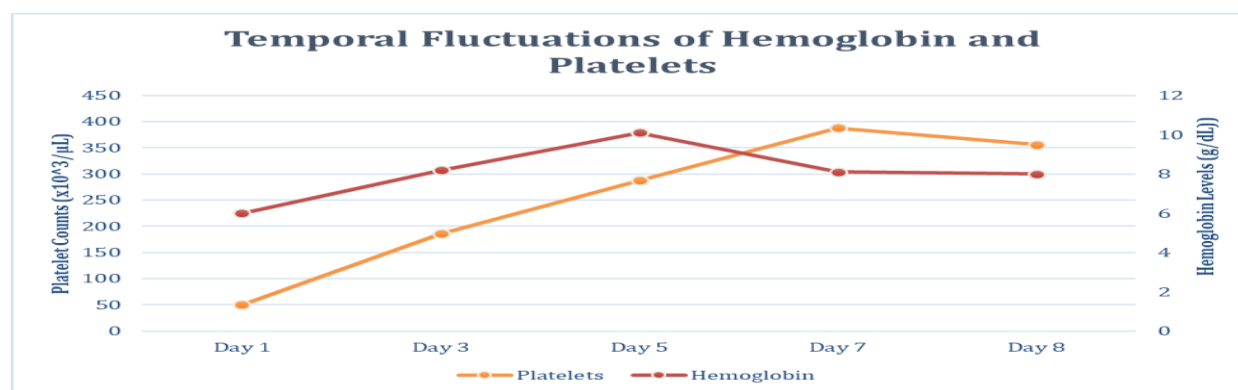
there are rare, unusual presentations and these include repetitive hepatitis, cholestasis lasting for prolonged periods, and complicated presentations with acute kidney injury (AKI). Hematologic HAV infection complications in the form of hemolytic anemia, bicytopenia, aplastic anemia, and red cell aplasia are uncommon [3,4,5]. Among the hepatitis-inducing viruses, the lowest incidence of such hematologic complications occurs with HAV infection [6].

Herein, we present a rare case of HAV infection with bicytopenia due to transient bone marrow suppression and AKI, emphasizing the need for heightened clinical awareness of these atypical but significant complications.

Case Presentation: A 23-year-old male patient with 2 weeks history of intermittent fever, jaundice, oliguria, anorexia, abdominal pain, diarrhea, and vomiting after meals. A week before the onset of symptoms, the patient consumed street food. Intrapartum treatment at a local medical center involved intravenous fluids, blood transfusions, acetaminophen for fever and

abdominal pain, and corticosteroids for symptom relief. The patient was, however, referred to our center due to worsening clinical condition.

The patient was admitted and noted to appear pale and tired. The vital signs were the following: temperature 37.6°C, blood pressure 110/70 mmHg, pulse 88 beats/min, respiratory rate 20 breaths/min, and oxygen saturation 98% on room air. Physical examination revealed jaundice and hepatomegaly without other significant findings. Laboratory investigations confirmed acute hepatitis A with marked elevations in liver enzymes. The patient exhibited bicytopenia, characterized by a hemoglobin of 6 g/dL and a platelet count of 50,000/ μ L, as well as AKI with a creatinine of 12.8 mg/dL. The white blood cell (WBC) count remained within the normal range, measuring 9,510/ μ L on Day 1, 7,060/ μ L on Day 2, 8,340/ μ L on Day 3, and 7,980/ μ L on Day 7. A line graph (Figure 1) illustrates the dynamic changes in hemoglobin and platelet counts over the course of hospitalization, demonstrating progressive recovery following supportive therapy.



Laboratory Parameter	Normal Range	Day 1	Day 2	Day 3	Day 4	Day 5	Day 7
Hemoglobin (g/dL)	12–16 (W), 14–18 (M)	6.0	8.1	8.2	—	10.1	—
Platelets ($\times 10^3/\mu$ L)	150–400	50	72	186	—	288	—

(— = not measured on that day)

Figure 1. Trends in hemoglobin and platelet counts during hospitalization, showing progressive improvement with treatment

Peripheral blood smear demonstrated normocytic, normochromic anemia. Coagulation studies revealed prolonged prothrombin time and international normalized ratio. Additional laboratory abnormalities included hyponatremia, elevated blood urea nitrogen, and hyperbilirubinemia.

Serological testing confirmed an acute hepatitis A infection, as evidenced by the presence of hepatitis A virus IgM antibodies. Results for hepatitis B surface antigen, hepatitis B core antibody IgM, and hepatitis C antibody were negative, excluding these etiologies. Additionally, serological markers for human immunodeficiency virus (HIV), Epstein-Barr virus, and parvovirus B19 were unremarkable. Autoimmune workup, including antinuclear antibody, rheumatoid factor, and direct Coombs test, was performed to assess potential autoimmune etiologies. Coombs' test was

positive, haptoglobin levels dropped to 5.6 mg/dL, but the D-dimer level was below 500 ng/mL. A chest X-ray, abdominal ultrasonography, and CT abdomen revealed no significant findings other than borderline hepatomegaly. No signs of gastrointestinal bleeding were observed.

Upon arrival at the Emergency Room (ER), the patient received initial care, including intravenous fluid resuscitation and correction of electrolyte imbalance (normal saline 80 mL/h) to address a decreased sodium level of 112 mEq/L. Subsequently, the patient was administered bicarbonate-based fluids and was admitted to the medical step-down unit for further observation and commenced on symptomatic treatment for hepatitis A. The patient presented with elevated liver enzymes consistent with cholestatic hepatitis A (Figure 2).

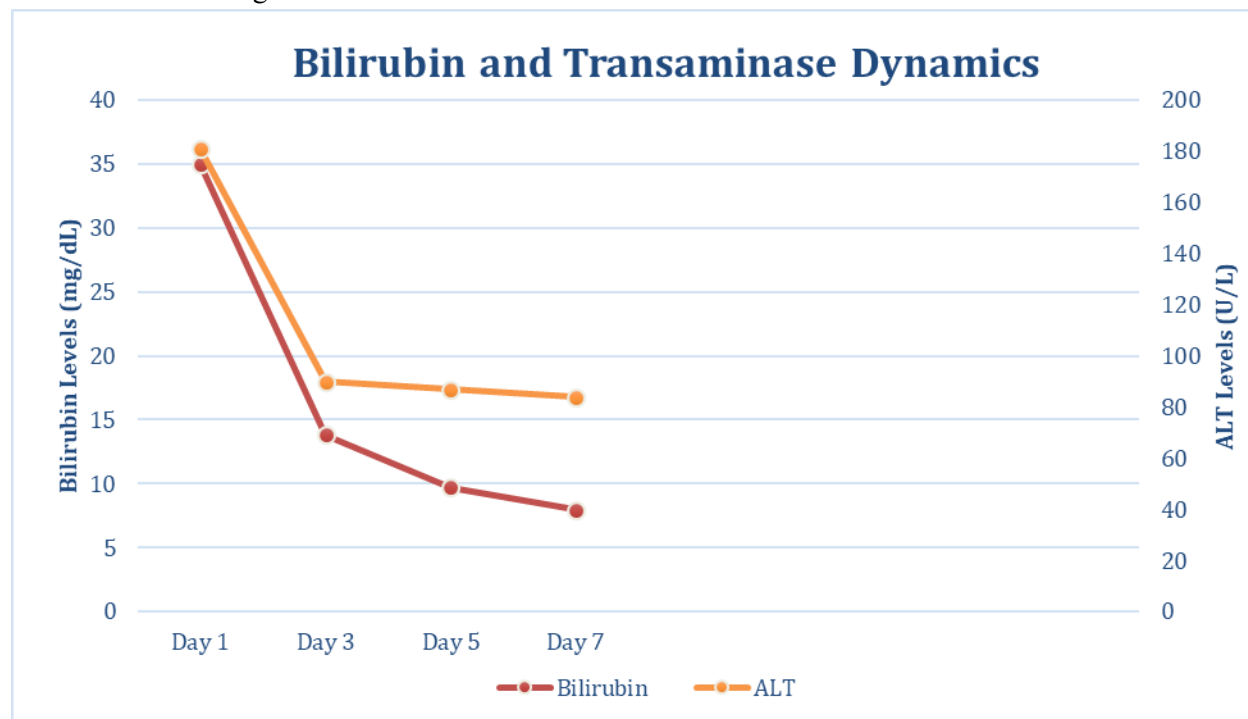


Figure 2. Changes in bilirubin and alanine aminotransferase (ALT) levels over time, illustrating the progression of liver function during the treatment period.

To address the risk of bacterial translocation and potential hepatic encephalopathy, the patient started oral rifaximin 550 mg three times daily. Additionally, the patient was prescribed ondansetron 8 mg every 8 hours and omeprazole 40 mg once daily to manage gastrointestinal symptoms.

On the third day of admission, based on hematology advice, the patient was transfused into 2 units of packed red blood cells and commenced on injection epoetin alfa 10,000 IU subcutaneously twice weekly, methylcobalamin 500 mg tablet once daily, ferrous sulfate 200 mg tablet once daily, and folic acid 500 micrograms tablet once daily to improve hematologic status.

Evaluation of renal function revealed AKI characterized by elevated creatinine, proteinuria, hematuria, and impaired renal concentration ability. The patient underwent hemodialysis due to the onset of uremic symptoms on the fifth day of hospitalization. Over time, there was an improvement in his symptoms and liver functions, so he was transferred to the medical ward for further management. Despite improved diuresis, the patient's renal function continued to decline, as evidenced by a persistently elevated serum creatinine level that peaked at 16.4 mg/dL on Day 5. Hemodialysis was initiated and maintained due to persistent renal impairment and metabolic derangements. The patient also received multiple doses of intravenous furosemide (40 mg) to induce diuresis and manage fluid overload. In addition, the patient was prescribed fosfomycin 667 mg tablet three times daily and allopurinol 50 mg tablet once daily to preserve renal function.

The patient was discharged on Day 8 with the aforementioned laboratory findings and was scheduled for twice-weekly hemodialysis sessions, which were completed on Days 11 and 15. He was advised to follow up with nephrology and gastroenterology outpatient departments after 1 week.

Discussion

Approximately 1.5 million clinical cases of hepatitis A are reported globally each year; however, the true incidence is estimated to be tenfold higher [7]. Hepatitis A is a viral liver infection caused by HAV and is primarily transmitted via contaminated food or water. Clinical manifestations range from asymptomatic infection to severe fulminant hepatitis, with fatigue, nausea, vomiting, abdominal pain, jaundice, and dark urine as common symptoms. A cholestatic variant of acute hepatitis A has been described in up to 10% of symptomatic cases in case reports and small series [8,9]. Clinicians should be aware of the diverse extrahepatic complications associated with hepatitis A to facilitate early diagnosis and management.

Bicytopenia is a hematological condition characterized by a simultaneous reduction in two of the three cell lines, i.e., erythrocytes, leukocytes, and platelets. In contrast to monocytopenia, which affects a single cell line, bicytopenia often signifies a more severe underlying pathophysiology. Etiologies encompass bone marrow suppression, autoimmune dysregulation, and infectious processes.

AKI is an acute impairment of renal function of diverse etiologies like infection, hypotension, nephrotoxicity, and direct renal injury. The AKI is a broad clinical spectrum that may range from mild to severe with potentially lethal consequences.

Even though the precise mechanisms of bicytopenia and AKI in hepatitis A are unknown, these sequelae may appear during severe illness. Bicytopenia may be a consequence of either direct viral damage to bone marrow or an underlying immunologic process. Similarly, AKI may result due to reduced renal perfusion, direct viral nephrotoxicity, or immune-mediated glomerulonephritis. Concurrent bicytopenia and acute kidney injury in hepatitis A are rather rare.

The case discussed shows the intricate interassociation between acute hepatitis A infection, bone marrow suppression, and AKI. Although hepatitis A is an infection of the liver, it sometimes occurs with extrahepatic manifestations such as autoimmune hemolytic anemia, aplastic anemia, pure red cell aplasia, bicytopenia, pleural or pericardial effusion, acute reactive arthritis, acute pancreatitis, and neurologic abnormalities such as mononeuritis and Guillain-Barré syndrome [10].

Bicytopenia here manifests as anemia with characteristics of extreme reticulocytopenia and the absence of erythroid precursors in the bone marrow, together with thrombocytopenia. The patient presented with deranged liver function tests and renal impairment. No evidence of gastrointestinal bleeding or thymoma was detected on chest radiography. Comprehensive laboratory investigations, including serological markers for HIV, Epstein-Barr virus, hepatitis B and C, autoimmune disorders, parvovirus B19, and rheumatoid arthritis, were negative.

Peripheral blood smear analysis revealed no lymphoma-associated abnormalities. The patient had no significant medical history.

A positive direct Coombs test was initially observed. However, the clinical significance of this finding was carefully considered. It is important to acknowledge that while the direct Coombs test exhibits high sensitivity, false-positive rates can occur in hospitalized patients, reaching up to 7–8% as reported in [11]. Furthermore, while the low haptoglobin level (5.6 mg/dL) initially suggested hemolysis, it is crucial to note that haptoglobin levels can be influenced by various factors, including hemodilution, blood transfusions, and liver dysfunction [12]. The absence of schistocytes on the peripheral blood smear and normal indirect bilirubin levels, coupled with the potential for a false-positive Coombs test and the limitations of haptoglobin interpretation, led us to favor a diagnosis of transient myelosuppression. D-dimer levels in this case were within normal limits, and there were no signs of widespread bleeding or abnormal clotting parameters, suggesting that DIC was not present.

The liver and bone marrow share components of the reticuloendothelial system, potentially rendering them susceptible to similar pathogenic insults [13]. While previous studies have implicated viral-induced autoimmune responses and direct viral infection of bone marrow progenitors in the pathogenesis of hepatitis-associated bicytopenia, the present case featuring a non-reactive antinuclear antibody and extractable nuclear antigen profile provides additional evidence supporting transient bone marrow suppression as the primary etiology.

Acute renal failure is a recognized complication of fulminant hepatic disease, although it is less frequently observed in hepatitis A. The mechanism underlying hepatitis A-associated

AKI remains incompletely elucidated. Prerenal factors, including anorexia, vomiting, and diarrhea, can contribute to reduced effective circulating volume, thereby activating the renin-angiotensin-aldosterone system [14]. Hyperbilirubinemia and cholestasis increase renal susceptibility to ischemia. Bilirubin and bile acids directly injure the kidney, exacerbating AKI, especially in hemodynamically unstable patients [15]. Several studies have demonstrated that bilirubin and bile salts exert direct nephrotoxic effects, inducing tubular injury and acute tubular necrosis [16]. Another potential mechanism involves immune complex-mediated nephritis, which may occur during acute hepatitis A. Management of renal failure in this context is primarily supportive, with generally favorable

outcomes; however, permanent renal sequelae remain a possibility [14].

Conclusion

We present the first documented case of hepatitis A complicated by bicytopenia due to bone marrow suppression and AKI. This case underscores the importance of recognizing and managing hematological and renal complications in HAV infections. Emphasizing supportive care over unnecessary bone marrow biopsy facilitated the resolution of bone marrow suppression, with the symptoms improving over time. Interventions, including hemodialysis and blood transfusions, led to complete remission within 2 weeks.

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