

Pleural Effusion Associated with Anicteric Hepatitis A Virus Infection – Unusual Manifestation of a Common Disease: A Case Report

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Background: Hepatitis A infection is common in children and often presents with mild hepatic disease. The clinical manifestations of hepatitis A virus are usually related to liver damage but sometimes extrahepatic manifestations may occur.

Case Presentation: We present a case of four-year- and eight-month-old male child with anicteric hepatitis A infection associated with a pleural effusion. The patient presented with abdominal pain, low-grade fever, loss of appetite, and vomiting of ten days duration. On examination, there was dullness and decreased air entry on the lower third of the lung field bilaterally and hepatomegaly of 6 cm below the costal margin. Ultrasonography revealed mild ascites, hepatosplenomegaly, and small bilateral pleural effusion. Immunoglobulin M anti-hepatitis A virus serology was positive. He was managed with supportive treatment and fully recovered after a month of follow-up. This case is reported to emphasize that hepatitis A infection should be considered in the differential diagnosis of pleural effusion in a patient with acute hepatitis even in the absence of jaundice. This is the first case of anicteric hepatitis A infection complicated with pleural effusion in children.

Conclusion: This report suggests that pleural effusion can be associated with anicteric hepatitis A infection and should be included in the differential diagnosis of pleural effusion.

Keywords: hepatitis A, unusual manifestation, pleural effusion, ascites

Background

Hepatitis A virus (HAV) is the most common cause of acute hepatitis in children. It is one of the public health problems particularly in low-income countries.¹

Worldwide, an estimated 10 million people are infected with hepatitis A virus annually.² HAV is transmitted primarily by ingestion of contaminated food, water, or direct contact with infectious individuals. The incidence is associated with socioeconomic status and access to safe water.^{3,4}

The clinical presentation of HAV infections is mostly related to liver damage. But it is seldom associated with atypical manifestations including anasarca,⁵ pleural effusion and ascites^{6,7} pleural effusion, ascites, and acalculous cholecystitis⁸ and isolated pleural effusion.^{9–12}

We report a child with anicteric acute hepatitis A infection with bilateral pleural effusion and ascites, who improved with supportive management.

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Case Presentation

Four-year- and eight-month-old, previously well, male child presented with abdominal pain, loss of appetite, low-grade intermittent fever, nausea, vomiting, and progressive abdominal distension of ten days duration. He has also cough of five days duration. There was no history of yellowish discoloration of eye or skin, bleeding or previous history of jaundice, urinary complaints, and change in urine or stool color. He has no history of contact with chronic cough or with tuberculosis-diagnosed patients.

On examination: Blood pressure 90/60mm, pulse rate 88/minute, respiratory rate 20/minute, and temperature 37°C. There was decreased air entry and dullness in the lower lung field bilaterally. Distended abdomen, fluid shift was positive; the liver was palpable 6cm below the right costal margin, total liver span 11 cm, and tender. There was some palmar pallor, otherwise normal.

On investigations, hepatitis A antibody immunoglobulin M was reactive, with a titer of >10.11. Other viral markers (hepatitis B, hepatitis C, and human immunodeficiency virus test was negative). Echocardiography study was normal. Other investigations are listed in [Table 1](#).

Ultrasonography examination revealed minimal ascites, hepatosplenomegaly, and small bilateral pleural effusion. Ultrasound guided-pleural tap revealed no cells, lactic acid dehydrogenase 15 IU/L, gene Xpert for tuberculosis was negative and bacteriologic culture was negative. Gastric aspirate was also done for gene Xpert and found to be negative.

Based on those investigations, the diagnosis of anicteric acute viral hepatitis A with unusual manifestations of pleural effusion and ascites was made. He was managed with supportive treatment (hydration, rest, antiemetics, a well-balanced diet). The liver enzymes were corrected within two weeks, ascites and pleural effusion disappeared after two weeks. Liver and spleen sizes were normalized after one month of follow-up.

Discussion

Hepatitis A infection in children may present in apparent, subclinical (there is evidence of liver damage on laboratory examination), symptomatic but without evidence of jaundice or with jaundice.¹⁰ Abdominal pain, fever, nausea, vomiting, fatigue, loss of appetite, abdominal distension and jaundice are common manifestations of hepatitis A virus infection in the symptomatic child. Children below 6 years are at less risk of symptomatic HAV infection and less than 10% of them manifesting with jaundice.¹

Infection with hepatitis A is associated with increased morbidity, and rarely mortality. Disease severity is dependent on age. It is mostly asymptomatic in children. Full recovery occurs in 85% of the patients within three months. Mortality increases as the age increase.¹³

Hepatitis A infection-related pleural effusion is a rare extrahepatic manifestation in children.¹⁴ Hepatitis A infection associated with pleural effusion was reported usually on the right side of the lung.^{9,11,12} But bilateral effusion has also been documented.^{6,7,15} The exact mechanism of pleural effusion in hepatitis A infection is not well known but the following mechanisms have been postulated. Transport of fluid from diaphragmatic lymphatics or leakage from a diaphragmatic defect to the pleural cavity from coexistent ascites.⁶ The second postulated mechanism is a virus-induced infection of the liver, with unknown mechanisms results in effusion.¹² Pleural effusion may also result from immune complex deposition,¹ or direct effect of viral on pleura.¹⁶ Ascites result from venous and lymphatic obstruction.⁶ Pleural effusion secondary to hepatitis A resolves spontaneously even though liver damage progresses.¹² Although the mechanism of pleural effusion in hepatitis A infection patient is speculated by the above mechanisms, there may not be different mechanisms for anicteric hepatitis A infection associated with pleural effusion.

Tuberculosis was ruled out for the fact that the patient had no history of contact with tuberculosis diagnosed patient or chronic cough and negative laboratory results. Therefore, the diagnosis of anicteric acute viral hepatitis A infection with associated pleural effusion and ascites was made.

Documented case reports of HAV infection with pleural effusions showed that the presence of effusion with HAV infection did not signify poor outcome and it resolves with supportive treatment alone.^{6,8,10,11,14,17-19}

Though the patient had nearly normal serum bilirubin (1.5mg/dl) and the liver enzymes were highly elevated especially the alkaline phosphatase which was 1000 mg/dl, but since it is nonspecific to the liver it may not be exclusively signal of liver damage and also the reference range for his age is 93–309 that means 3 to 5 times elevated. However, the other enzymes specific to the liver like alanine amino transaminase were also highly elevated. The good thing was the synthetic function of the liver was not affected and that why he recovered fully.

All previously reported cases had elevated bilirubin while this child did not, so this is the first case report of

Table I Investigations of the Patient at Presentation and During Follow-Up

Investigations	At First Visit	Normal Values for His Age Range	Follow-Up (After 2 Weeks)
Hemoglobin (gm/dl)	10	11.5–14.5	10.5
White blood cell count (cells/mm ³)	13.9 × 10 ³	4.0–12.0 × 10 ³	12.6 × 10 ³
Differential cell count	Neutrophils 46.5% Lymphocytes 42.8% 158 × 10 ³	54–62% 25–33%	
Platelet count (cells/mm ³)		150–400 × 10 ³	160 × 10 ³
Peripheral smear	Normocytic normochromic		
Urinalysis	Non revealing		Negative
Bilirubin (mg/dl) total	1.5	0.3–1.0	
Direct	0.5		
Serum albumin (mg/dl)	3.8	3.5–5.6	
Aspartate transaminase (U/L)	911	15–50	46
Alanine amino transaminase (U/L)	800	5–45	34
Alkaline phosphatase (U/L)	1000	93–309	80
Serum creatinine (mg/dl)	0.4	0.03–0.59	
Prothrombin time (second)	12 seconds	10.6–11.4	
International normalized ratio	1.5	1–3	
Erythrocyte sedimentation rate	32 millimeters/hour	3–13	20 millimeters/hour

anicteric hepatitis A infection complicated with pleural effusion in children. Therefore, a patient with symptoms of acute hepatic damage and pleural effusion even without jaundice hepatitis A infection has to be considered but in developing countries like Ethiopia tuberculosis and other bacterial causes must be ruled out.

Conclusions

Pleural effusion has not been reported previously to be associated with anicteric hepatitis A viral infection. We would like to stress that although pleural effusion is rarely seen during anicteric hepatitis A, hepatitis A infection should be considered in the differential diagnosis in patients with pleural effusions, especially in developing countries. Pleural effusion is a benign and early extrahepatic complication of anicteric acute hepatitis A infection that resolves spontaneously.

Data Sharing Statement

All data generated or analyzed during this study are included in this case report.

Ethics Approval and Consent to Participate

Expedited approval was obtained from Mekelle University College of Health Sciences, Health Research Ethics Review Committee (HRERC) on 10/12/2018, (ERC 1531/2018).

The patient's father has provided written informed consent, confirming that the father has agreed on the case to get published.

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Disclosure

The authors declare that they have no competing interests.

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