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پروپوزال نویسی

آموزش مهارت‌های کاربردی در ندوین و چاب مقاوم
**Hepatitis A with Pleural Effusion, Ascites and Acalculous Cholecystitis**

Ela Erdem*, MD; Nafiye Urgancı, Ass. Prof, MD; Yasemin Ceylan, MD; Nursu Kara, MD; Gul Ozcelik, MD, and Seda Geylani Gulec, MD

Department of Pediatrics, Sisli Etfal Education and Research Hospital, Istanbul, Turkey

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**Abstract**

**Background:** Hepatitis A virus (HAV) infection constitutes an important health problem in developing countries. It is usually a benign self-limiting disease, but may present with atypical clinical findings.

**Case Presentation:** A twelve-year-old male with ascites, pleural effusion, and acalculous cholecystitis during the course of HAV infection is reported. He was managed conservatively and clinical improvement was observed with resolution of HAV infection.

**Conclusion:** To our knowledge, this is the first case in which all these three rare complications were observed in a single patient in the early period of disease.

**Key Words:** Pleural effusion; Ascites; Acalculous cholecystitis; Hepatitis A virus; Hepatitis

**Introduction**

Acute hepatitis A virus (HAV) infection is a self limiting viral disease in childhood. The most important cause of transmission is contamination of water with feces. Although hepatitis A usually presents with mild symptoms or is asymptomatic in children, extrahepatic manifestations are reported in 6.4%-8% of cases[1,2]. These manifestations are arthralgia, cutaneous vasculitis, cryoglobulinemia, hemophagocytic syndrome, acalculous cholecystitis, pancreatitis, aplastic anemia, Guillane-Barre syndrome, transverse myelitis, acute tubular necrosis, nephrotic syndrome, vasculitis, reactive arthritis and pleural effusion. Among these, pleural effusion and acalculous cholecystitis are rare complications of acute viral hepatitis A, especially in childhood. Pleural effusion occurs during early period of the disease and resolves spontaneously with resolution of hepatitis[3-5]. Ascites is a known complication of HAV infection. Pleural effusion accompanying ascites in the course of hepatitis A is reported only in three cases in literature[6-8]. However, there is not a single case in the literature with all these three complications being presented simultaneously. Herein we
Case Presentation

A twelve-year-old boy was admitted to our clinic with seven days history of nausea, vomiting, anorexia and fatigue; the patient was febrile and icteric with normal vital signs. There was no significant medical history. The medical history was unremarkable. He had no underlying disease and there was no exposure to other patient with hepatitis A. On physical examination there was a tender liver, palpable 3 cm below the costal margin and the spleen was not palpable.

Laboratory examination yielded the following; hemoglobin: 10.9 g/dL; hematocrit: 32%; white blood cell count: 4200 cells/mm³; platelet count: 172,000/mm³; serum aspartate aminotransferase and alanine aminotransferase: 1364 and 1838 U/L (respectively); total (direct) bilirubin: 6.3 (5.6) mg/dl; gamma-glutamyl transferase: 89 U/L; alkaline phosphatase: 132 U/L; total protein: 5.2 g/dL; albumin: 1.9 g/dL; prothrombin time: 16 seconds; blood urea nitrogen, glucose, serum electrolytes levels and erythrocyte sedimentation rate were in normal limits. HAV IgM and HAV IgG were positive, whereas all other viral markers including hepatitis B, C and E markers were interpreted as negative. Serological analysis for cytomegalovirus, parvovirus, Epstein Barr virus, leptosira and salmonella were also found to be negative. So diagnosis of HAV infection was confirmed according to positive IgM and IgG antibody titers.

On the 4th day of admission patient complained of abdominal distension and mild respiratory distress. Chest X-ray showed closure of right costophrenic sinus and there was no parenchymal infiltration (Fig 1). Thoracic ultrasonography revealed a right-sided pleural effusion and ascites. In abdominal ultrasound there was a mild hepatomegaly with increased echogenicity, a hydroptic, thickened, not calculous gallbladder (4 mm), and intra-abdominal fluid (Fig. 2). Thoracocentesis revealed pleural fluid with no leukocytes or atypical cells. Bacteriological culture of pleural fluid remained sterile including for M. tuberculosis. PPD was also negative.

He was managed with supportive parenteral fluids and was given a protein-lipid restricted and carbohydrate enriched diet. One dosage of vitamin K was enough for mildly elevated prothrombin time level. During the follow-up there was no progression of clinical findings. Ten days after admission, chest X-ray and ultrasonographic examinations showed regression of pleural effusion, ascites and

![Fig. 1: Closure of right costophrenic sinus without parenchymal infiltration in chest X-ray](www.SID.ir)
hydroptic changes in the gall bladder.

With supportive therapy considerable improvement was observed in biochemical tests and periodical ultrasound controls (Table 1). Hepatic enzyme levels gradually returned to normal values within two months. He continued to do well during a three month follow-up.

**Discussion**

Hepatitis A virus (HAV) causes acute hepatitis associated with significant morbidity and occasional mortality. Although it can infect other tissues, clinical manifestations are associated solely with liver inflammation. The severity of disease is age dependent. In children, it manifests usually with mild symptoms or asymptomatic and jaundice is usually absent. In this self limiting infection, in which 85% of patients recover completely in three months, mortality risk increases with age[9]. HAV infection may present also with rare complications such as acalculous cholecystitis, pleural effusion and ascites. Pleural effusion is known to be an early and benign complication of the disease[8]. The exact pathogenesis of the effusion is unknown but it seems likely to be related with inflammation of the liver, immune complexes or secondary to ascites[8,10]. In all cases pleural effusion resolved spontaneously except the case reported by Tesovic et al which resulted in death[3]. Ascites that has been reported in later stages of disease especially in older children and adults, is thought to occur from venous or lymphatic obstruction due to liver involvement or reduction of oncotic pressure due to hypoalbuminemia during the

| Test                        | 1st  | 2nd  | 3rd  | 4th |
|-----------------------------|------|------|------|-----|
| Aspartate aminotransferase (AST) (U/L) | 1364 | 1100 | 500  | 43  |
| Alanine aminotransferase (ALT) (U/L) | 838  | 1400 | 340  | 40  |
| Gamma-glutamyl transferase (U/L) | 89   | 90   | 100  | 50  |
| Alkaline phosphatase (U/L) | 132  | 230  | 215  | 175 |
| Total bilirubin (mg/dl) | 6.3  | 5.4  | 2.5  | 1.3 |
| Direct bilirubin (mg/dl) | 5.6  | 3.8  | 1.8  | 1.0 |
course of infection\cite{9,10}. Acalculous cholecystitis, rare in children, has an uneventful course an usually recovers in two to three weeks. Very little is known about the exact pathogenesis of this manifestation\cite{11,12}. Mourani et al detected HAV antigen in bile duct epithelium and the gall bladder wall suggesting a direct effect of viral antigen rather than a secondary phenomenon\cite{13}.

Gallbladder changes may be variable during the course of HAV infection. Gallbladder thickening is the most common finding\cite{14}. In our patient pleural effusion, ascites and acalculous cholecystitis were detected in HAV infection. Since acalculous cholecystitis is transient and gradually disappears when viremia becomes low, surgical intervention was not required in our case similar to other previously reported cases in literature\cite{15}. To our knowledge, this is the first case with the presence of three rare complications in single patient in the early period of disease. We can explain the recovery of signs with supportive therapy by occurrence of pleural effusion due to transport of fluid from diaphragmatic lymphatics or directly through a diaphragmatic defect secondary to ascites or hypoalbuminemia that was present in our patient.

Since these three complications were seen at the same time, serosal involvement due to immune complexes gains importance as the possible etiological agent.

**Conclusion**

Although HAV infection is known to be a self-limiting disease, it is not so innocent and may reveal very rare, serious and atypical complications in the course of disease as seen in our patient. This may result in performing unnecessary diagnostic tests. One should remember, especially in developing countries, children vaccinated against HAV in infancy, can be protected from unnecessary laboratory investigations and atypical complications of HAV infection.

**References**

1. Amarapurkar DN, Amarapurkar AD. Extra-hepatic manifestations of viral hepatitis. Ann Hepatol. 2002;1(4):192-5.
2. Willner IR, Uhl MD, Howard SC, et al. Serious hepatitis A: an analysis of patients hospitalized during an urban epidemic in the United States. Ann Intern Med. 1998;128(2):111-4.
3. Tesovic G, Vukelić D, Vuković B, et al. Pleural effusion associated with acute hepatitis A infection. Pediatr Infect Dis J. 2000;19(6):585-6.
4. Alhan E, Yildizdağ D, Yapıcıoğlu H, et al. Pleural effusion associated with acute hepatitis A infection. Pediatr Infect Dis J. 1999;18(12):1111-2.
5. Selimoglu MA, Ziraatci O, Tan H, et al. A rare complication of hepatitis A: pleural effusion. J Emerg Med. 2005;28(2):229-30.
6. Dagan R, Yagupsky P, Barki Y. Acute ascites accompanying hepatitis A infection in a child. Infection. 1988;16(6):360-1.
7. Cohen HA, Amir J, Frydman M, et al. Infection with the hepatitis A virus associated with ascites in children. Am J Dis Child. 1992;146(9):1014-6.
8. Gürkan F. Ascites and pleural effusion accompanying hepatitis A infection in a child. Clin Microbiol Infect. 2000;6(5):286-7.
9. Ciocca M. Clinical course and consequences of hepatitis A infection. Vaccine. 2000;18(suppl 1):S71-4.
10. Kamath SR, Sathiyasekaran M, Raja TE, et al. Profile of hepatitis A in Chennai, India. Indian Pediatrics. 2009;46(7):642-3.
11. Fuoti M, Pinotti M, Miceli V, et al. Acute acalculous cholecystitis as a complication of hepatitis A: a report of 2 pediatric cases. Pediatr Med Chir. 2008;30(2):102-5.
12. Melero Ferrer JL, Ortuno Cortes J, Nevarez Heredia A, et al. Acute acalculous cholecystitis associated with acute hepatitis A virus infection. Gastroenterol Hepatol. 2008;31(7):433-5.
13. Mourani S, Dobbs S, Genta RM, et al. Hepatitis A-virus associated cholecystitis. Ann Intern Med. 1994;120(5):398-400.
14. Portincasa P, Moschetta A, Di Ciula A, et al. Changes of gallbladder and gastric dynamics in patients with acute hepatitis A. Eur J Clin Invest. 2001;31(7):617-22.
15. Arroud M, Benmiloud S, Oudghiri B, et al. Acute acalculous cholecystitis revealing hepatitis A virus infection in children. Saudi J Gastroenterol. 2009;15(4):277.
