Cukurova Medical Journal

Olgu Sunumu / Case Report

Autoimmune Thrombocytopenic Purpura in Hepatitis A Infection

Hepatit A Enfeksiyonunda İmmün Trombositopenik Purpura

Can Acıpayam[1], Sadık Kaya[2], Özlem Sangün[3], Gül İlhan[4], Canan Altunay[2], Gönül Oktay[5]

[1] Hatay Antakya State Hospital Department of Pediatric Hematology and Oncology, [2]Department of Pediatric, [3]Department of Pediatric Endocrinology, [4]Department of Hematology, [5]Department of Hemoglobinophaty Center, HATAY

Cukurova Medical Journal 2014; 39 (3):646-649.

ABSTRACT

In undeveloped countries, Hepatitis A is common and endemic because of unimmunization, unhygienic nutrition and poor living conditions. Secondary immune thrombocytopenia is frequently seen in hepatitis B and C infections. It is rarely reported with acute hepatitis A. Two cases of autoimmune thrombocytopenic purpura with acute hepatitis A is presented here.

Key Words: Hepatitis A, autoimmune thrombocytopenic purpura, intravenous immunoglobulin

ÖZET

Gelişmemiş ülkelerde, yetersiz aşılama, kötü hijyen ve yaşam koşulları nedeniyle hepatit A yaygındır. Sekonder immun trombositopeni, Hepatit B ve C enfeksiyonlarında sık görülürken, akut hepatit A enfeksiyonu bulgusu olarak nadiren bildirilmiştir. Sekonder immun trombositopenik purpurası olan akut hepatit A enfeksiyonlu 2 olgu burada sunulmuştur.

Anahtar Kelimeler: Hepatit A, immun trombositopenik purpura, intravenöz immunglobulin

INTRODUCTION

HAV infection is generally self limited and the clinical findings range of the disease are from asymptomatic to death from fulminant hepatitis[1]. Age of patients effects clinical manifestations of hepatitis A. Although in children under 6 years of age, 70% of infections are asymptomatic; 70% of adults symptomatic with jaundice and high levels of serum transaminases. After incubation period, fever, nausea, abdominal discomfort, dark urine and jaundice develop. Myalgia, pruritus, diarrhea, arthralgia and skin rash are less common symptoms. Relapsing hepatitis, prolonged hepatitis, acute renal injury and autoimmune hepatitis are reported as atypical complications of HAV infection. Autoimmune hemolytic anemia, aplastic anemia, pure red cell aplasia, pleural or pericardial effusion, acute reactive arthritis, acute pancreatitis, mononeuritis, mononeuritis multiplex and Guillain-Barré syndrome are other autoimmune and hematological immune manifestations of the disease[2]. These complications are rare in acute HAV infection, whereas common in adult patients with hepatitis B and hepatitis C[3].

It is well known that hematologic abnormalities may ocur during HAV infection because of bone marrow depression4. Autoimmune complications like ITP and hemophagosytic syndrome reported rarely during

HAV infection5. We presented an 8 year old boy and a 6 year old girl with thrombocytopenia as an initial manifestation of acute HAV infection.

CASE REPORT

Case 1

A 8 year old boy with epstaxis, ecchymosis, purpura on trunk, arms and legs for 3 days admitted to our hospital. He had no hepatic and hematological disease in the past. He was antiicteric and hemodynamically stable. Spleen and liver were non palpable. Liver enzyme levels were elevated (AST 1208 U/L, ALT 1351 U/L) with normal alkaline phosphatase, bilirubin, total protein, albumin, prothrombin time, activated partial thromboplastin time, and fibrinogen. Complete blood cell count showed hemoglobin 11.7 g/dl, white blood cell count 7.340/mm^3 with a differential of 64% neutrophil, 34% lymphocyte, and 2% monocyte, platelet count 3000/mm^3. Viral serologic tests were positive for anti-HAV IgM antibody and anti-HAV IgG negative for HIV, hepatitis B and C. Abdominal ultrasonography showed minimal diffuse thickening of the gallbladder wall. Direct Coombs tests were negative. Normocellular marrow with trilineage hematopoiesis and megakaryocytic hyperplasia with many mature and immature megakaryocytes seen in bone marrow. There was no hemophagocytosis. We diagnosed Immune thrombocytopenia and gave IVIG with a 1 g/kg dose for two day. On the 7th day of treatment his platelet count was 90.000/mm^3.

Case 2

A 6 year old girl with purpuric lesions over his trunk, ams and legs for 3 days admitted to our hospital. He had no hepatic and hematological disease in the past. She was anicteric and hemodynamically stable. Widely purpuric, petechial lesions and ecchymoses on his trunk, arms and legs and hematoma measuring 2x2 cm on the right frontal area were detected on physical examination. On physical exam, patient's liver is palpable 3 cm below the costal margin and the spleen are non-palpable. Liver enzyme levels were elevated (AST 149 U/L, ALT 469 U/L). Complete blood cell count showed hemoglobin 12.4 g/dl, white blood cell count 4.500/mm^3 with a differential of 16% neutrophil, 72% lymphocyte, and 8% monocyte, platelet count 8000/mm^3. Viral serologic tests were positive for anti-HAV IgM antibody and anti-HAV IgG negative for HIV, hepatitis B and C. Abdominal ultrasonography was normal. Direct Coombs tests were negative. Bone marrow aspiration examination revealed normocellular marrow with trilineage hematopoiesis and megakaryocytic hyperplasia with many mature and immature megakaryocytes. There was no hemophagocytosis. Immune thrombocytopenia due to acute HAV infection was diagnosed and IVIG with a 1 g/kg dose was given for two days. Her platelet count was found 80.000/mm^3 on the seventh day of the treatment and reached to normal level (215.000/mm^3) in one month. Her clinical and biochemical profiles normalized in a month.

DISCUSSION

HAV is an important cause of acute viral hepatitis in the Turkey and it occurs worldwide. The disease is generally self limited but the severity of illness is age dependent. While in children it is usually asymptomatic, symptomatic infection and jaundice is common in adults. Althaough classic form of HAV infection with jaundice, abdominal pain, fever, and diarrhea is seen in most of patients, rare extrahepatic and hematological complications develop in few patients. Extrahepatic complications such as urticarial rash and acute arthritis may ocur with acute hepatitis B, but not found in acute hepatitis A[6,7].

In a study conducted with Willner et al[8] in 256 patients mean age 26 hemolysis, acalculous cholecystitis, acute renal failure, pleural /pericardial effusion, acute reactive artritis and pancreatitis were reported as complications of hepatitis A.

Acalculous cholecystitis may often be complicated, as illustrated by an edematous gallbladder on radiological images and compatible clinical findings, many of which manifest transiently with spontaneous recovery[2]. We found diffuse thickening on gallbladder wall and acalculous cholecystitis in our 8 year old case and he had spontaneous recovery. Autoimmune manifestations are rare with acute HAV, especially in children. Maiga et al[9] reported 3 cases of acute hepatitis A infection with haematological complications. In the first case, severe aplastic anemia occurred in a 6 year-old child and in the second and third cases, severe anemia and thrombocytopenia occurred.

Thrombocytopenic purpura is rarely described in association with hepatitis A[4,10]. The possible causes of thrombocytopenia during hepatitis A infection could be due to direct marrow suppression, viral-associated hemophagocytosis syndrome with emperipolesis, immune-mediated peripheral destruction of platelets, or increased platelet consumption associated with disseminated intravascular coagulopathy[11]. Bone marrow examination of our patients showed megakaryocytic hyperplasia and it suggested peripheral destruction of platelets. Severe thrombocytopenia can be treated with IVIG, corticosteroid, and anti-D immunoglobulin. The comparative efficacy between IVIG and corticosteroid in treatment of immune thrombocytopenia is questionable. IVIG has high cost and risk of infection transmission whereas corticosteroids may cause dysglycemia, altered behavior, bone changes, and weight gain even when used for short durations. The presence of adequate megakaryocytes in the bone marrow of our patient suggests that the thrombocytopenia is most probably secondary to peripheral destruction of platelets. Absence of splenomegaly, other coexisting viral infections, and autoimmune conditions suggests the relation between hepatitis A and immune-mediated thrombocytopenia. The certain mechanism of thrombocytopenia is still unknown in hepatitis A. Generalized immune deregulation may be a hypotesis[10].

In a study conducted with Samantha et al[12] among 229 patients, hematological problems were reported in 8 patients. One of the two children with isolated thrombocytopenia (<50.000/mm3), bone marrow examination showed features of ITP.

CONCLUSION

Hepatitis A may present with thrombocytopenia findings as other viral infections. Transient autoimmune thrombocytopenia is a rare but definite entity in patients with acute hepatitis A and needs to be thought as a differential diagnosis of immune thrombocytopenic syndromes.

Conflicts of Interest: The authors have no conflicts of interest.

REFERENCES

1. Nainan OV, Xia G, Vaughan G, Margolis HS. Diagnosis of hepatitis a virus infection: a molecular approach. Clin Microbiol Rev. 2006;19:63-79.
2. Jeong SH, Lee HS. Hepatitis A: clinical manifestations and management. Intervirology. 2010;53:15-9.
3. Schiff ER. Atypical clinical manifestations of hepatitis A. Vaccine. 1992;10:18-20.
4. Cohen O, Mevorach D, Ackerman Z, Oren R. Thrombocytopenic purpura as a manifestation of acute hepatitis A. J Clin Gastroenterol. 1993;17:166-7.
5. Ertem D, Acar Y, Pehlivanoglu E. Autoimmune complications associated with hepatitis A virus infection in children. Pediatr Infect Dis J. 2001;20:809-11.
6. Koff RS. Clinical manifestations and diagnosis of hepatitis A virus infection. Vaccine. 1992;10:15-7.
7. Lemon SM. Type A viral hepatitis: epidemiology, diagnosis, and prevention. Clin Chem. 1997;43:1494-9.
8. Willner IR, Uhl MD, Howard SC, Williams EQ, Riely CA, Waters B. Serious hepatitis A: an analysis of

patients hospitalized during an urban epidemic in the United States. Ann Intern Med. 1998;128:111-4.

9. Maiga MY, Oberti F, Rifflet H, Ifrah N, Calès P. Hematologic manifestations related to hepatitis A virus. 3 cases. Gastroenterol Clin Biol. 1997;21:327-30.

10. Shenoy R, Nair S, Kamath N. Thrombocytopenia in hepatitis A--an atypical presentation. Journal of tropical pediatrics. 2004;50:241-2.

11. Tanir G, Aydemir C, Tuygun N, Kaya O, Yarali N. Immune thrombocytopenic purpura as sole manifestation in a case of acute hepatitis A. Turk J Gastroenterol. 2005;16:217-9.

12. Samanta T, Das AK, Ganguly S. Profile of hepatitis A infection with atypical manifestations in children. Indian J Gastroenterol. 2010;29:31-3.

Yazışma Adresi / Address for Correspondence:
Dr. Can Acıpayam
Hatay Antakya State Hospital,
Department of Pediatric Hematology and Oncology
31040 Hatay, Turkey.
Tel: 90 326 219 40 00
Fax: +90 326 227 24 40
Email : cacipayam@hotmail.com

Geliş tarihi/Received on: 26.12.2013
Kabul tarihi/Accepted on:29.01.2014