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Immune thrombocytopenic purpura as sole manifestation in a case of acute hepatitis A

İmmun trombositopenik purpuranın tek bulgu olduğu akut hepatit A olgusu

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Acute hepatitis due to hepatitis A virus is usually a benign self-limiting disease during childhood. Although many viral infections such as hepatitis B virus, Parvovirus, and Epstein-Barr virus are associated with extrahepatic autoimmune phenomena, such manifestations are rare in patients with acute hepatitis A infection. Immune thrombocytopenia is a benign, self-limiting disease in children, responding well to treatment and generally associated with viral infections. Immune thrombocytopenic purpura is rarely reported as a manifestation of acute hepatitis A. We report a five-year-old boy with immune thrombocytopenic purpura as the sole manifestation of anicteric acute hepatitis A infection. Acute hepatitis A should be included in the differential diagnosis of immune thrombocytopenic purpura.

Key words: Acute hepatitis A, childhood, immune thrombocytopenia, purpura

Hepatit A virüsüne bağlı akut hepatit, çocukluk çağında genellikle kendi kendini sınırlayan ve iyileşen bir hastalıktır. Hepatit B virüsü, Parvovirus, Ebstein-Barr virus enfeksiyonları gibi birçok viral enfeksiyon, ekstrahepatik otoimmun fenomenle ilişkili olmasına rağmen, akut hepatit A enfeksiyonlu hastalarda ekstrahepatik otoimmun bulgular nadirdir. İmmun trombositopeni, çocuklarda iyi seyirli, kendini sınırlayan, tedaviye iyi yanıt veren ve genellikle viral enfeksiyonlarla ilişkili bir hastalıktır. İmmun trombositopenik purpura akut hepatit A enfeksiyonu bulgusu olarak nadiren bildirilmiştir. İmmun trombositopenik purpuranın tek bulgu olduğu anikterik akut hepatit A enfeksiyonlu 5 yaşında erkek hasta sunulmuş, akut hepatit A enfeksiyonunun immun trombositopenik purpuranın ayırıcı tanısında yer alması gerektiği düşünülmüştür.

Anahtar kelimeler: Akut hepatit A, çocukluk çağı, immun trombositopeni, purpura

INTRODUCTION

Acute hepatitis A infection is generally a self-limited disease in childhood. Hepatitis A virus (HAV) infection can be inapparent, subclinical, anicteric or icteric. The likelihood of having symptoms with HAV infection is directly related to age. Most children younger than six years have asymptomatic infection or mild nonspecific symptoms with hepatitis A. Hepatitis A has several atypical manifestations including relapsing hepatitis A, cholestatic hepatitis, triggering of autoimmune hepatitis A, and extrahepatic symptoms (1). Immune thrombocytopenic purpura in children is usually a self-limiting disorder presenting most commonly with a short history of purpura and bruising. It may follow a viral infection or immunization and is caused by an inappropriate response of the immune system (2).

Transient hematologic abnormalities due to bone marrow depression in the course of HAV infection are well known (3). Several cases with thrombocytopenia following hepatitis B and C infection have been described (2). Autoimmune manifestations such as immune thrombocytopenic purpura, aplastic anemia and hemophagocytic syndrome have been rarely reported during the course of acute HAV infection (4).

We describe a five-year-old boy whose only manifestation of acute anicteric HAV infection was immune thrombocytopenic purpura.

CASE REPORT

A previously healthy five-year-old boy presented with complaints of bruises and purpuric lesions

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over his legs beginning two days prior to hospitalization. His past history did not reveal any hepatic or hematological disease. At admission the child was alert, anicteric and hemodynamically stable. Several purpuric, petechial lesions and ecchymoses on his upper and lower extremities were detected on physical examination. His liver and spleen were not palpable. Laboratory investigations revealed elevated liver enzyme levels (AST 1031 U/L, ALT 840 U/L) with normal alkaline phosphatase, gamma-glutamyl transferase, bilirubin, total protein, albumin, prothrombin time, activated partial thromboplastin time, fibrinogen and D- dimer. Complete blood cell count showed hemoglobin 11.7 g/dl, white blood cell count 6,200/mm^3 with a differential of 66% neutrophil, 30% lymphocyte, and 4% monocyte, platelet count 2,000/mm^3, and reticulocyte count 0.8%. Viral serologic studies were positive for anti-HAV IgM antibody and negative for anti-HAV IgG, hepatitis B and C, Epstein-Barr virus, cytomegalovirus, Toxoplasma, rubella, and Parvovirus B_{19}. Minimal hepatomegaly and minimal ascites were established on abdominal ultrasonography. Direct and indirect Coombs tests, antinuclear antibody, anti-dsDNA, anticardiolipin and antiphospholipid IgM and IgG antibodies were negative. Quantitative serum immunoglobulins and complement (C_3 and C_4) levels were normal. Examination of the bone marrow aspiration revealed normocellular marrow with trilineage hematopoiesis and megakaryocytic hyperplasia with many mature and immature megakaryocytes. There was no hemophagocytosis or emperipolesis. Immune thrombocytopenia due to acute hepatitis A infection was diagnosed and IVIG with a 0.8 g/kg dose was given for a day. Platelet counts returned to normal (154,000/mm^3) in 72 hours. His clinical and biochemical profiles normalized in two weeks. He developed anti-HAV IgG at the end of the 3rd week. He was well after a period of six months of outpatient follow-up.

DISCUSSION

Immune-mediated extrahepatic manifestations and hematological complications are mainly reported in adults with acute and chronic hepatitis B and C. However, they are relatively rare in acute hepatitis A (5). A variety of extrahepatic manifestations can be observed in patients with acute hepatitis A, mainly in adults. In a study including 256 patients with a median patient age of 26 years, the complications of HAV infection were reported as hemolysis, acalculous cholecystitis, acute renal failure, pleural or pericardial effusion, acute reactive arthritis, and pancreatitis, whereas no thrombocytopenia was reported in this study (6).

Thrombocytopenia may be a result of bone marrow depression, viral-associated hemophagocytic syndrome with emperipolesis, immune-mediated peripheral destruction of platelets or increased platelet consumption associated with disseminated intravascular coagulopathy (2, 7-9). Immune-mediated thrombocytopenia occurring during the course of acute hepatitis A may be related to the presence of transient anticardiolipin and antiphospholipid antibodies, anti-platelet antibodies or circulating immune complexes (4, 8-10). We could not find any evidence of hemophagocytic syndrome, disseminated intravascular coagulopathy or bone marrow suppression in our patient. No known autoantibodies were found; however, increased megakaryocytes in bone marrow aspiration and the rapid response of the platelet counts to IVIG therapy suggested an immune-mediated platelet destruction.

To our knowledge, immune thrombocytopenic purpura associated with HAV infection has been reported in four children to date. In three of them, thrombocytopenic purpura was the initial symptom. In these reports, thrombocytopenia had occurred in association with hemophagocytosis, anticardiolipin antibody positivity or cholestatic hepatitis A. The authors suggested that thrombocytopenia may be the result of viral-associated hemophagocytic syndrome with emperipolesis or immune-mediated peripheral destruction (2, 4, 11, 12).

In conclusion, immune thrombocytopenic purpura may be the only manifestation of acute hepatitis A, without other manifestations such as jaundice, vomiting and abdominal pain. The cause of thrombocytopenia-associated hepatitis A is not exactly known. Acute hepatitis A should be considered in the differential diagnosis of immune thrombocytopenic purpura in children.

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