

Response of anti-D in a Case of Immune Thrombocytopenic Purpura Secondary to Acute Hepatitis A

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Abstract

Acute hepatitis A is usually a benign and self-limiting disease. 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 (ITP) is rarely reported as a manifestation of acute hepatitis A. We report a case of four and a half years old boy with immune thrombocytopenic purpura as a manifestation of acute hepatitis A infection which responded to Anti-D. Acute hepatitis A should be included in the differential diagnosis of immune thrombocytopenic purpura.

Introduction

Acute hepatitis A infection is generally a self-limiting disease. 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 manifestations.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 case of 4.5-year-old boy presenting with immune thrombocytopenic purpura secondary to acute HAV

infection which responded to anti-D.

Case Report

A previously healthy four and a half years-old boy presented with complaints of bruises and purpuric rash over his legs for previous two days. His past history did not reveal any hepatic or hematological disease. At presentation the patient was alert, icteric and hemodynamically stable. On physical examination several purpuric, petechial and ecchymotic lesions were observed on his face, abdomen, and upper as well as lower extremities. His liver was palpable 6 cm below costal margin and was tender and spleen was not palpable. Laboratory investigations revealed elevated liver enzyme levels (AST 805 U/L; ALT 1507 U/L), serum bilirubin 1.8 mg/dl with normal alkaline phosphatase, total protein, albumin, prothrombin time, and activated partial thromboplastin time. Complete blood cell count showed hemoglobin 11.1 g/dl, white cell count $7.3 \times 10^9/l$ with a differential of 43% neutrophil, 53% lymphocyte, and 4% monocyte. Platelet count was $18 \times 10^9/l$, and reticulocyte count was 1.2%. Viral serologic studies were positive for anti-HAV IgM antibody and negative for anti-HAV IgG, hepatitis B and C. Examination of the bone marrow aspiration revealed normocellular marrow showing megakaryocytic hyperplasia with left shift. Erythroid and myeloid cell lines were normal and there were no abnormal cells. Based on bone marrow findings diagnosis was thrombocytopenia due to excessive peripheral platelet destruction (ITP). So the final diagnosis, Immune thrombocytopenia following acute hepatitis A infection was made and IV anti D with a 50µg/kg dose was given. Platelet counts increased to 50,000/mm³ in 72 hours. Only side-effect reported was decreased Hb level to 9.1 gm/dl. His clinical and biochemical profiles normalized in 10 days (his Hb returned to 11.5 gm/dl with platelet count to $285 \times 10^9/l$).

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 of 256 patients with a median 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, immune-mediated peripheral destruction of platelets or increased platelet consumption associated with disseminated intravascular coagulopathy.^{2, 7} Increased megakaryocytes in bone marrow aspiration and the rapid response of the platelet counts to Anti-D therapy in our patient suggested an immune-mediated platelet destruction. To our knowledge, immune thrombocytopenic purpura associated with HAV infection has been reported in only few children to date. In three of them, thrombocytopenic purpura was the initial symptom. The authors suggested that thrombocytopenia may be the result of viral-associated or immune-mediated peripheral destruction.^{8,9}

There is no consensus on the criteria of response to anti-D therapy in ITP. Bussel et al defined a response as a rise in platelet count of more than 20,000/ml.¹⁰ Salama et al observed a rise in platelet count following administration of anti-D in patient of ITP.¹¹ Anti-D therapy has been given to Rh positive healthy volunteers and inadvertently to neonates without any side effects.¹² Mechanism of action of Anti-D in ITP is not fully understood. Blockade of Fc receptors of the monocyte-macrophage system by anti-D is one of the possible mechanisms. Studies have found that anti-D is at least as good as IVIG with respect to magnitude and frequency of effect, but IVIG is associated with higher cost and prolonged infusion times.¹³ It is suggested that larger studies are essential to study the effect of anti-D in ITP. Such studies are of great relevance to our country, as the cost of anti-D therapy is less than 10% that of IVIG therapy.¹⁴

In conclusion, immune thrombocytopenic purpura may be one of manifestations of acute hepatitis A. 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 and anti-D is the cost effective treatment option for such cases.

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