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CASE REPORT

Use of steroids for prolonged cholestasis secondary to acute hepatitis A infection

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ABSTRACT

Hepatit A is usually a self-limited, asymptomatic infection. However, severe manifestations of hepatitis may occur rarely in adult patients. Here, we present a case of prolonged, relapsed cholestasis secondary to acute hepatitis infection in an adult patient. A 25-year old male patient had been given symptomatic treatment for weakness, abdominal pain, loss of appetite, pruritis, nausea and generalized jaundice. A week later, he had been diagnosed with acute hepatitis A infection. He admitted to our clinic two months after the first episode with complaints of pruritis and jaundice. His laboratory results included a serum alanine aminotransferase (ALT) level of 86 U/L, aspartate transferase (AST) of 91 U/L, total bilirubin of 46.5 mg/dl and direct bilirubin of 33.9 mg/dl. ursodeoxycholic acid (UDCA) therapy was started due to protracted jaundice, severe itching and a marked elevation in bilirubin levels, which was replaced with prednisolone therapy at a dose of 1 mg/kg/day at 12 days. Most of his clinical symptoms resolved with much lower serum bilirubin levels. No clinical or biochemical deterioration was observed after discontinuation of therapy. One year later his general condition was good with no relapse. There are few case reports in literature about the use of corticosteroids for treatment of prolonged cholestatic jaundice in patients with hepatitis A infection. Based on our findings, we suggest that this type of therapy may be beneficial for relief of symptoms and improvement of serum biochemistry. *J Microbiol Infect Dis 2014; 4(4): 162-164*

Key words: Hepatitis A, prolonged cholestatic hepatitis, hyperbilirubinemia, corticosteroids

Uzamış kolestazı olan akut hepatit A enfeksiyonunda steroid kullanımı

ÖZET

Hepatit A kendi kendini sınırlayan, genellikle asemptomatik seyreden bir enfeksiyondur. Nadiren bazı erişkin olgularda ağır hepatit tablosu görülebilir. Burada tekrarlayan ve uzun sure kolestatik formla seyreden bir olgu sunuldu. Yirmi beş yaşında erkek hasta halsizlik, karın ağrısı, bulantı ve tüm vücutta sararma yakınmaları ile başvurdu. Başvurmadan önce semptomatik tedaviler almış ve bir hafta sonra akut hepatit A tanısı konulmuştu. İlk ataktan iki ay sonra hastanın tekrar kaşıntı ve sarılık şikayeti olduğu için bize başvurmuştu.

Başvuruda serum alanin aminoasit transferaz (ALT):86 U/L, aspartat transferaz (AST):91 U/L, T. Bil:46,5 mg/dl, D. Bil:33.86 mg/dl' idi. Uzun süren sarılık, yoğun kaşıntı ve bilirübin seviyelerinde artma nedeniyle ursodeoxycholic acid (UDCA) tedavisi verildi. Daha sonra tedavi 1 mg/kg/gün prednisolon tedavisiyle değiştirildi. Klinik semptomların çoğu kayboldu ve bilirübin düzeyleri düştü. Bir yıllık takibinde relaps görülmedi. Literatürde kortikosteroit kullanılan uzamış kolestatik tipte sarılıkla seyreden az miktarda hepatit A olguları bulunmaktadır. Bunun, bizim olgumuzda olduğu gibi semptomları giderici ve serum biyokimya değerlerini iyileştirici etkisi olduğu düşünülmektedir.

Anahtar kelimeler: Hepatit A, uzamış kolestatik hepatit, hiperbilirübini, kortikosteroitler

INTRODUCTION

Hepatitis A virus (HAV) is a member of the picornaviridae family and the most common cause of viral hepatitis cases worldwide.[1] Globally, about 1.5 million new cases of HAV infection occur each year but the true incidence is estimated to be 10-fold greater.[2] HAV infection exhibits three different patterns of endemicity (high, intermediate and low) based on its incidence. Our country has an intermediate endemicity level.[3] HAV usually causes self-limiting,

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asymptomatic, subclinical infections in chidlhood, whereas the clinical spectrum in the adult age group ranges from mild, anicteric form to fulminant hepatitis.[4,5] Atypical HAV infections occur in approximately 7% of cases and three forms of hepatitis A were identified including prolonged cholestatic, relapsing and fulminant forms. Prolonged cholestatic form is characterized by persistently elevated bilirubin levels for more than eight weeks above 15 mg/dl as well as itching, fatigue, diarrhea and weight loss.[6] Here, we present a case of prolonged, relapsing cholestatic form of hepatitis A infection in an adult patient who failed to show clinical response to initial adjuvant therapy but successfully treated with methylprednisolone.

CASE REPORT

A 25-year old male patient had visited a physician while he was in Afghanistan about four months ago due to complaints of malaise, abdominal discomfort, nausea and generalized jaundice and received therapy. Subsequently, he had admitted to a hospital in Izmir for his persistent, unrelenting symptoms. He had been hospitalized following diagnosis of acute hepatitis A and discharged upon normalization of his liver function tests with a recommendation to return for follow-up visits at the outpatient clinic. However, one month after his discharge, he was referred to our clinic due to elevated bilirubin values. On admission, he had generalized itching and jaundice. There were no remarkable characteristics in his personal and family histories. Laboratory work-up showed: hemoglobin: 12.9 g/dL, leukocyte count: 6250 /mm3 (61.8% neutrophils, 22.7% lymphocytes, 10.1% monocytes, 4.6% eosinophils), platelet count: 356.000/mm3, AST: 91 U/L, ALT:86 U/L, GGT: 28 U/L, ALP:233 U/L, total bilirubin: 46.5 mg/dl, direct bilirubin: 33.86 mg/dl, indirect bilirubin:12.64 mg/dl, PT:13.6 sec, INR:1.2, APPT:28.7 sec, urinary urobilinogen 24 g/dl and bilirubin 13 g/dl. Abdominal ultrasonography examination showed no pathology. Indirect and direct Coombs' tests were negative. Serologic assays showed: HAV-IgM positive, HAV-IgG positive, HBsAg negative, Anti-HBs negative, AntiHBc-total negative, Anti-HCV negative, Anti-HEV IgG negative, CMV IgM negative, CMV IgG positive, EBV-VCA IgM negative, EBV-VCA IgG positive. Autoimmune liver disease panel revealed no pathology. His initial treatment regimen included N-aceytlcysteine ampoules (1 ampoule given via a one-hour infusion), ursodeoxycholic acid capsules (3x1), lactulose suspension (3x1/2 measuring cups). His bilirubin levels ranged between 45 and 50 mg/dL and on the fifth day of hospitalization, INR value increased from 1.2 to 1.8 which required addition of Vitamin K for 3 days. Subsequently, INR values returned to normal. Ursodeoxycholic treatment was stopped and Prednisolone at a dose of 1 mg/kg was added to his treatment regimen on Day 13 of hospitalization (approximately 75 days after reoccurrence of his symptoms) due to persistently elevated bilirubin levels. On the third day of this therapy, blood bilirubin level fell to 34.35 mg/dL and continued to decrease in the following days. Prednisolone dosage was gradually tapered beginning from the fifth day and discontinued at Day 50 when bilirubin levels were completely normal. All of his clinical and laboratory findings were normal at the one- year follow-up.

DISCUSSION

While hepatitis A virus infections are common in developing countries, they rarely occur and cause epidemics in developed countries depending on variable conditions of tourism and migration. Hepatitis A disease may manifest itself in clinical and subclinical forms depending on age and cases of prolonged, relapsing or cholestatic hepatitis were reported at a global incidence of 5-10% in literature.[5]

The cholestatic form of hepatitis A was first identified in 1984 in a patient who presented with cholestasis accompanied by severe pruritis, diarrhea and weight loss and was treated successfully with corticosteroid therapy without any sequelae. Since then, cholestatic form which is defined as a variant of acute hepatitis A was reported in 10% of symptomatic patients as isolated cases or in small case series.[7-9] However, there is one report in literature concerning a case of hepatic necrosis and persistently elevated transaminase levels despite use of corticosteroid therapy.

Our patient represents a typical case of hepatitis A with normalization of transaminase and bilirubin levels and clinical recovery following acute hepatitis A infection. However, at the end of one month, he presented with the cholestatic form of the disease which was associated with moderate elevation of transaminases, severe abdominal pain and significantly elevated bilirubin levels. In literature, cases of cholestatic hepatitis A infections have been reported to occur particularly during the second clinical phase of relapsing hepatitis A disease, as in our case.[5,10]

Concurrent cholestasis in the setting of a clinical hepatitis A infection is the result of an inflam-

matory process. Excessive secretion of systemic and intrahepatic endotoxins as well as cytokines including TNF-alpha and IL-1 were implicated. Additionally, the synthesis of a transporter protein, multidrug resistance-associated protein 2 (mrp2) was reported to be inhibited during this process; mrp2 is responsible for excretion of bilirubin out of hepatocytes during bilurubin metabolism. In literature, treatment of patients with cholestatic form of hepatitis A using corticosteroids has been described in case reports. Experimental studies on animals have shown that corticosteroids provide beneficial effects by inhibiting synthesis of inflammatory cytokines and improving actions of mrp2.[11,12]

For our patient, use of corticosteroid was deemed necessary due to a significantly elevated level (48 mg/dL) of total bilirubin (direct bilirubin 33.86 mg/dL) before steroid treatment, persistence of bilirubin elevations and particularly the presence of severe itching. It is interesting to note that Yoon et al. reported three patients who started treatment with oral prednisolone at a dose of 30 mg/day despite having much lower levels of direct bilirubin (19, 27 and 31 mg/dL, respectively). In that study, patients were given steroid therapy with gradually reduced doses for variable durations (8 to 12 weeks). For all of the three patients, direct bilirubin started to fall through the end of one week showed a marked decrease (10 mg/dl reduction weekly) at 2-3 weeks. Direct bilirubin fell from 48 mg/dL to 17 mg/dL within seven days and clinical symptoms showed a considerable improvement within 4-5 days in our patients. Yoon et al. suggested that administration of a higher dose of prednisolone (1 mg/kg) might have resulted in a more rapid decrease in bilirubin. Prednisolone therapy was administered for 10 weeks to our patient and was not associated with any clinical or biochemical deterioration during or after that period.

In this report, we presented a patient with cholestatic hepatitis A infection who had very high direct bilirubin levels and was successfully treated with prednisolone. The value of corticosteroids in the treatment of hepatitis is controversial. Steroid therapy was reported to provide no improvement in the clinical manifestations of viral hepatitis among 77 patients with acute hepatitis.[11,13]

In conclusion, spontaneous clinical improvement was reported in some cases with cholestatic form of the disease.[4] However, use of corticosteroids may provide rapid correction of clinical manifestations in selected non-immunocompromised patients presenting with very severe symptoms associated with cholestasis or relapsing patients with prolonged cholestatic form of the disease under close supervision.

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