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Pegylated interferon treatment of acute pericarditis associated with acute hepatitis C

Akut hepatit C'ye eşlik eden akut perikarditin pegile interferon ile tedavisi

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A 65-year-old female patient was admitted to our hospital with the symptoms of chest pain, dyspnea and fatigue. She had undergone a tooth extraction three months before. She took no medication. Echocardiography revealed pericardial effusion. The serum alanine aminotransferase (ALT) at presentation was 650 IU/L and aspartate aminotransferase (AST) was 600 IU/L. Hepatitis C virus (HCV) RNA level was 150,000 IU/ml. Genotype was 1b. Acute pericarditis was considered to be caused by acute HCV infection. The patient was followed without treatment. One month later, AST and ALT were found as 65 IU/L and 82 IU/L, respectively; there were symptoms of effort dyspnea and fatigue. Echocardiography showed minimal decrease in pericardial effusion compared to one month previously. HCV RNA level was again checked and found as 155,000 IU/ml. The patient was given pegylated interferon. One month later, the pericardial effusion and related symptoms had disappeared. The pegylated interferon treatment was sustained for 24 weeks and HCV-RNA was found negative at the 3rd and 6th months of the treatment and six months after the end of treatment. We conclude that pegylated interferon may be offered to patients with symptomatic acute HCV-related pericarditis.

Key words: Acute hepatitis C, acute pericarditis, pegylated interferon

Altmışbeş yaşında bayan hasta göğüs ağrısı, dispne ve yorgunluk şikayetleriyle kliniğimize başvurdu. Hikayesinde başvurudan 3 ay önce diş çekimi hikayesi vardı. Hastanın herhangi bir ilaç kullanımı yoktu. Ekokardiyografide perikardiyal effüzyon saptandı. İlk değerlendirmede alanin aminotrasferaz (ALT) düzeyi 650 IU/L, aspartat aminotransferaz (AST) düzeyi ise 600 IU/L saptandı. Hepatit C virüsü (HCV) RNA'sının kantitatif değeri 150.000 IU/mL bulundu. HCV'nün genotipi 1b idi. Akut perikardite sebep olan etiyolojik faktör olarak akut HCV infeksiyonu düşünüldü. Hasta tedavisiz izleme alındı. Takibin 1. ayında, AST ve ALT düzeyleri sırasıyla 65 IU/L ve 82 IU/L olarak bulundu. Hastanın efor dispnesi ve halsizlik şikayetleri devam etmekteydi. Kontrol ekokardiyografide perikardiyal efüzyonda minimal azalma mevcuttu. HCV RNA düzeyine tekrar bakıldı ve 155.000 IU/L bulundu. Hastaya pegile interferon tedavisi başlandı. Tedavinin 1. ayında yapılan kontrolde perikardiyal efüzyonun ve ilgili semptomların kaybolduğu görüldü. Pegile interferon tedavisine 24 hafta devam edildi. Tedavinin 3., 6. aylarında ve tedavi bitiminden 6 ay sonra yapılan kontrollerde HCV RNA düzeyleri negatif bulundu. Sonuç olarak, akut HCV infeksiyonuna sekonder gelişen semptomatik akut perikarditin tedavisinde pegile interferon kullanılabilir.

Anahtar kelimeler: Akut hepatit C, akut perikardit, pegile interferon

INTRODUCTION

Acute hepatitis C virus (HCV) infection is a rare cause of acute pericarditis. Infections are believed to account for the majority of pericarditis cases. Most cases of acute pericarditis are viral or idiopathic and self-limited; however, other etiologies should also be considered (1). Acute pericarditis has many possible causes (2), including bacterial infection, myocardial infarction, trauma, malignancy, uremia, hypothyroidism, collagen vascular disease, and the effects of certain drugs, notably hydralazine and procainamide. Autoimmunity covers an important part in the findings of HCV infection. Serological markers of autoimmunity, especially rheumatoid factor, smooth muscle antibodies (SMA) and antinuclear antibodies, are present in approximately 90% of patients infected with HCV (3).

The challenge in the treatment of acute HCV infection is deciding whether the initiation of

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antiviral treatment should be immediate or can be delayed. Analysis of the acute course of HCV infection has demonstrated that a spontaneous clearance of HCV RNA can occur within 2-3 months (4). Thus, treating these patients within 2-3 months may cause high therapeutic costs and unnecessarily put them at risk for adverse events. The indications for early treatment of acute HCV infection remain unknown at present.

In this paper, we report a case with acute HCV-associated pericarditis in whom resolution of pericarditis-related symptoms and findings was achieved with pegylated interferon (peg-IFN) alfa-2a.

CASE REPORT

In January 2006, a 65-year-old female patient presented with chest pain, dyspnea and fatigue. Physical examination revealed decreased heart sounds. She had a history of tooth extraction three months before. The patient was a housewife. She did not smoke, drink alcohol, or use illicit drugs. Serology for hepatitis A, B and C, acute infection of cytomegalovirus, herpes simplex virus, Epstein-Barr virus and toxoplasma was negative. Hepatitis C virus RNA by means of polymerase chain reaction was 150,000 IU/ml. Genotype was 1b. Standard blood tests including hemogram, serum ferritin, ceruloplasmin, and coagulation tests as well as serum protein electrophoresis and albumin were within normal limits, except for aspartate aminotransferase (AST) 600 IU/L and alanine aminotransferase (ALT) 650 IU/L. Thyroid function was normal and tuberculin test was negative. Antinuclear antibodies, SMA, antibodies to liver/kidney microsome type 1 and soluble liver antigen were found negative. Electrocardiography (ECG) was normal. The chest radiography showed an enlarged cardiac silhouette. Echocardiography showed pericardial effusion with no tamponade. Diagnostic pericardiocentesis was performed, but HCV RNA was found negative in the pericardial fluid. Acute pericarditis associated with acute HCV infection was diagnosed. Ibuprofen was given to the patient for symptomatic relief.

In February 2006, AST and ALT were found as 65 IU/L and 82 IU/L, respectively. The patient was free of pain but dyspnea and fatigue and pericardial effusion in echocardiography persisted. HCV RNA load was checked again and found as 155,000 IU/ml. The patient was given peg-IFN alfa-2a at a dose of 180 μg once a week.

In March 2006, echocardiography revealed no pericardial effusion and pericarditis-related symptoms had disappeared.

The peg-IFN alfa-2a treatment was sustained for 24 weeks and HCV-RNA was determined to be negative at the 3rd and 6th months of the treatment in the follow-up period. In addition, the patient had sustained HCV RNA negativity six months after the end of treatment.

DISCUSSION

We have reported a case of acute pericarditis caused by acute HCV infection in a female patient. After the diagnosis of acute pericarditis, the clinical and laboratory evaluations were committed to excluding other possible etiological factors causing acute pericarditis. The clinical course was not consistent with bacterial infection. Laboratory values regarding the thyroid and renal functions were normal. ECG was normal. The patient history was unremarkable for trauma or drug use causing pericarditis. Pericardiocentesis revealed no specific findings about bacterial, malignant or fungal etiology. Due to elevations in the transaminase levels up to 15 times normal, viral hepatitis was suspected. The positive value of HCV RNA with the elevated hepatic transaminase levels and the history of tooth extraction three months before led us to the diagnosis of acute pericarditis associated with acute HCV infection.

The possible mechanism for causing pericarditis may be related to direct or indirect effects of acute HCV infection. Invasion of the pericardium by HCV may result in acute pericarditis. Based on this theory, pericardial fluid was investigated for the presence of HCV RNA genome and found negative, which may be explained by two possible mechanisms: The low HCV load in the pericardial fluid and the presence of autoimmune associated-pericarditis. Due to association of HCV infection with autoimmune phenomena (5), a possible indirect mechanism for the complication of pericarditis may be autoimmunity. Although no antibody was found positive in the laboratory evaluation, unknown antibodies may play a role in the pathogenesis of pericarditis.

What are the mechanisms for HCV to induce autoimmunity? Potential mechanisms include viral-induced changes in self-antigen expression, molecular mimicry, alterations in the idiotypic network, formation of heat shock proteins, and induction of major histocompatibility complex antigens on nonimmune cells (6). Autoimmunity

may be induced in patients with HCV due to genetic risk factors (7).

An interesting point of this case was the finding of a normal ECG. It has been reported that neither ST nor PR deviations were found in patients with hypothyroidism and renal failure (7).

Indeed, classic uremic pericarditis is unique. Despite even life-threatening inflammatory effusions and intrapericardial hemorrhage, the ECG does not change, since even a brisk uremic intrapericardial inflammation does not penetrate the myocardium (8). Based on these explanations, the normal ECG finding was unexpected for this patient. HCV core and nonstructural 3 proteins activate inflammatory pathways via toll-like receptors that may affect viral recognition and contribute to activation of the innate immune system (9). Any deterioration by mutation or unknown factors in those steps including in the way of HCV entry and inflammatory response of the host may reduce inflammation and result in normal ECG in patients with acute HCV infection and acute pericarditis.

Most patients with idiopathic pericarditis can be managed conservatively with a non-steroidal anti-inflammatory drug (NSAID) or acetylsalicylic acid. These agents are believed to be equally effective, and the literature does not indicate a NSAID of choice for pericarditis. Patients who do not respond to the NSAID may need a short course of a corticosteroid, usually prednisone in a dosage of 5 to 10 mg per day for one to two weeks (10). We waited one month in order to allow for the opportunity of spontaneous recovery from acute HCV infection. Although the transaminase levels decreased, the patient's symptoms and pericardial effusion persisted. In order to verify the ongoing acute HCV infection, viral load was again checked and determined as 155,000 IU/ml. Peg-IFN alfa-2a at a dose of 180 μg once a week was started. One month after the start of the treatment, pericardial effusion and symptoms of the patient had disappeared and transaminase levels returned to normal. To our knowledge, this is the first case of acute HCV infection-associated pericarditis treated with peg-IFN alfa-2a.

There is no randomized trial comparing immediate versus delayed acute HCV infection therapy in the literature. The analysis of the acute HCV infection revealed that 10% to 50% of patients with acute hepatitis C may clear the infection spontaneously (11). There are no reliable markers that help to predict which patients would recover from the acute HCV infection or develop chronic HCV infection. Thus, in the early treatment, overtreatment is always a risk in the absence of trustworthy predictive factors for the natural course of the disease. In our case, the primary standpoint for the early therapy was to treat the patient for the presence of acute pericarditis associated with acute HCV infection. The patient had clinical and laboratory improvement in pericarditis in the first month of the treatment. In addition, the patient had biochemical and virological response after three months of follow-up and at the end of the treatment.

In conclusion, acute HCV infection is a rare cause of acute pericarditis. In patients with acute pericarditis, transaminase levels must be monitored and acute HCV infection should be suspected in the event of increases, especially to levels more than 10 times normal. Patients with acute HCV infection-associated acute pericarditis may present with normal ECG. Peg-IFN alfa-2a may be offered to the patients with symptomatic acute pericarditis associated with acute HCV infection without considering the starting time of treatment.

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