



Hepatitis-A Virus Induced Acute Myocarditis

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The viral myocarditis is the most common cause of heart failure in previously healthy children. We herewith present an adolescent girl admitted with acute myocarditis findings, heart failure and arrhythmia. Cardiological studies verified the diagnosis and patient received intravenous immunoglobuline solution in addition to supportive therapy. Her clinical picture was finally attributed to unicteric hepatitis A virus infection.

Keywords: Viral myocarditis, Hepatitis A, Intravenous immunoglobuline

Hepatit A Enfeksiyonu Sonucu Gelişen Miyokardit

Sağlıklı çocuklarda kalp yetersizliğinin en sık sebebi viral miyokarditlerdir. Yazımızda kliniğimize kalp yetersizliği, aritmi bulguları ve akut miyokardit tablosu ile başvuran bir adölesan kız vakayı sunmak istedik. Kardiyolojik testlerin akut miyokardit tanısını doğrulaması üzerine, hastaya destekleyici tedaviye ek olarak intravenöz immunglobulin uygulandı. İleri tetkiklerde hastanın klinik tablosunun altında sarılık gelişmeden gerçekleşen hepatit A enfeksiyonu olduğu tespit edildi.

Anahtar Kelimeler: Viral miyokardit, Hepatit A, İntravenöz immunoglobulin

Myocarditis is an inflammatory process that primarily involves the myocytes,¹ and can be a manifestation of severe infection caused by almost any infectious agent. The viral myocarditis is the most common cause of heart failure in previously healthy children and adolescents.² The majority of the myocarditis cases have viral etiology. Clinical expression of acute myocarditis (AM) ranges from inapparent disease to fulminant cardiac failure with rhythm abnormalities. Hepatotropic viruses rarely cause AM. We herewith present an adolescent girl admitted with myocarditis findings, including heart failure and arrhythmia, and finally attributed to asymptomatic hepatitis A virus (HAV) infection.

CASE REPORT

A fourteen years old girl was referred because of malaise, nausea, vomiting, fever and mild diarrhea for the last week. She had received empirical ceftriaxone therapy for 3 doses in a district hospital. The worsening nausea, vomiting and hypotension caused her transfer to our tertiary-care teaching hospital. On admission, physical examination revealed mild fever (37,9°C), tachycardia (123/min), hypotension (84/34 mm Hg), 2/6 systolic murmur on the left sternal border, diminished respiratory sounds on both basal lung sides, 1 cm palpable liver, and mild pretibial edema. Her skin and neurological examinations were within normal range. Laboratory examination showed mild anemia (Hb: 10,4 gr/dl), increased leukocyte count (16,500/mm³ with PMNL predominance) and normal thrombocyte count. Erythrocyte sedimentation rate was 120 mm/hr, and CRP was 6,5 mg/dl (0-5mg/dl). Urine analysis showed 5 WBCs and 33 RBCs per high-resolution field. Her biochemistry tests showed mild azotemia (BUN 49, kreatinin 1,3 mg/dl); but liver function tests, CPK-MB and bilirubin levels were within normal range. Plain chest radiography revealed mild cardiomegaly (CTI:0,54), pulmonary venous congestion and minimal bilateral pleural effusion. The electrocardiogram (ECG) showed sinus tachycardia at a rate of 112/minute with widened QRS complexes (110 msec), inverted T waves on precordial leads, flattened T waves on limb leads. A 24 hour Holter monitoring showed

frequent unifocal ventricular extrasystoles without ventricular tachycardia and couplet beats. Echocardiography showed a dilated left ventricle with poor contractility (LVEDD 52 mm; LVEF 56 %) which were suggestive of mild cardiomyopathy. A presumptive diagnosis of viral myocarditis was entertained. Inotropic agents, diuretics were commenced, and the patient received high-dose intravenous immunoglobulin (IVIG), as well. After obtaining cultures, the ceftriaxone therapy was continued as she had fever, leukocytes in urine analysis and increased infection parameters. Dopamine and dobutamine therapy was tapered as her blood pressure levels recovered within 4 days. Renal parameters and liver function tests were within normal range after 5 days. No pathological organisms were isolated from blood, urine and stool cultures. Second urine analysis showed no leukocytes, and ceftriaxone was discontinued after 6 days. Serological tests for Rubella, Mumps, Brucella, Salmonella, HBV, HCV, HIV, EBV and CMV were negative, but anti-HAV IgM and IgG were positive. The second echocardiographic evaluation before discharge revealed improvement of left ventricular contractility. Twenty days after discharge, the second serological testing showed positive anti-HAV IgG but negative anti-HAV IgM. The last echocardiogram showed normal ventricular function (LVEDD 47 mm, LVEF 69 %), and the ECG findings were also within normal limits.

DISCUSSION

The spectrum of AM includes asymptomatic patients who may have only electrocardiographic abnormalities; patients with signs and symptoms of clinical heart failure and ventricular dilatation; and patients with symptoms of fulminant heart failure and severe left ventricular dysfunction, with or without cardiac dilatation.³ The incidence of myocarditis is elusive as AM is frequently asymptomatic and self-limited. Data from autopsies report that 6–21% of children with sudden death had myocarditis.²

Enteroviruses, especially coxsackievirus B serotypes 1 to 5, are implicated up to 40% of all pediatric AM and dilated cardiomyopathy (DCM)⁵. The peak season for AM, the spring and summer months, coincides with peak activity of enteroviruses. The majority of the remaining cases are due to viral etiology⁶; cytomegalovirus, echovirus, Epstein-Barr, herpes simplex, human immunodeficiency, influenza A and B, measles, mumps, parvovirus, rubella, and etc. The incidence of AM related to other organisms,

bacterial, spirochetal, fungal, protozoal, parasitic, rickettsial, is relatively low. There are very rare reports of AM caused by hepatotropic viruses, hepatitis A and C virus.

Enteroviruses and HAV both belong to family Picornoviridae, and similarly transmitted by the fecal-oral route. HAV infection course can be inapparent, subclinical, anicteric or icteric. Children younger than 6 years often have asymptomatic infection or mild nonspecific symptoms, and only 10% have jaundice. However, 76% to 97% have symptoms when infected with HAV, and 40-70% of patients with symptoms are icteric. Although HAV infection has usually a self-limited course, complications are occasionally observed. Fulminant hepatitis is the most devastating picture. Other complications are, while rare, cholestatic or relapsing hepatitis, pancreatitis, acute renal failure and rashes. Myocarditis and ventricular arrhythmias are infrequently reported in the literature.

Viral cultures of the nasopharynx and stool, virus-specific IgM titer or 4-fold rise in IgG titers may suggest recent viral infection, but do not definitively establish causation in AM. The endomyocardial biopsy remains the gold standard for the diagnosis, particularly for staging and prognosis. We did not perform the invasive cardiac biopsy since the patient responded well to supportive therapy. On the other hand, its limited sensitivity and specificity⁷ suggest that the diagnosis of myocarditis should not be based on histologic findings alone. Our patient had anti-HAV IgM and IgG positivity in acute stage and resolution of anti-HAV IgM after 20 days, indicating that she was diagnosed on convalescent phase of infection.

The mainstay of management for AM patients is supportive. Although viruses may be responsible for some forms of acute myocarditis, studies in animals suggest that persistent inflammation may instead be mediated by autoimmune mechanisms. The long-term consequences of AM appear to be related to the activation of cellular and humoral autoimmunity. That's why many clinicians believe that immunosuppression should be beneficial in patients with myocarditis. The Myocarditis Treatment Trial failed to show significant improvements in ventricular function or survival with prednisone, azathioprine or cyclosporin.⁸

The intravenous immune globulin (IVIG) therapy has immunomodulatory and anti-inflammatory effects that render it a valuable agent in the treatment of

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several autoimmune or inflammatory disorders. By the help of various mechanisms, IVIG remove autoimmune antibodies, down-regulates immune activation and neutralizes viral antigens. Controlled IVIG trials in viral-specific AM have not been conducted yet. The results of a recent randomized, placebo-controlled trial studying the use of IVIG in AM and DCM have failed to demonstrate beneficial effects of immunosuppression in general population.⁹ On the other hand, Drucker et al showed that IVIG caused marked improvement in left ventricular performance in pediatric AM patients¹⁰. Our patient showed improvement in cardiac functions upon receiving IVIG therapy which is well-tolerated in infants and children unlike adults. Taken together, the use of IVIG may be promising in the management of viral-mediated pediatric AM cases.

Inactivated HAV vaccines were studied extensively above 2 years of age. Vaccination should be recommended for all young children living in endemic areas. Nevertheless, large community-wide outbreaks of hepatitis A continue to occur throughout not only developing countries but also developed nations, i.e., United States, with consequent disruption, hospitalizations, and deaths. Although it is not current policy, the universal vaccination of children should be implemented, with catch-up immunization for all older children through adolescence, to minimize the complications of HAV infection.

As a result, HAV infection occasionally results in complications, yet severe. Myocarditis incidence may be underestimated during HAV infection because of self-limited nature in childhood period. Vaccination against HAV should be encouraged worldwide.

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