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Transient sinus bradycardia in a child during the course of acute hepatitis A

Çocukluk çağında akut hepatit A seyri sırasında görülen geçici sinüsal bradikardi

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Cardiovascular complications in acute hepatitis A are reported rarely. In this report, we describe a case of a previously healthy girl who developed transient sinus bradycardia during the course of acute hepatitis A.

Key words: Sinus bradycardia, acute hepatitis A, childhood

Akut hepatit A enfeksiyonunun kardiyovasküler komplikasyonları nadiren bildirilmiştir. Bu yazıda daha önceden sağlıklı olan ve akut hepatit A enfeksiyonunun seyri sırasında geçici sinüzal bradikardi gelişen bir kız çocuk olgu sunulmuştur.

Anahtar kelimeler: Sinüzal bradikardi, akut hepatit A, çocukluk çağı

INTRODUCTION

Cardiovascular complications in viral hepatitis occur rarely. Cases of hypotension and dysrhythmias associated with viral hepatitis have been reported, but most were described before the advent of specific viral markers (1). Bradycardia can be seen in diseases that are associated with profound hyperbilirubinemia; however, it has been reported very rarely during the course of acute viral hepatitis (2). We report a case of a previously healthy child who developed sinus bradycardia during the course of acute hepatitis A.

CASE REPORT

A previously healthy nine-year-old girl presented with a three-day history of abdominal pain and vomiting. She had scleral icterus alone and other physical examination findings were normal. She was hospitalized because she could not tolerate oral feedings. On admission, her pulse rate was regular, 92 beats/min, and blood pressure was 100/60 mmHg. Complete blood cell count showed hemoglobin, 14.1 g/dl, white blood cell count, 4900/mm^3, with a differential of 46% neutrophils, 44% lymphocytes, 10% monocytes, and platelet count 285,000/mm^3. Results of initial biochemical and coagulation tests included total bilirubin 3.36 mg/dl, direct bilirubin 1.78 mg/dl, aspartate aminotransferase (AST) 5408 U/L (normal 0-47 U/L), alanine aminotransferase (ALT) 4569 U/L (normal 0-39 U/L), alkaline phosphatase (ALP) 821 U/L (normal < 720 U/L), gamma-glutamyl transferase (GGT) 109 U/L (normal 0-23 U/L), lactic dehydrogenase (LDH) 4405 U/L (normal 370-440 U/L), glucose 85 mg/dl, total protein 6.32 g/L, albumin 3.43 g/L, prothrombin time (PT) 26.3 sec (normal 10-14 sec), and partial thromboplastin time (PTT) 47.9 sec (normal 25-39 sec). She was managed as probable liver failure according to increased serum bilirubin, prolonged PT and borderline hypoalbuminemia findings. PT and PTT returned to normal after three days of treatment with vitamin K. Viral serologic studies were positive for anti-HAV IgM antibody and negative for anti-HAV IgG and hepatitis B and C with enzyme immunoassay method.

On the third day of her admission, bradycardia was detected by physical examination. There was a sinus rhythm with a pulse rate of 50/min on the

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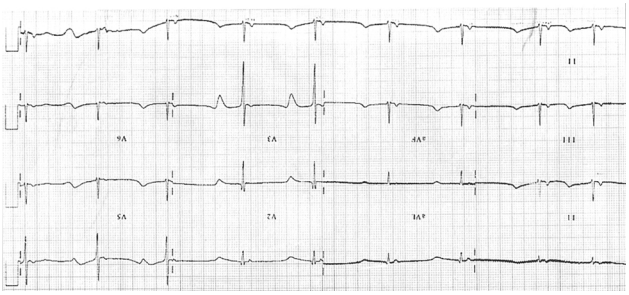

Figure 1. Electrocardiogram demonstrating sinus bradycardia in the patient with acute hepatitis A

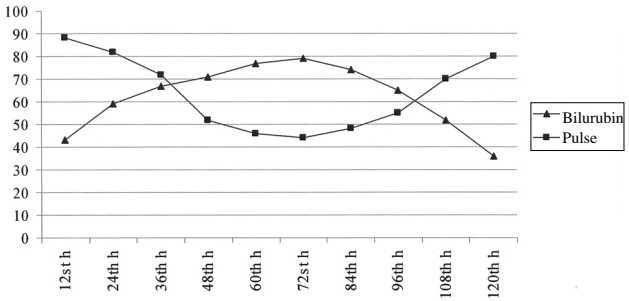

Figure 2. Relationship between bilirubin levels and heart rate in the patient with acute hepatitis A
(Note: The bilirubin levels are multiplied by 10 on the graph.)

electrocardiogram (Figure 1). Her blood pressure and echocardiographic examination were normal. Abdominal ultrasonographic examination showed increased gallbladder echogenicity and bile duct wall thickness. The results of the biochemical tests on the third day of the admission were as follows: AST 1615 U/L, ALT 2930 U/L, ALP 931 U/L, total bilirubin 6.74 mg/dl, direct bilirubin 3.64 mg/dl, GGT 171 U/L, serum ammonia level 44 µmol/L (normal 14.7-55.3 µmol/L) and serum bile acid level 490 µmol/L (normal 0-14 µmol/L). General status of the patient was good and there were no signs of hepatic encephalopathy or increased intracranial pressure such as headache, blurring of vision or papilledema. Thyroid hormone levels were within normal ranges. Her peak total and direct bilirubin levels during the course of her illness were 7.7 mg/dl and 4.06 respectively, while her heart rate fell to 44 beats/min. Bilirubin levels and heart rates during the course of her illness are demonstrated in Figure 2. Bradycardia continued for four days without any symptom and resolved spontaneously. On the 14th day of her hospitalization, the results of biochemical tests were as follows: AST 84 U/L, ALT 189 U/L, total bilirubin 2.7 mg/dl, direct bilirubin 0.84 mg/dl, and GGT 104 U/L. She was discharged and followed on an outpatient basis. Her biochemical tests returned to normal at the end of the third month. She is well after a six-month period of outpatient follow-up.

DISCUSSION

Hepatitis A virus causes a typically minor illness in childhood, with more than 80% of cases being asymptomatic (3). Our patient had a symptomatic course with abdominal pain, vomiting and scleral icterus. Transient sinus bradycardia as an extrahepatic complication developed during the clinical course of hepatitis A. A variety of extrahepatic manifestations can be observed in patients with acute hepatitis A. Hemolysis, aplastic anemia, autoimmune thrombocytopenic purpura, acute renal failure, interstitial nephritis, acalculous cholecystitis, pleural or pericardial effusion, pancreatitis, acute reactive arthritis, immune complex mesangial proliferative glomerulonephritis, acute tubular necrosis, mononeuritis, Guillain-Barré syndrome, postviral encephalitis, and transverse myelitis have all been described in patients with acute hepatitis A. The exact mechanism(s) involved has not been defined. Occasionally, patients with hepatitis A virus infection manifest symptoms consistent with circulating immune complex formation. These include cutaneous vasculitis, arthritis, and cryoglobulinemia (4). The cardiovascular complications of viral hepatitis are not widely recognized. Profound hypotension and a variety of dysrhythmias, including sinus arrest, transient left ventricular hypertrophy, myocarditis and cardiomyopathy have been reported in association with viral hepatitis, but most of these cases were described before the advent of specific viral serologic markers (5-8). Gordon et al. (1) reported two previously healthy adult cases who presented with unexplained hypotension and bradycardia as the initial manifestations of acute icteric hepatitis A. Bradycardia may be seen in some clinical settings other than cardiovascular diseases such as increased intracranial pressure, head and neck cancers, myxedema and hypothermia (9-12). These clinical conditions were not present in our case. It has been reported that bradycardia and sinus node dysfunction may be seen in obstructive jaundice caused by liver and bile duct pathologies (13, 14). In our case, when serum bilirubin level reached the peak value of 7.7 mg/dl, her heart rate was the lowest of the course of illness, and high bile

acid levels were demonstrated. It has been considered that direct viral invasion of the conduction system or toxicities of increased levels of serum bilirubin or bile acid could be responsible for the development of sinus bradycardia (13). In a case report, a patient with obstructive jaundice and profound sinus dysfunction was presented. It was postulated that parasympathetic activation originating from the mechanical distention of the bile ducts caused vasovagal activation and bradycardia due to the fact that sinus arrest occurred at the same time bilirubin levels peaked and the arrest was responsive to atropine (6). However, in another case report of a patient with viral hepatitis A, who had hypotension, bradycardia and nodal arrest, the patient was unresponsive to atropine, and a pacemaker was needed (1). Patients with fulminant liver failure frequently develop multiorgan failure, placing them at risk of systemic infections, cerebral edema, hemodynamic instability, coagulopathy and various renal and metabolic complications (15). Our patient had none of these features.

In conclusion, we suggest that sinus bradycardia may be a transient manifestation of acute hepatitis A in previously healthy children and in the absence of fulminant liver failure.

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