A case of myocarditis mimicking acute coronary syndrome associated with H1N1 influenza A virus infection

Akut koroner sendromu taklit eden ve H1N1 influenza A virüs enfeksiyonu ile ilişkili miyokardit: Olgu sunumu

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Myocarditis due to H1N1 influenza infection has not been previously described. We report on a case of acute fulminant myocarditis caused by H1N1 influenza A virus infection that mimicked acute coronary syndrome. A 50-year-old man was admitted with dyspnea, fever, cough, vomiting, and atypical chest pain of three-day history. His body temperature, pulse rate, and blood pressure were 39.2 °C, 115 beats/min, and 80/40 mmHg, respectively. Electrocardiography showed sinus tachycardia, 1-mm ST-segment elevation, and absence of R wave progression in anterior leads, and ST depression in anterolateral leads. The chest radiogram revealed diffuse bilateral alveolar infiltrates. Cardiac enzymes were elevated. Despite treatment with aspirin, clopidogrel, low-molecular weight heparin, metoprolol, and an ACE inhibitor, he developed hemodynamic instability on the first day of admission. Echocardiographic examination showed anteroseptal, apical, and lateral wall hypokinesia, left ventricular diastolic dysfunction, and dilatation of all the chambers. There was no abnormal finding on coronary angiography. The diagnosis was considered to be myocarditis; thus, anticoagulant and antiaggregant therapies were discontinued, and empirical broad-spectrum antimicrobial treatment was initiated together with antiviral oseltamivir (2x75 mg/day). The patient's clinical condition significantly improved. Nasopharyngeal samples were positive for H1N1 influenza A virus. He was discharged on the 15th in good medical condition.

Key words: Acute coronary syndrome; influenza A virus, H1N1 subtype/complications; myocarditis/diagnosis/therapy.

H1N1 influenza virüsüne bağlı miyokardit daha önce bildirilmemiştir. Bu yazıda, akut koroner sendromu taklit eden ve H1N1 influenza virüsünün neden olduğu akut fulminant miyokarditli bir olgu sunuldu. Elli yaşında erkek hasta üç gündür var olan nefes darlığı, ateş, öksürük, kusma, ve atipik göğüs ağrısı ile yatırıldı. Vücut ısısı 39.2 °C, nabzı 115 atım/dk ve kan basıncı 80/40 mmHg olan hastanın elektrokardiyografisinde anteriyor derivasyonlarda sinüs taşikardisi, 1 mm ST-segment yükselmesi ve R dalga yokluğu, anterolateral derivasyonlarda ise ST çökmesi görüldü. Göğüs radyogramında iki taraflı, yaygın alveolar infiltratlar izlendi. Kardiyak enzimleri yükselmiş idi. Aspirin, klopidogrel, düşük molekül ağırlıklı heparin, metoprolol ve ACE inhibitörü ile tedaviye rağmen, yatışın ilk gününde hastada hemodinamik instabilite gelişti. Ekokardiyografik incelemede anteroseptal, apikal ve lateral duvarda hipokinezi, sol ventrikül diyastolik disfonksiyonu ve tüm kalp odacıklarında genişleme saptandı. Koroner anjiyografide anormal bulguya rastlanmadı. Miyokardit öntanısıyla antikoagülan ve antiagregan tedaviler kesilerek, ampirik olarak geniş spektrumlu antimikrobiyal tedaviye ve oseltamivir (2x75 mgr/gün) ile antiviral tedaviye başlandı. Hastanın klinik durumu belirgin derecede düzeldi. Nazofarengeal örneklerin inceleme sonucu H1N1 influenza A virüsü için pozitif bildirildi. Hasta yatışın 15. gününde durumu iyi olarak taburcu edildi.

Anahtar sözcükler: Akut koroner sendrom; influenza A virüs, H1N1 alttipi/komplikasyon; miyokardit/tanı/tedavi.

Myocarditis is an inflammatory disorder characterized by necrosis of myocytes and inflammatory infiltrate of the myocardium. Clinical manifestations may vary from latent to very severe clinical forms, such as acute congestive heart failure, cardiogenic shock, and sudden death.[1] Although the etiological agent is usually a virus, bacterial or fungal infections, autoimmune disorders, and medical drugs may also be involved.[2] Influenza accounts for 3-5 million cases of severe illness and up to 300,000 deaths annually. It

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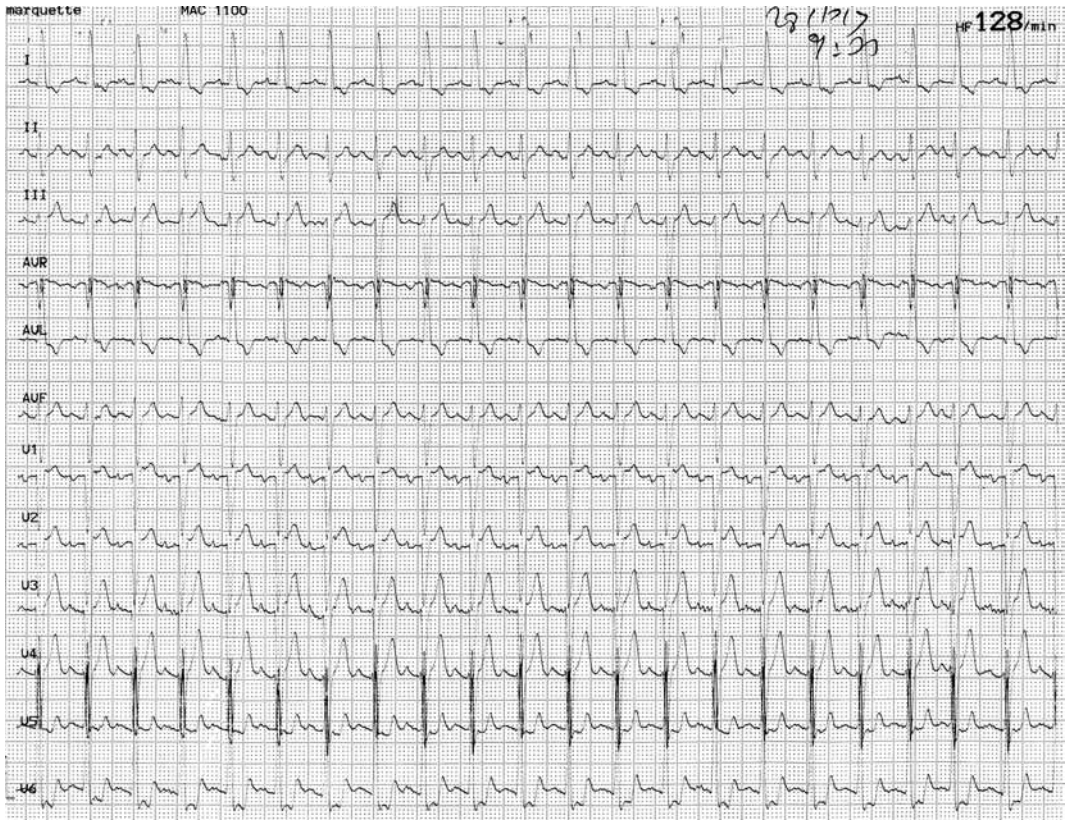

Figure 1. ST-T changes suggestive of acute coronary syndrome on 12-lead electrocardiography.

is caused by RNA viruses that infect the respiratory tract of many animals, birds, and humans. Influenza pandemics are rare events with at least three pandemics in the 20th century (1918, 1957 and 1968).[3] There are three types of influenza viruses: A, B and C. Current subtypes of influenza A viruses found in people are H1N1 and H3N2 viruses. H1N1 primarily involves children and young adults.[4] Myocarditis due to H1N1 influenza infection has not been previously described. We report on a case of acute fulminant myocarditis caused by H1N1 influenza infection that mimicked acute coronary syndrome.

CASE REPORT

A 50-year-old man was admitted to the emergency room with dyspnea, fever, cough, vomiting, and atypical chest pain of three-day history. He had no risk factors for atherosclerosis. He was receiving azathioprine for rheumatoid arthritis. Crackles in the middle zones were heard on lung examination, and cardiac examination revealed an S_3 gallop. His body temperature, pulse rate, and blood pressure were 39.2 °C, 115 beats/min, and 80/40 mmHg, respectively. Electrocardiography showed sinus tachycardia, 1-mm ST-segment elevation, and absence of R wave progression in anterior leads, and ST depression in anterolateral leads (Fig. 1). Chest radiography revealed diffuse bilateral alveolar infiltrates. Creatine phosphokinase-MB isoenzyme was measured as 417 ng/ml and troponin T as 1.79 ng/ml. White blood cell count, erythrocyte sedimentation rate, C-reactive protein, and procalcitonin values were 26.3×10^9/l, 25 mm/h, 48.8 mg/l, and 0.619 ng/ml, respectively. Blood urea nitrogen, creatinine, sodium, potassium levels were normal, and liver function tests were slightly increased. The patient was admitted to the coronary intensive care unit for the differential diagnosis of acute coronary syndrome, myocarditis, and shock (cardiogenic or septic). He was given aspirin, clopidogrel, low-molecular weight heparin, metoprolol, and an ACE inhibitor. On the first day of admission, he developed hemodynamic instability and dopamine infusion was initiated. Echocardiographic examination showed anteroseptal, apical, and lateral wall hypokinesia, left ventricular diastolic dysfunction (ejection fraction 40%), and dilatation of all chambers. There was no abnormal finding on coronary angiography (Fig. 2). Based on echocardiographic and angiographic findings, the diagnosis was considered to be myocarditis and medical treatment of the patient was arranged accordingly. Anticoagulant

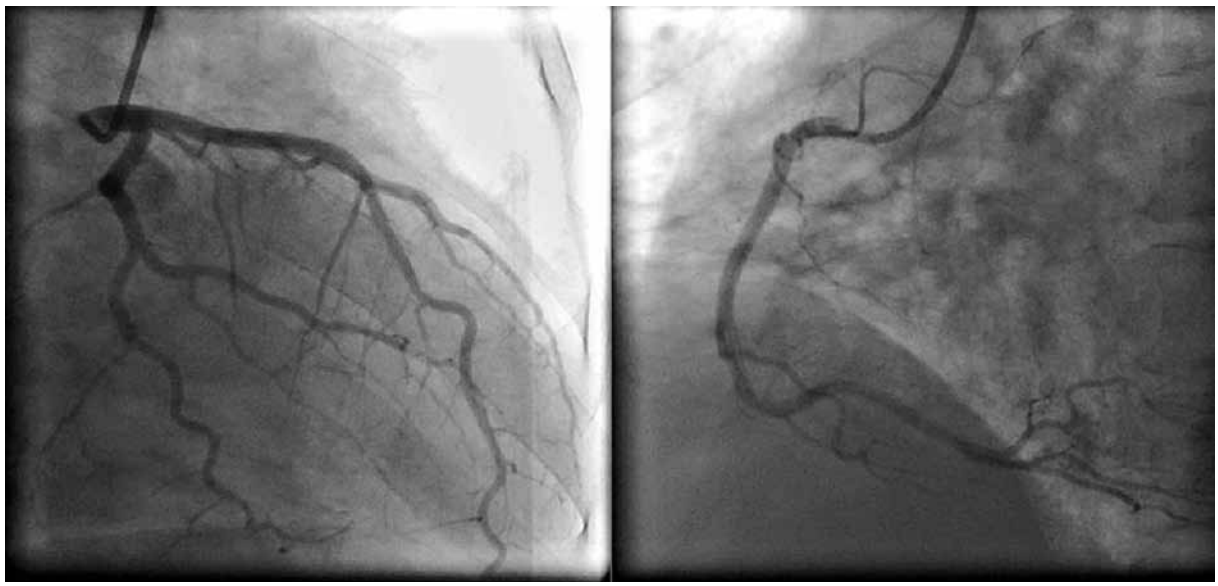

Figure 2. Normal coronary angiograms that support the diagnosis of myocarditis.

and antiaggregant therapies were stopped. Because of high body temperature and influenza-like clinical symptoms, nasopharyngeal samples were taken for H1N1 virus tests. On the third day of admission, consultation with the infection diseases department yielded a diagnosis of probable septic shock or cardiogenic shock caused by viral myocarditis. Empirical broad-spectrum antimicrobial treatment was initiated including intravenous vancomycin (2 x 1 g/day), sulperazon (2 x 2 g/day), gentamicin (1 x 240 mg/day), and antiviral oseltamivir (2 x 75 mg/day). The patient's clinical condition significantly improved after the third day of treatment. Serum creatine kinase levels were 312 IU/l on the second day of illness and 54 IU/l on the third day of admission. Real-time reverse transcription polymerase chain reaction assay of the nasopharyngeal smear performed at the Ankara Refik Saydam Hygiene Center Presidency was positive for influenza A, identified as 2009 H1N1 influenza A virus. He was discharged on the 15th day of hospitalization because of decreases in enzyme levels to normal and significant improvement in medical condition. There were slight improvements in wall motion and ejection fraction (50%) on echocardiographic evaluation. Improved clinical and laboratory condition of the patient obviated the use of cardiovascular magnetic resonance imaging and myocardial biopsy.

DISCUSSION

Myocarditis refers to myocardial inflammation caused by infections, drug toxicity, or immunological reactions.[2] Enteroviruses, specifically Coxsackie B serotype, have been implicated as the predominant viral cause.[5] Influenza-associated myocarditis has been reported in few cases.[6] Patients may develop fever, myalgia, respiratory symptoms, or gastroenteritis that may result in sudden hemodynamic collapse.

Elevated troponin levels have shown to be a more reliable predictor of myocardial injury than levels of creatine kinase in myocarditis.[7] Electrocardiographic manifestations of acute myocardial ischemia may typically include ST-segment elevation in two contiguous leads (54%), T wave inversion (27%), widespread ST-segment depression (18%), and pathological Q waves (18% to 27%).[8] Segmental or global echocardiographic wall motion abnormalities are frequently seen despite angiographically normal coronary anatomy.[8] In our patient, electrocardiography showed sinus tachycardia, ST-segment elevation, and absence of R wave progression in anterior leads, and ST depression in anterolateral leads. Echocardiography showed anteroseptal, apical, and lateral wall hypokinesia and coronary angiography was absolutely normal.

H1N1 influenza continues to be a disease primarily afflicting children and young adults. The incubation period for H1N1 influenza is 1 to 4 days, sometimes extending to seven days. The clinical features of influenza are well-known and include sudden onset of high fever, extreme tiredness, headache, dry cough, sore throat, runny nose, muscle aches, and stomach symptoms. Complications of H1N1 influenza are frequent in patients with an underlying chronic disease. Our patient had a history of azathioprine use for rheumatoid arthritis. A wide variety of complications may develop including myositis, rhabdomyolysis, central

nervous system complications such as encephalopathy, encephalitis, seizures, sinusitis and otitis, pulmonary complications including bronchitis or asthma, acute exacerbations of chronic bronchitis, secondary bacterial pneumonia, and septic shock syndrome.[4] Our patient developed shock on the first day of admission and recovered after dopamine, antibiotic, and antiviral treatment.

Data on the clinical benefits of antiviral treatment for H1N1 influenza A infection are limited, and different authorities have different recommendations. It has been recommended by the Central Committee on Infectious Disease and Emergency Responses (CCIDER) that empirical antiviral treatment be started immediately to those patients with influenza-like illness who are at higher risk for developing complications.[9] Antiviral treatment should also be considered in patients with a high risk for complications, including those younger than six years, current smokers, morbidly obese, asthmatic, immunocompromised, or pregnant subjects, patients showing no improvement in symptoms 48 hours after medical treatment, and in patients in whom influenza A (H1N1) infection has been confirmed.[4] According to the Centers for Disease Control and Prevention, either oseltamivir 75 mg twice daily or inhaled zanamivir 10 mg twice daily should be given to all hospitalized patients with confirmed, probable, or suspected influenza A (H1N1) infection.[10] Our patient presented three days after the onset of symptoms and oseltamivir 75 mg twice daily was started six days after symptom onset. Oseltamivir treatment combined with supportive cardiac and antimicrobial medications resulted in significant improvement in the clinical status of our patient and he became asymptomatic after 15 days of treatment.

In conclusion, myocarditis due to H1N1 influenza infection must be suspected in patients presenting with influenza-like manifestations, cardiac symptoms, and signs related to myocarditis. Clinical manifestations of myocarditis due to H1N1 influenza virus infection may be severe and can mimic acute coronary syndrome.

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