Acute Fulminant Myocarditis and the 2009 Pandemic Influenza A Virus (H1N1)

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ABSTRACT

The 2009 Pandemic Novel Influenza A [H1N1] resulted in mild disease mostly but severe cases and death were associated with pneumonia, respiratory failure and multi-organ failure. We present a case of severe disease with acute heart failure and arrhythmia due to fulminant myocarditis in a 50- year old obese man with diabetes mellitus.

Keywords: Influenza myocarditis, H1N1 myocarditis, viral myocarditis

Miocarditis Fulminante Aguda y el Virus (H1N1) de la Pandemia de la Gripe A de 2009

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RESUMEN

La nueva gripe A [H1N1] pandémica resultó ser una enfermedad leve en su mayor parte, pero se produjeron casos graves y muertes asociadas con neumonía, insuficiencia respiratoria y fallo multiorgánico. Presentamos un caso de enfermedad severa con insuficiencia cardíaca aguda y arritmia debido a miocarditis fulminante en un hombre obeso de 50 años de edad con diabetes mellitus.

Palabras claves: Miocarditis por gripe, miocarditis por H1N1, miocarditis viral

INTRODUCTION

The 2009 Pandemic influenza A virus (H1N1) affected an estimated 41–84 million people worldwide causing an average of 11 690 deaths (1). Severe disease and hospitalization was mostly associated with viral pneumonia, secondary bacterial pneumonia, respiratory failure and multi-organ dysfunction (2, 3). This is a report of severe cardiac complication due to fulminant myocarditis in a patient with H1N1 and no known pre-existing cardiac disease.

CASE REPORT

A 50-year old white male was seen at the George Town Hospital, Cayman Islands on July 29, 2009. He presented to the emergency room about 2:55 am with an acute onset of shortness of breath and severe orthopnoea. He had no chest pain and no previous history of cardiac disease. His cardiac symptoms were preceded by a two-day history of fever and productive cough. His other medical problem was diabetes mellitus treated with oral hypoglycaemic agents.

On examination, he was obese with body mass index [BMI] of 41 and was in severe respiratory distress. He was apprehensive and very diaphoretic. His temperature was 38.5°C, respiration 36/minute and heart rate 214 beats/minute; blood pressure was initially 180/127 mm Hg but decreased to 90/50 mmHg over 24 hours. His lungs had extensive bilateral crepitations, and heart sounds were S1, S2 with tachy-cardia. His abdomen was normal and he had no pedal edema.

His laboratory findings showed a white cell count of 10.10 x 10^9/L, haemoglobin [Hb] 17.1g/dL, haematocrit (Hct) 48.10% and platelets 174 X 10^9/L. His blood chemistry, sodium (Na) was 136mmol/L, potassium (K): 3.9 mmol/L, chloride (Cl): 100 mmol/L, bicarbonate: 18 mmol/L, blood urea nitrogen (BUN): 13 mg/dL, creatinine: 1.0 mg/dL, blood glucose: 490 mg/dL, aspartate aminotransferase (AST): 10 iu/L, alanine aminotransferase (ALT): 105

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iu/L, alkaline phosphatase (AP): 108 iu/L and B-type natriuretic peptide (BNP): 197.3ng/L [normal < 100]. His serial cardiac enzymes (CK-MB, Troponin I) were negative.

A nasopharyngeal swab screening test was positive for influenza A and confirmed as 2009 Pandemic novel influenza A virus [H1N1] using real time polymerase chain reaction [RT-PCR] at the Caribbean epidemiology centre in Trinidad and Tobago. His sputurm showed numerous pus cells and grew S*treptococcus agalactiae*.

His initial electrocardiogram showed monomorphic wide-complex tachycardia but a repeat after amiodarone treatment showed left bundle branch block (LBBB). He had extensive pulmonary oedema on chest X-ray.

His echocardiography showed severely impaired left ventricular function with an ejection fraction of 30–35%, a normal left ventricular wall thickness, marked hypokinesis and akinesis of the inferior wall, interventricular septum and anterior wall.

He was treated with intravenous frusemide for pulmonary oedema, intravenous amiodarone for arrhythmia, oseltamivir 75 mg twice a day for seven days and also a course of broad spectrum antibiotics.

On day 3 of hospitalization, he developed an acute cephalic vein thrombosis in the right upper limb and was treated with subcutaneous enoxaparin. He improved progressively and was discharged on day 12 with a referral to a tertiary centre for cardiac catheterization. His cardiac catheterization showed no significant stenosis in both left and right coronary circulation but left ventriculography showed left ventricular dilatation with severe global hypokinesis and reduced ejection fraction of 25% due to non-ischaemic cardiomyopathy.

DISCUSSION

The patient presented with acute onset of congestive cardiac failure, ventricular arrhythmia and eventually non-ischaemic dilated cardiomyopathy preceded by a two-day history of influenza- like illness during the early period of the 2009 pandemic influenza A virus [H1N1] in Cayman Islands. He was screened early for influenza virus and a positive influenza A virus was confirmed as 2009 novel influenza A [H1N1].

The clinical picture of acute congestive heart failure and arrhythmia preceded by an acute viral illness as in our patient is consistent with acute viral myocarditis (4).

His echocardiographic findings of extensive myocardial hypokinesis and akinesis as well as low ejection fraction is consistent with myocardial damage from acute myocarditis which can mimic an acute myocardial infarction (4).

Cardiac biomarkers are only elevated in a small number of patients with myocarditis thus a negative cardiac marker does not exclude myocarditis (4). In a study of elevation of cardiac biomarkers in biopsy proven myocarditis, cardiac troponin I [cTnI] was elevated in 18 of 53 patients [34%] and creatinine kinase MB[CK-MB] in 3 patients (5).

His cardiac catheterization did not show any significant coronary artery obstructive lesion. Though he had an initial transient hypertension,he became hypotensive subsequently as he had no previous history of hypertension. Endomyocardial biopsy is definitive but was not done in this case. Influenza virus is a known but very rare cause of acute viral myocarditis and may be responsible for death. In an autopsy review of 47 deaths from the influenza virus during 2003–2004 seasonal influenza in the USA by Guarner et al, myocarditis was seen in 6 out of 20 cases [30%] (6).

The clinical presentation of influenza associated myocarditis may range from mild progressive dyspnoea to acute fulminant cases with arrhythmia and haemodynamic instability as in this case (7). There may be electrocardiographic changes of left bundle branch block, S-T elevation and Q waves, as well as echocardiographic findings of hypokinesis and akinesis (7). The cardiac symptoms are usually preceeded by a flu-like illness in all cases.

The mechanism of viral myocarditis may include viral induced cell mediated cytotoxicity or myocardial damage by pro-inflammatory cytokines (4). Acute influenza virus is associated with release of cytokines which includes pro-inflammatory cytokines as IL-1beta, IL-6, IL-18 and tumour necrosis factor alpha [TNF-alpha] (8).

The over-expression of pro-inflammatory cytokine Tumour Necrosis Factor [TNF] alpha as well as TNF-alpha receptors 1 and 11 in patients with acute viral myocarditis including influenza virus correlated with severe myocardial necrosis on histology as well as clinically severe cardiac dysfunction (9).

In a recent review of the immunologic profile and disease severity due to the 2009 Pandemic H1N1, a higher level of pro-inflammatory cytokines were seen in patients with Adult Respiratory Distress Syndrome [ARDS] and death compared with mild disease (10). Out of the 23 patients with severe disease due to ARDS or death, 21.7% had myocarditis (10). In another case series, EL-Said *et al* reported four cases of H1N1 influenza associated myocarditis in children (11). Our case is the first fully reported case in an adult not associated with pneumonia using Pubmed search though this complication was noted in 5 cases with severe disease by Too *et al,* ages not known, and 3 were post-mortem findings (10). The patient developed an acute thrombosis of the cephalic vein possibly due to endothelial damage from pro-inflam-matory cytokines.

Diabetes mellitus and obesity are both associated with critical illness due to H1N1 virus (3, 12). Obesity was the most prevalent underlying disease in a review of 58 patients critically ill with H1N1 in Mexico occurring in 36.2% of patients while diabetes mellitus was seen in 17.2% (12).

We report that the 2009 pandemic influenza A virus (H1N1) may cause severe heart disease in adults and cardiac

complications should be looked for during all influenza outbreaks.

ACKNOWLEDGEMENT

The authors acknowledge the assistance of Dr Joseph Barefoot in doing echocardiography, Dr Kevin Coy, cardiac catheterization and the Caribbean Epidemiology Centre in performing H1N1 confirmatory testing.

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