INTRODUCTION

The 2009 pandemic of H1N1 influenza is of concern to paediatricians as it is not clear as to what pattern of illness patients will manifest in response to the virus (1). Will there be an increased risk of secondary bacterial infection, encephalopathy or other symptoms? The following case demonstrates that damage to the myocardium may be a significant factor underlying the deterioration in a child during H1N1 infection.

CASE REPORT

A.S. was an eight-year old boy who developed a high fever, vomiting and diarrhoea while in the Yemen. He presented to Hospital in the UK four days later with coughing, shortness of breath, vomiting and diarrhoea. While in the Yemen a number of family members suffered mild upper respiratory tract symptoms with fever.

A.S. was born in Holland; a diagnosis of propionyl-CoA carboxylase deficiency was made there in the first year of life. A.S. was the youngest of five siblings; the others are well. He had a gastrostomy placed at the age of a year and after this was fed a low protein diet using this device; he was managed with Carnitine (30% solution, 4.5 mls bd) and biotin (0.5 mg od). His care after 2003 in London was shared between a tertiary metabolic unit and a district general Hospital. A.S. had developmental delay and attended special school. His metabolic condition was stable; he had one episode of lactic acidosis when aged 4 years that resolved rapidly. He was admitted aged 6 years with a severe lower respiratory tract infection; he required ventilation for 24 hours for this episode. ECG recordings from 2006 and 2007 demonstrated a normal rhythm but borderline prolonged QTc interval of 442 msecs, which is just below the 95th centile for this value (14).

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On admission in summer 2009 A.S appeared unwell with tachypnoea and fever. He had clinical signs of a right lower lobe pneumonia confirmed on a chest radiograph. He was treated with intravenous cefotaxime and oseltamivir (Tamiflu). Over the course of the first night he required mask oxygen; he became more distressed and on the morning of the second day developed drowsiness. His white cell count fell, as did his platelet count. The chest radiograph showed progressive deterioration in both lungs suggestive of viral pneumonitis. An ECG showed no arrhythmia but a QTc of 450 ms. His blood tests showed no decompensation of his acid base balance; the ammonia remained at 71 umol/l. The creatinine kinase was raised at 1849 IU/l and troponin was 0.05 ug/l (normal up to 0.01 ug/l). Cultures and swabs were negative to bacterial testing but positive for H1N1 influenza. Treatment with vancomycin was added to protect against secondary bacterial infection. A.S. remained normotensive, but on the ward suffered a bradycardia and a cardiac arrest on day three. He responded to resuscitation and was stabilised, intubated and transferred to a paediatric intensive care unit. There A.S. proved progressively more difficult to ventilate. He developed a adult respiratory distress-type of lung disorder with increasing pulmonary oedema. He showed reduce left ventricular shortening on echocardiography and inotropes were started. A further antibiotic, colomycin, was commenced. Cardiac contractility decreased rapidly on day 5 despite supportive care. A.S. died of a cardiorespiratory arrest related to an influenza infection complicated by myocarditis.

DISCUSSION

Our patient had several reasons to be predisposed to suffer more severely from influenza. He was young and had required ventilation two years previously for a lower respiratory tract infection. Cardiac pathology may have been more likely in his case as he had a pre-existing prolonged QTc interval related to his propionic academia (2,3). In his previous clinical course A.S. had shown no evidence of cardiac problems, but the role of H1N1 influenza in aggravating this previous cardiac condition was significant. As was evident from the rise in troponin and further prolongation of his QTc interval, the virus involved his myocardium. His clinical course suggested that treatment with oseltamivir did not prevent his progressive deterioration although it was commenced on the day of Hospital admission.

Although influenza infections commonly present with myalgia during the early febrile phase of the illness, subsequent respiratory symptoms usually predominate. It is never evident to what extent the virus has spread or caused damage outside the respiratory tract (4). Children often have more limited immune responses that may permit greater viral invasion and spread to other tissues. Encephalopathy for instance is seen more often in such cases. Animal
models of “immature” or youthful immune systems suggest influenza virus has a strong tropism for the central nervous system and muscle: myosits of all types is more common in these (5). The virus infects both mature myocytes and immature myotubes. Myotubes may lack basal lamina; additionally they express surface acetylcholine receptors, thought to promote viral entry. For these reasons children’s muscle is thought to be more susceptible to influenza infection. Similarly injured or denervated muscle, and muscle with infiltrating fibroblasts, is also more susceptible to this virus (5).

Myocarditis is a complication in children with all influenza strains (6-10) although coxsackie A and B or enteroviruses more commonly cause myocarditis. Acute deaths specifically caused by myocarditis during influenza in children are few and descriptions of myocarditis as an isolated presenting symptom are rare (9-10). Cardiac function in influenza may also be impaired by deranged autonomic nerve function, as seen in encephalopathic infections (7). Individuals with prolonged QTc intervals in influenzal infection may develop arrhythmias (10, 11). These considerations are significant both to acute presentations of influenza and following recovery as some individuals may go on to develop a dilated cardiomyopathy. This condition is a recognised cause of arrhythmia and sudden death in the young. An asymptomatic and unsuspected cardiac infection may therefore lead to compromised health in the longer term (12). It therefore becomes important for clinicians to establish whether a particular patient may suffer myocarditis as well as other problems, when infected with influenza virus.

The case presented poses the question as to whether troponin and creatinine phosphokinase levels should be examined earlier and more frequently in children suffering significant illness with influenza. Should they be monitored with an ECG, and should the QT interval be checked at regular intervals (14)? Should biochemical responses, such as troponin release or Early echocardiographic diagnosis be employed more frequently? Critically, there are no data on the merits of antiviral treatment for influenza on myocardial function. An early series of three cases showed intravenous ribavirin had little effect (15). The progress of our case suggests that a neuraminidase inhibitor, oseltamivir may have little impact on the progression of combined pneumonitis and myocarditis. Vaccination will therefore offer the most cost-effective alternative to preventing infections of this severity in children with predisposing medical problems. Optimal Hospital treatment in cases such as that presented must therefore be supportive with a view to actively excluding underlying complications, including myocarditis.

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