



Reversible Cardiac Dysfunction Associated With Pandemic 2009 Influenza A(H1N1)

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Historical influenza A epidemics have carried elevated rates of cardiovascular disease, including transient cardiac dysfunction. Whether such an association holds for the novel influenza A strain, pandemic 2009 influenza A(H1N1) [A(H1N1)], remains unknown. We report an index case of transient cardiac dysfunction associated with A(H1N1) infection. Next, we reviewed 123 sequential cases of patients hospitalized with pandemic A(H1N1) at a single academic medical center in the United States from April 1, 2009, through October 31, 2009. We identified that 4.9% (6/123) of patients had either new or worsened left ventricular dysfunction. These cases ranged in age from 23 to 51 years, and all had preexisting medical conditions. ICU level care was required in 83% (5/6) of the cases. Sixty-seven percent (4/6) of the cases had follow-up echocardiograms, and left ventricular function improved in all four. We conclude that potentially reversible cardiac dysfunction is a relatively common complication associated with hospitalized pandemic A(H1N1) influenza. CHEST 2010; 137(5):1195–1197

Abbreviations: A(H1N1) = 2009 influenza A(H1N1); RT-PCR = reverse transcriptase polymerase chain reaction

In September 2009, a 43-year-old black man was referred to our ED from his local urgent care center with 5 days

of fever, cough, sore throat, and dyspnea. His medical history was significant for benign hypertension and mild intermittent asthma. His dyspnea was refractory to home nebulizer treatments.

Presenting vital signs were: temperature, 36.5°C; pulse, 95; BP, 91/59 mm Hg; respiratory rate, 18 breaths/min; and oxygen saturation, 87% on room air. The patient appeared in acute respiratory distress. He had crackles and wheezes on lung examination; chest radiograph revealed bilateral nodular and confluent opacities.

The patient was initially treated in our ED for an exacerbation of asthma and bacterial pneumonia with supplemental oxygen, IV fluids, antibiotics, and steroids, as well as nebulized bronchodilators. Despite these measures, his hypoxemic respiratory failure and shock progressed. He was admitted from the ED to the ICU, where he was intubated within 24 h and required mechanical ventilation for the duration of his 55-day hospitalization.

On hospital day 1, a transthoracic echocardiogram demonstrated global left ventricular hypocontractility with an ejection fraction of 35% without evidence of left ventricular hypertrophy. He responded partially to IV diuresis and inotropic support. Although a nasal wash obtained at admission was negative for influenza A by reverse-transcriptase polymerase chain reaction (RT-PCR), viral cultures from bronchoscopy performed upon ICU arrival returned positive for influenza A on hospital day 6. The patient was then initiated on oseltamivir (Tamiflu; Roche; Basel, Switzerland) 75 mg daily (adjusted for severe renal impairment). Strain typing at the state laboratory confirmed the isolate to be pandemic 2009 influenza A(H1N1) [A(H1N1)]. His cardiac dysfunction was attributed to A(H1N1) infection; there was no evidence of myocardial infarction (normal cardiac biomarkers) or pericarditis on ECG. Repeat echocardiogram on hospital day 13 revealed that his left ventricular function had returned to normal. The patient was discharged to a long-term acute care facility still requiring nocturnal mechanical ventilation. This is the first report, to our knowledge, of pandemic A(H1N1) association with reversible cardiac dysfunction. The patient described is one in a series of patients identified at our institution with such an association.

MATERIALS AND METHODS

We retrospectively reviewed medical charts of all pediatric and adult patients sequentially hospitalized at Duke University Medical Center with pandemic A(H1N1) from April 1, 2009, to October 31, 2009. Our case definition required hospitalization for at least 24 h because of an influenza-like illness (fever plus cough or sore throat) with pandemic A(H1N1) infection confirmed by RT-PCR

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Table 1—Clinical Characteristics of Patients With Pandemic 2009 Influenza A(H1N1) and Cardiac Dysfunction

| Characteristic | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 |
|------------------------------------|---------------|-----------------|-------------------|-------------------|---------------------------|------------------------------|
| Age, y | 43 | 23 | 51 | 49 | 33 | 25 |
| Sex | Male | Female | Female | Male | Female | Female |
| Race | Black | Black | White | Black | Black | Black |
| Medical history | Asthma HTN | SLE Seizures | COPD HTN DM | CHD CHF SLE | Pregnancy HTN DM(G) | Pregnancy Asthma DM(G) |
| Time to presentation | 5 d | “Recent” | 5 d | “Weeks” | 1 d | 1 d |
| Pao ₂ /FIO ₂ | 79 | 46 | 110 | 108 | 371 | 91 |
| APACHE II | 25 | 28 | 13 | 21 | 1 | 20 |
| Chest radiograph | | | | | | |
| Bilateral infiltrates | + | + | + | + | + | + |
| Pleural effusion | + | ... | ... | + | ... | + |
| Days hospitalized | 55 | 50 | 23 | 26 | 8 | 36 |
| Days in ICU | 55 | 45 | 13 | 26 | 0 | > 21 |
| Elevated CMs | ... | + | ... | + | ... | ... |
| New on ECG | | | | | | |
| Sinus tachycardia | + | + | ... | ... | + | + |
| NSTWA | + | + | ... | + | ... | + |
| Conduction delay | ... | + | ... | ... | ... | ... |
| Days to index TTE | 1 | 0 | 5 | 0 | 1 | 23 |
| Ejection fraction | 35% | 40% | 45% | 25% | 30% | “Moderate impairment” |
| Pericardial effusion | ... | ... | ... | + | ... | ... |
| Chamber dilation | ... | ... | ... | ... | + | ... |
| Days to repeat TTE | 12 | 22 | ... | 4 | 5 | ... |
| Ejection fraction | > 55% | > 55% | ... | 30% | 35% | ... |
| Disposition | LTAC | LTAC | Home | Expired | Home | Expired |

Day of admission is day 0. Pao₂/FIO₂ and APACHE II (a severity of disease classification used in the ICU; higher score indicates greater severity) were calculated as the worst values within 24 h of admission. Cases 5 and 6 were both in their third trimester of pregnancy. Baseline ejection fraction for case 4 was 40%. APACHE = Acute Physiology and Chronic Health Evaluation; CHD = coronary heart disease; CHF = congestive heart failure; CM = cardiac biomarkers (CK-MB, troponin T); DM = type 2 diabetes mellitus; DM(G) = gestational diabetes mellitus; HTN = hypertension; LTAC = long-term acute care facility; NSTWA = nonspecific T-wave abnormalities; SLE = systemic lupus erythematosus; TTE = transthoracic echocardiogram.

or viral culture. All testing used standard Centers for Disease Control and Prevention-based primers. Because >99% of influenza A in our state was pandemic A(H1N1), a new policy was enacted in September 2009 to confirm pandemic A(H1N1) strain only in ICU patients (relevant to 59.3% [73/123] of charts reviewed). Our chart review strategy was to identify subjects who had an echocardiogram for any reason during their hospitalization, then assess for reduced left ventricular function, which, if present, triggered extraction of the variables in Table 1. This study was reviewed and approved by the Duke University Medical Center Institutional Review Board for Human Studies.

RESULTS

In our series of 123 patients, 24 (19.5%) had at least one echocardiogram during their hospitalization, and six (4.9%) had new (cases 1-3, 5, 6) or worsened (case 4) left ventricular dysfunction during their hospitalization, as summarized in Table 1. The age range was 23 to 51 years. All had preexisting medical conditions, five required hospitalization > 3 weeks with prolonged ICU care, and two died. All four in whom follow-up echocardiograms were obtained, at a range of 4 to 22 days into hospitalization, demonstrated improved or normalized ejection fraction.

DISCUSSION

Historically, influenza has been linked to cardiovascular disease. Epidemiologic analyses have illustrated an increase in cardiovascular deaths during influenza epidemics.¹ Although the mechanism of increased cardiovascular deaths remains unknown, previous reports suggest the possibility of influenza myocarditis, exacerbation of pre-existing coronary disease, or worsening of congestive heart failure.² A recent systematic review of 39 studies found diverse but consistent observational evidence of influenza association with myocardial infarction.³ The multiple organ dysfunction syndrome, common in critically ill patients and associated with systemic inflammation, represents yet another etiologic consideration.

Similar to the timing in our index case, prior case series of influenza myocarditis^{4,5} describe the onset of cardiac dysfunction within the first week of illness. Extending this older data, this case series highlights to care providers that reversible cardiac dysfunction is a common complication associated with hospitalized pandemic A(H1N1). Early recognition of this syndrome could facilitate initiation of both timely and appropriate therapy.

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Air Within the Spinal Canal in Spontaneous Pneumomediastinum

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Spontaneous pneumomediastinum is an uncommon benign condition that is occasionally associated with air within the spinal canal. We describe a further case in a 14-year-old girl and suggest a classification system based on a detailed review of the previous literature. Forty-eight patients with spontaneous pneumomediastinum and intraspinal air accumulation (36 men and 12 women, age range 4-72 years, median age 18 years) were grouped into those with underlying lung disease (n = 13), those with other underlying etiologic factors (n = 22), and those arising spontaneously (n = 13). Neurologic symptoms or signs were noted in one case. The remaining cases were successfully managed conservatively. In spontaneous pneumomediastinum, accumulation of air within the spinal canal is self-limiting and benign. The same management is advised in spontaneous pneumomediastinum with and without intraspinal air accumulation. *CHEST* 2010; 137(5):1197-1200

Air within the spinal canal, termed pneumorrhachis, occurs in a variety of settings, including epidural anesthesia, lumbar puncture, skull or spine injury, epidural abscess, and traumatic pneumothorax or pneumomediastinum.¹ We report on a recently encountered case in which pneumorrhachis occurred in an adolescent with spontaneous pneumomediastinum (ie, not due to previous injury or surgery) and extensively review the corresponding literature.²

CASE REPORT

A 14-year-old girl was admitted for investigation of the sudden onset of chest pain. She had no significant past medical or surgical history, did not use illicit drugs, and denied recent episodes of vomiting, coughing, or air travel. BP was 117/76 mm Hg; heart rate, 83 beats/min; respiratory rate, 16 breaths/min; axillary temperature, 36.9°C; and oxygen saturation, 95%. Examination revealed mild subcutaneous crepitus over the neck. Her respiratory effort was unlabored, and breath sounds were clear and equal bilaterally. On cardiac auscultation, a crunching sound was noted over the precordium with each heartbeat. The remainder of her general and neurologic examination was normal and without abnormal skeletal findings, such as disproportionately long thin limbs and fingers, anterior chest deformity, column deformity, or joint laxity.

Chest radiograph demonstrated pneumomediastinum with moderate amounts of subcutaneous air (Fig 1). CT scanning of her neck and thorax demonstrated, in addition to the above findings, air in the spinal space at the cervical level (Fig 2). Because the clinical examination demonstrated complete resolution of the subcutaneous emphysema within 2 days, the girl was discharged home after 3 days.

DATA ASSESSMENT

We recently performed a search of the terms intraspinal air, pneumorrhachis, epidural pneumatosis, and pneumomediastinum and found 42 reports³⁻⁴⁴ in English (n = 39), German (n = 2), and Italian (n = 1) for a total of 47 cases of spontaneous, nontraumatic pneumomediastinum complicated by pneumorrhachis, which were published between 1989 and 2009 as full-length articles or letters. The case of an Italian boy reported two times in the literature was considered only once.^{9,35} In the patients, the diagnosis of pneumorrhachis was made using a CT scan. From each patient we excerpted age, sex, the lung disease predisposing to pneumomediastinum, the presence of pneumothorax, the possible occurrence of either neurologic complaints or a pathologic neurologic examination, and the management. Respiratory maneuvers with elevated pulmonary pressure,

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