HHS Public Access

Author manuscript

Pediatr Crit Care Med. Author manuscript; available in PMC 2015 May 08.

Published in final edited form as:

Pediatr Crit Care Med. 2011 March ; 12(2): e99–e101. doi:10.1097/PCC.0b013e3181e28887.

Fulminant pH1N1-09 influenza-associated myocarditis in pediatric patients

Erica R. Gross, MD, **Jeffrey W. Gander, MD**, **Ari Reichstein, MD**, **Robert A. Cowles, MD, FACS, FAAP**, **Charles J. H. Stolar, MD, FACS, FAAP**, and **William Middlesworth, MD, FACS, FAAP**

Division of Pediatric Surgery, Morgan Stanley Children's Hospital, New York-Presbyterian, New York, NY

Abstract

Objective—To report an atypical presentation of pH1N1-09 influenza infection in children as fulminant myocarditis and tamponade and the successful treatment with extracorporeal membrane oxygenation.

Design—Case report.

Setting—Pediatric cardiac intensive care unit in a quarternary care children's hospital.

Patients—Two girls, 5 and 7 yrs of age, infected with pH1N1-09 influenza virus who presented in cardiogenic shock with a pericardial effusion and echocardiographic evidence of tamponade from fulminant myocarditis.

Interventions—Both patients received a pericardiocentesis. One was managed with multiple, high-dose inotropic agents, whereas the other required institution of extracorporeal membrane oxygenation.

Measurements and Main Results—Acute respiratory distress syndrome is the major reported clinical manifestation of pH1N1-09 influenza virus infection in hospitalized pediatric patients. In this report we describe two children with confirmed pH1N1-09 influenza infection that required intensive care for fulminant myocarditis. Neither patient had the typical symptoms of influenza-like illness, respiratory compromise, or evidence of pulmonary involvement. One child required extracorporeal membrane oxygenation. Both children survived to hospital discharge.

Conclusions—pH1N1-09 influenza infection can cause fulminant myocarditis in the healthy pediatric population. The clinical presentation may be nonspecific, and the lack of pulmonary symptoms may make diagnosis difficult. Extracorporeal membrane oxygenation support may offer an effective bridge to the recovery of heart function.

The authors have not disclosed any potential conflicts of interest.

For information regarding this article, eg2561@columbia.edu

Keywords

influenza A virus; pH1N1 subtype; shock; cardiogenic; myocarditis; pericardial effusion; cardiac tamponade; extracorporeal membrane oxygenation

Both seasonal and novel (pH1N1-09) influenza commonly present with fever, cough, sore throat, and myalgias, a constellation of symptoms known as influenza-like illness. Pulmonary complications, pneumonia and acute respiratory distress syndrome, are the major reported causes of morbidity and mortality associated with seasonal and novel (pH1N1) influenza. Patients with these complications require intensive care with mechanical ventilation and possibly extracorporeal life support.

Between April and December 2009, five patients at our institution required extracorporeal membrane oxygenation (ECMO) for treatment of confirmed or suspected pH1N1-09 influenza infection. The indication for ECMO in four of these patients was acute respiratory distress syndrome. The fifth patient was treated for cardiogenic shock from fulminant pH1N1-09 influenza-associated myocarditis. Five additional pediatric patients with severe pH1N1-09 influenza infections were evaluated for ECMO: four with pulmonary complications and one with cardiogenic shock. One patient declined ECMO and died, whereas the other four stabilized with aggressive medical therapy and recovered without ECMO support.

Fulminant myocarditis secondary to seasonal influenza infection has been well described but has not been reported with pH1N1-09 influenza virus. In this report we summarize the clinical characteristics of two patients who presented in cardiogenic shock secondary to fulminant pH1N1-09 influenza myocarditis. Neither child had a significant medical history, and both presented after 1 week of fever, abdominal pain, and lethargy but no respiratory complaints or diagnosis of influenza-like illness. Echocardiography revealed pericardial effusion with tamponade in both patients. Neither child underwent endomyocardial biopsy, but their acute clinical presentation, echocardiography findings, and positive serology results were highly suggestive of a clinical diagnosis of fulminant myocarditis.

CASE PRESENTATIONS

The institutional review board at Morgan Stanley Children’s Hospital waived the need for informed consent.

Patient A

A 5-yr-old girl with no known medical history presented after a 5-day prodrome of fever to 103°F, lethargy, and emesis. She had been immunized against seasonal influenza 2 months before presentation. Her pediatrician had obtained a rapid influenza enzyme immunoassay (EIA), the results of which were negative, and treated her for presumed gastroenteritis. She then developed altered mental status and ataxia and was referred to a local emergency department. Intravenous fluids were administered. A computed tomography scan of the brain was normal, and results of a second rapid influenza test (EIA) were negative. She clinically improved with intravenous fluid hydration and was discharged home.

Within 24 hrs of discharge from the emergency department, the lethargy worsened, she complained of diffuse headache, and she refused to walk. Upon return to the emergency department, she was found to be hypotensive (68/49 mm Hg). The results of laboratory investigations were significant for elevations in white blood cell count, aspartate transaminase, alanine aminotransferase, and serum lactate (Table 1). Magnetic resonance imaging of the brain was normal. Lumbar puncture results were unremarkable for infection. Ceftriaxone was given, and she was admitted for observation to rule out meningitis.

Within 6 hrs of admission, she lost consciousness, was intubated, fluid resuscitated, and started on dobutamine at 15 μg/ kg/min and dopamine at 5 μg/kg/min. An electrocardiogram showed flattening of T waves and low voltage. A transthoracic echocardiogram showed severely decreased left ventricular function, an ejection fraction of 37%, a shortening fraction of 17%, and a moderately sized pericardial effusion. The child was then transferred to our institution for further treatment.

She was hypotensive on arrival, and an epinephrine infusion (0.1 μg/kg/min) was started. Repeat echocardiography showed evidence of cardiac tamponade with a moderate pericardial effusion that was causing right atrial compression and decreased biventricular function. She underwent pericardiocentesis that drained 60 mL of serous fluid without immediate hemodynamic improvement. Milrinone was added (5 μg/kg/min). She was evaluated for ECMO, but her blood pressure remained stable on inotropic support, her urine output was >2 mL/kg/hr, and she was oxygenating adequately.

At our institution, results of the influenza A/B EIA (nasopharyngeal swab) were positive for influenza A, and we used polymerase chain reaction to confirm the strain as pH1N1-09. Pericardial fluid was sent for culture, EIA, and polymerase chain reaction, the results of which were all negative for influenza A. Cell count was consistent with a transudative pericardial effusion. Peramivir, corticosteroids, and broad-spectrum intravenous antibiotics (piperacillin/tazobactam and vancomycin) were started for fulminant myocarditis. Intravenous immunoglobulin was administered but discontinued secondary to a hypotensive reaction.

Within 24 hrs, her blood pressure improved, and inotropic support was weaned. She was extubated on hospital day 3, and all support was discontinued by day 4. She was discharged home on hospital day 10 on enalapril for mild residual left ventricular dysfunction.

Patient B

A 7-yr-old girl with no known medical history presented 9 days after patient A. She had a 5-day history of fever, abdominal pain, and emesis. Results of her initial rapid influenza EIA were negative, and she was also treated for presumed gastroenteritis by her pediatrician. She had received the seasonal influenza vaccine 1 month before presentation. The patient became more lethargic with worsening abdominal pain 2 days before admission. She was seen at a local emergency department, where she became hypotensive and lost consciousness during an abdominal computed tomography scan. A pericardial effusion was seen on computed tomography, and subsequent echocardiography revealed poor biventricular function, in addition to the pericardial effusion. She was started on dopamine.

Results of a repeat influenza A EIA were positive, and polymerase chain reaction confirmed pH1N1-09. She was then transferred to a tertiary care facility, where she was intubated. Pericardiocentesis with drain placement was performed, and 150 mL of serous fluid was removed. Tamiflu and intravenous immunoglobulin were started. Analysis of the pericardial fluid could not be performed because of a clot, and the specimen did not undergo polymerase chain reaction analysis for presence of influenza A. After 24 hrs without improvement on dopamine (12.5 μg/kg/min) and epinephrine (0.2 μg/kg/min), she was transferred to our center for extracorporeal life support.

During transport, she required increasing doses of dopamine (20 μg/kg/ min). Examination on arrival was significant for hypotension with mottled extremities. Vasopressin (0.002 μg/kg/ min) was added to the epinephrine and dopamine, but normal blood pressure was not sustained. Echocardiography revealed no significant residual pericardial effusion but did show global hypokinesis. The patient was well oxygenated and adequately ventilated but remained hemodynamically unstable with poor perfusion on maximal medical therapy. Given the reasonable likelihood of recovery of cardiac function, we chose ECMO support over a ventricular-assist device, which allowed us to avoid sternotomy and ventriculotomy.

The patient was transported to the cardiac catheterization laboratory, where a balloon atrial septostomy was performed by using a 7-mm × 2-cm OPTA Pro PTA dilation catheter (Cordis, Bridgewater, NJ) at 12 atmospheres (atm) followed by a 16-mm × 2-cm Atlas PTA dilation catheter (Bard Peripheral Vascular, Tempe, AZ) at 20 atm through a 14F sheath in the right femoral vein. The ECMO cannulas were then inserted. Venous drainage was achieved through a 15F (18-cm) cannula in the right internal jugular vein and a 17F (50-cm) cannula in the right common femoral vein. Arterial inflow was accomplished through a 15F (18-cm) cannula in the left femoral artery. An attempt to place a left superficial femoral artery distal limb perfusion catheter under sonographic guidance was unsuccessful but was later accomplished by arterial cut-down in the pediatric intensive care unit. Inotropes were discontinued within 10 mins of commencement of ECMO support. After intravascular volume repletion, a flow of 2550 mL/min was achieved. She remained hemodynamically stable on ECMO for 125 hrs. Her cardiac function normalized, and she was decannulated in the operating room with primary repair of the left femoral artery. Her ECMO course was complicated by left lower extremity limb ischemia, rhabdomyolysis, and acute renal failure that required continuous renal replacement therapy. She received a full 10-day course of peramivir, piperacillin/tazobactam, and vancomycin for 48 hrs with negative cultures, along with a steroid taper for myocarditis. She has required no long-term diuretic or inotropic support.

DISCUSSION

Worldwide, seasonal influenza accounts for approximately 3–5 million cases of severe respiratory illness and 300,000 deaths each year (1). In the United States, from April to November 2009, there have been 40,399 confirmed pH1N1 influenza-associated hospitalizations, 1,719 adult deaths, and 210 pediatric deaths (2, 3). Because many patients are being treated without laboratory confirmation of the specific influenza strain, it is difficult to know the true incidence or compare the mortality rate of pH1N1-09 influenza to

seasonal influenza. During the 2007–2008 influenza season, there were only 83 pediatric deaths associated with confirmed influenza reported to the Centers for Disease Control and Prevention (4). Argentina has reported a two-fold increase in the rate of pediatric hospitalizations and a dramatic increase in pediatric deaths, from zero to 13, between the 2008 and 2009 influenza seasons (5).

Despite this large number of affected patients, only one case description of pH1N1-09 influenza-associated myocarditis with cardiogenic shock has been published. This case involved an adult without respiratory compromise who recovered after requiring ECMO (6). In addition, the ECMO Registry of the Extracorporeal Life Support Organization in Ann Arbor, MI, keeps data on individuals supported with ECMO and contains eight other patients (three adults and five children) with myocarditis from pH1N1 influenza infection who required ECMO support.

Influenza is a well-documented cause of myocarditis in both adults and children, but the incidence is low. In a Canadian case series of 505 children admitted with confirmed influenza from 2003 to 2004, only two (<1%) of the children had documented myocarditis (7). During the same influenza season, the United States reported six (4%) pediatric cases of myocarditis or pericarditis from a cases series of 146 pediatric hospitalizations (8).

In children, the diagnosis of myocarditis can be difficult, because the presentation may be vague and nonspecific. There is a wide clinical spectrum, with signs and symptoms depending on the severity of cardiac decompensation and the age of the child. Myocarditis can be subclinical, acute, or fulminant. The spectrum of presentation varies from completely asymptomatic to cardiogenic shock, with dyspnea, arrhythmias, and congestive heart failure along the continuum (9). Children <1 yr of age often present with poor appetite, fever, irritability, cyanosis, or diaphoresis. Older children more commonly present with abdominal pain, diarrhea, and lethargy (10).

The two case presentations of pH1N1-09 influenza discussed here are of interest because neither patient presented with a classic influenza-like illness in the initial phase of the infection or with respiratory compromise in the later phase. This atypical presentation, along with false-negative influenza testing, led to a delay in diagnosis. In retrospect, each patient had unrecognized signs and symptoms of cardiogenic hypoperfusion. Patient A had neurologic and gastrointestinal symptoms at initial presentation, whereas patient B had only gastrointestinal symptoms. It is notable that neither patient presented with dyspnea or cough, which is the most common clinical symptom in children with myocarditis and influenza, respectively.

CONCLUSION

The pH1N1-09 influenza infection can cause fulminant myocarditis in the healthy pediatric population. The clinical presentation may be nonspecific, and the lack of pulmonary symptoms may make diagnosis difficult. Pericardial effusion in the setting of influenza should raise suspicion for viral myocarditis. Significant effusions should be drained, but drainage alone may be insufficient treatment for cardiogenic shock. As with other types of

viral myocarditis, ECMO support may offer an effective bridge to recovery of heart function. Influenza-associated myocarditis requires a high index of clinical suspicion for a timely diagnosis, especially in pediatric patients for whom pH1N1-09 influenza infection is suspected.

References

1. Mamas MA, Fraser D, Neyses L. Cardiovascular manifestations associated with influenza virus infection. Int J Card. 2008; 130:304–309.
2. Centers for Disease Control and Prevention. [Accessed December 28, 2009] 2009 H1N1 flu situation update. Available at http://www.cdc.gov/h1n1flu/updates/090409.htm
3. Centers for Disease Control and Prevention. [Accessed December 28, 2009] 2009 H1N1 flu U.S. situation update. Available at http://www.cdc.gov/h1n1flu/updates/us
4. Centers for Disease Control and Prevention. 2007–08 U S influenza season summary. MMWR Morb Mortal Wkly Rep. 2008; 57:692–700. Available at http://www.cdc.gov/flu/weekly/weeklyarchives2007-2008/07-08summary.htm. [PubMed: 18583957]
5. Libster R, Bugna J, Coviello S, et al. Pediatric hospitalizations associated with 2009 pandemic influenza A (H1N1) in Argentina. N Engl J Med. 2010; 362:45–55. [PubMed: 20032320]
6. The Australia and New Zealand Extracorporeal Membrane Oxygenation Influenza Investigators. Extracorporeal membrane oxygenation for 2009 influenza A (H1N1) acute respiratory distress syndrome. JAMA. 2009; 302:1888–1895. [PubMed: 19822628]
7. Moore DL, Vaudry W, Scheifele DW, et al. Surveillance for influenza admissions among children hospitalized in Canadian immunization monitoring program active centers, 2003–2004. Pediatrics. 2006; 118:e610– e619. [PubMed: 16950953]
8. Bhat N, Wright JG, Broder KR, et al. Influenza-associated deaths among children in the United States, 2003–2004. N Engl J Med. 2005; 353:2559–2567. [PubMed: 16354892]
9. Batra AS, Lewis AB. Acute myocarditis. Curr Opin Pediatr. 2001; 13:234–239. [PubMed: 11389357]
10. Vashist S, Singh GK. Acute myocarditis in children: Current concepts and management. Curr Treat Options Cardiovasc Med. 2009; 11:383–391. [PubMed: 19846036]

Table 1

Laboratory values

	Patient A	Patient B
WBCs	28.0 (3.3–11 10^9/L)	8.0 (4.5–13.5 10^9/L)
Hematocrit	41.6 (37–47%)	41.3 (34–40%)
Platelets	276 (13–400 10^9/L)	140 (165–415 10^9/L)
Potassium	4.2 (3.7–5.1 mEq/L)	4.4 (3.6–5 mM/L)
CO_2	20 (22–29 mEq/L)	14 (25–33 mM/L)
BUN	11 (7–24 mg/dL)	31 (7–20 mg/dL)
Creatinine	0.2 (0.5–1.6 mg/dL)	0.8 (0.5–0.9 mg/dL)
AST	124 (12–33.9 U/L)	207 (12–38 U/L)
ALT	44 (8–38.2 U/L)	50 (7–41 U/L)
Total bilirubin	0.2 (0.1–1.5 mg/dL)	0.4 (0.3–1.3 mg/dL)
LDH	456.3 (135–214 U/L)	—
Arterial blood gas	7.40/32/177/19/−4	7.45/27/98/19.1/−3
INR	1.4 (0.7–1.3)	1.32 (0.87–1.16)
Lactate	38.2 (4.5–19.8 mg/dL)	3.5 (0.5–1.6 mmol/L)
Troponin (0–0.8 ng/mL)	5.65	51.04
CK-MB (0–5.5 ng/mL)	224.7	70.1
BNP (0–100 pg/mL)	4629	7292
CSF	RBCs 2	—
	WBCs 3	—
	Neutrophils 0	—
	Protein 17	—
	Glucose 100	—
	Gram stain (−)	—

WBCs, white blood cells; BUN, blood urea nitrogen; AST, aspartate transaminase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; INR, international normalized ratio; CK-MB, creatine kinase MB; BNP, brain natriuretic peptide; CSF, cerebrospinal fluid; RBCs, red blood cells.