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Myocardial dysfunction during H1N1 influenza infection☆,☆☆

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Abstract

Purpose: The purpose of the study is to evaluate the incidence and hemodynamic consequences of right ventricular (RV) and left ventricular (LV) dysfunction in critically ill patients with H1N1 infection.

Patients and methods: This is a retrospective analysis of all patients admitted to the intensive care unit of an academic hospital between October 2009 and March 2011 with severe H1N1 infection. Hemodynamic measurements and respiratory conditions were noted daily during the intensive care unit stay.

Results: Forty-six patients were admitted with severe H1N1 infection. Echocardiography was obtained in 39 patients on admission: 28 (72%) had abnormal ventricular function, of whom 13 (46%) had isolated LV abnormalities, 11 (39%) had isolated RV dysfunction, and 4 (14%) had biventricular dysfunction. Echocardiography was repeated in 19 of the 39 patients during their hospitalization: RV function tended to worsen with time, but LV function tended to normalize. The ventricular abnormalities were not associated with history, severity of the respiratory failure, or hemodynamic status. However, patients with ventricular dysfunction needed more aggressive therapy, including more frequent use of vasopressor and inotropic agents and of rescue ventilatory strategies, such as inhaled nitric oxide, prone positioning, and extracorporeal membrane oxygenation.

Conclusions: These observations emphasize the high incidence of cardiac dysfunction in patients with H1N1 influenza infections.

1. Introduction

During the H1N1 influenza pandemic in 2009 to 2011, some patients developed severe complications leading to hospitalization in an intensive care unit (ICU) [1–5]. These complications often occurred in young individuals, pregnant women, or morbidly obese patients or in patients with comorbidities, such as chronic lung or cardiac disease or immunosuppression [6,7]. Most reports of complications associated with influenza infection focused on respiratory failure [6,7], but although most patients had single organ failure, other organs may be involved. Indeed, influenza infection is associated with cytokine release and activation of inflammation [8,9], and microcirculatory alterations were common in these patients [10], suggesting a systemic disease. Myocarditis may occur during acute influenza infection [11,12], and there have been a few reports of myocardial involvement specifically during H1N1 infection

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[13–15]. In addition, myocardial depression is present in most severe cases of septic shock, and shock was present in up to 58% of patients with H1N1 [3,5]. Although the exact mechanisms underlying the myocardial depression of sepsis have not been well defined, release of cytokines seems to be involved [16]. One may thus hypothesize that myocardial depression may also occur in influenza infection, either as a result of viral-triggered inflammation or direct myocardial viral infiltration.

The prevalence of myocardial dysfunction in H1N1 influenza infection and, if present, its hemodynamic consequences are not well known. On the one hand, the myocardial depression may be masked by the decrease in left ventricular (LV) afterload, related to peripheral vasodilatation, and the tachycardia. On the other hand, the severe respiratory conditions, including high positive end-expiratory pressure (PEEP) levels, may alter right ventricular (RV) function [17]. Several factors may, therefore, influence myocardial alterations in H1N1 infections.

We reviewed the hemodynamic and echocardiographic data of all patients with suspected or confirmed H1N1 influenza A infection hospitalized in our department during the pandemic period of 2009 to 2011, to determine the incidence and hemodynamic consequences of RV and LV dysfunction in these patients.

2. Methods

All patients with H1N1 infection admitted to our department of intensive care between October 2009 and March 2011 were included. Patients were divided into 3 groups according to the World Health Organization definition [18]: probable, suspected, or confirmed H1N1 infection. Diagnosis was based on real-time polymerase chain reaction or detection of influenza antigen from nasal swabs or bronchoalveolar lavage specimens.

Baseline characteristics were collected for all patients, including preexistent cardiopathy (known ischemic cardiac disease, moderate to severe valvular disease), and an Acute Physiology and Chronic Health Evaluation II score was calculated. Extracorporeal membrane oxygenation (ECMO) was initiated for the treatment of refractory hypoxemia, associated or not with hypercapnia, which occurred despite optimization of mechanical ventilation settings and use of rescue acute respiratory distress syndrome therapies (including prone positioning and inhaled nitric oxide [NO]). The initial mode of ECMO was veno-venous with centrifugal blood pump-driven circuit flow and low-resistance oxygenators.

Echocardiography was performed routinely on admission and repeated later during the ICU stay if considered necessary by the attending physician to address specific clinical questions. All echocardiographic examinations were performed by an experienced echocardiographer with several years of echocardiography practice (DF and LB) according to standard protocol following the American Society of Echocardiography guidelines and reviewed by a senior echocardiographist (DDB). Measurements were not performed in duplicate.

A Philips Sonos 5500 (Philips, Eindhoven, The Netherlands) was used for transesophageal echocardiography and a Toshiba Xario (Toshiba Xario SSA-660A; Toshiba Medical systems, Zoetermeer, The Netherlands) for transthoracic echocardiography. The LV ejection fraction (LVEF) was estimated by eyeball examination on short-axis views. Left ventricular function was further classified into normal (LVEF >60%), slightly to moderately altered (LVEF, 45%-60%), moderately to severely altered (LVEF, 30%-45%), and severely altered (LVEF<30%) [19]. Stroke volume was determined as the area of the LV outflow tract multiplied by the velocity time integral of the pulse wave Doppler across the aortic valve. Cardiac output was computed as stroke volume multiplied by heart rate.

Right ventricular function was assessed in several ways. The RV end-diastolic area (EDA) was measured, and the ratio between EDAs of the right and left ventricles was calculated (RVEDA/LVEDA). This ratio classifies RV function as normal (<0.6), moderately altered (0.6-0.8), moderate to severely altered (0.8-1), and severely altered (>1) [20]. The peak systolic velocity of the tricuspid annulus was also obtained on a 4-chamber view using tissue Doppler imaging. Systolic pulmonary artery (PA) pressure was determined by measuring the peak systolic pressure gradient from the RV to the right atrium. This was calculated using the modified Bernoulli equation, $4v^2$, where v is the maximum velocity of the tricuspid valve regurgitant jet, measured by continuous wave Doppler, added to the estimated right atrial pressure. The presence of paradoxical movement was evaluated in short-axis and longitudinal views. Finally, we also measured respiratory variations in the inferior vena cava [21] and, with transesophageal echography, the respiratory collapse of the superior vena cava [22].

Hemodynamic variables (cardiac output, PA occlusion pressure [PAOP]) were collected at the time of the echocardiographic examination using a PA catheter (PAC) when inserted, with the exception of systolic pulmonary pressure, which was obtained from the PAC or estimated by echography. All measurements were performed at end expiration. Ventilatory variables and vasoactive drug doses were collected online using a data management system (Critical Care Manager; PICIS SAS, Paris, France). We also retrieved laboratory values closest to the time of the echocardiographic study, notably creatine kinase, lactate dehydrogenase, and high-sensitivity cardiac troponin I levels.

2.1. Statistical analysis

Statistical analyses were performed using SPSS (IBM SPSS Statistics 19 for windows; Chicago, IL). Descriptive statistics were computed for all study variables. A