

Influenza A (H1N1) Pneumonia in an Immunossuppressed Patient after Heart Transplantation

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The role of the immune response during Influenza H1N1 virus infection is not yet fully established, but it is believed that it decisively participates in the severity of the disease as well as in the development of acute respiratory distress syndrome. The role of immunomodulating therapies in the control of viral infections is not a consensus either, and data from the literature defining the indications for their use are lacking. The present report is, to our knowledge, the first on a heart transplant patient who developed H1N1 virus infection and had a favorable outcome, thus generating discussion on the real role of immunosuppressive therapy as a risk factor for the severe form of the disease.

O papel da resposta imunológica durante a infecção pelo vírus Influenza H1N1 não está totalmente estabelecido, mas acredita-se que atue de forma decisiva no agravamento do quadro e no aparecimento da síndrome de desconforto respiratório agudo. O papel de terapias imunomoduladoras no controle de infecções virais também não é consensual e faltam dados de literatura para se definir as indicações de seu uso. Neste relato de caso, apresentamos, segundo nosso conhecimento, pela primeira vez, o relato de um paciente transplantado cardíaco que apresentou infecção pelo vírus H1N1 e evoluiu de forma favorável, trazendo um questionamento sobre o real papel da terapia imunossupressora como fator de risco para a forma grave da doença.

Introduction

In the current influenza pandemic with the Influenza H1N1 virus, some factors have been associated with an increased risk for a more severe disease, among which, immunosuppressive conditions. In this case report, for the first time, to our knowledge, we present a heart transplant patient who was receiving immunosuppressants and developed Influenza A (H1N1) virus infection; we also discuss the role of these drugs in the treatment and consequent clinical outcome of the disease.

Case Report

A 45-year-old female Caucasian patient underwent heart transplantation one year and seven months earlier due to cardiomyopathy secondary to chemotherapeutic agent toxicity. The patient had a history of hypertension, diabetes mellitus, and multiple sclerosis. She received home oxygen therapy via nasal cannula, at a 2 L/min flow, due to a chronic lung disease resulting from recurrent pneumonia and right paralysis of the diaphragm following previous cardiac surgeries. She was receiving immunosuppressive therapy with corticosteroid, cyclosporine and sodium mycophenolate, in addition to medication to control hypertension and diabetes mellitus (oral hypoglycemic agents).

The patient sought the emergency care service of *Instituto do Coração* on August 2, 2009 with a complaint of productive cough and progressive worsening of dyspnea for ten days. She reported to have had fever in the three previous days. On baseline physical examination, the patient was in good general state of health, hemodynamically stable, however with worsening of hypoxia, thus requiring a higher oxygen concentration (oxygen mask). A nasopharyngeal swab was collected for Influenza A (H1N1) virus test using the real-time PRC technique (RT-PCR). Empirical treatment was started with oseltamivir, ceftriaxone and clarithromycin.

CT scan of the chest was performed at the beginning of treatment (Figure 1), showing: right middle and inferior lung lobes with reduced volume with elevation of the right diaphragm dome (already seen in previous tests); pulmonary consolidation in the right inferior lobe with air bronchograms; and extensive involvement of the left lung with diffuse ground glass opacities. Baseline C-reactive protein level was 160.00 mg/mL (reference value of 5 mg/L) and complete blood count was normal: hemoglobin 13.1g/dL; white blood cells 5,600/mm³; neutrophils 4,032/mm³ with no band cells; and platelets 201,000/mm³. Blood cultures (two aerobic/anaerobic pairs) were negative and qualitative test for Influenza A (H1N1) virus using RT-PCR was positive.

During hospitalization, the patient required non-invasive ventilation support, which was used intermittently. There was progressive improvement of dyspnea and hypoxia, with return to the baseline pattern after approximately seven days. Clinical improvement was accompanied by a reduction in C-reactive protein levels: 101 mg/dL (08/04); 39 mg/dL (08/07); 16 mg/dL (08/12); and 2.25 mg/dL (08/17). In relation to the immunosuppressive drugs, usual doses were maintained during hospitalization. The patient was discharged 14 days after admission in conditions similar to those prior to the infection.

Key Words

Influenzavirus A (H1N1); Heart Transplantation; Immunosuppression; Pneumonia.

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Case Report

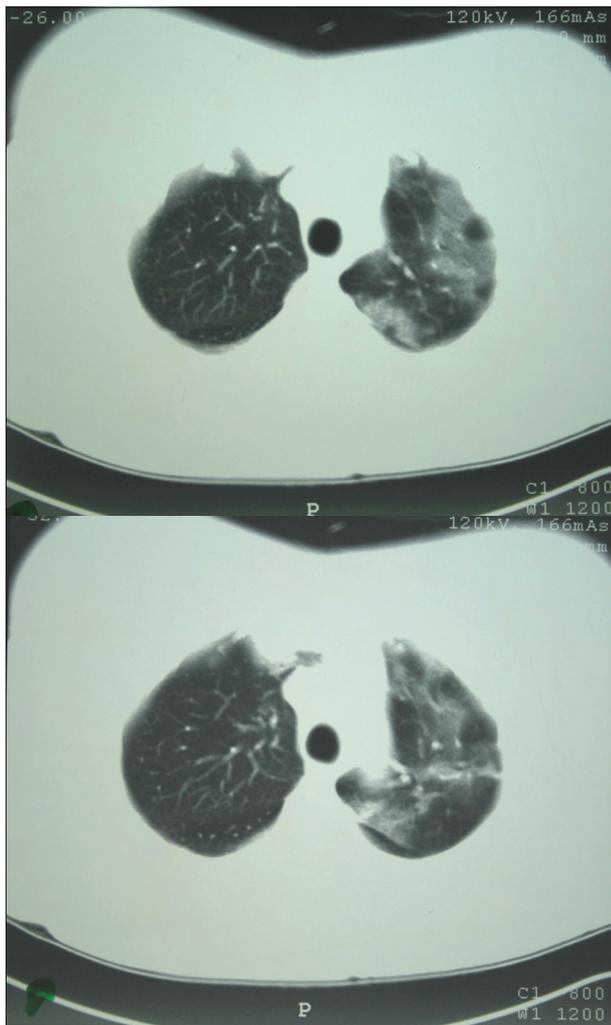


Figure 1 – CT-scan of the chest images showing extensive involvement of the left lung with diffuse ground glass opacities.

Discussion

In March 2009, there was an outbreak of Influenza A H1N1 virus infection in Mexico¹. It rapidly spread worldwide and, in June 11, 2009, the World Health Organization (WHO) moved the alert level to the highest level of a pandemic. The

latest WHO's data show more than 200 thousand confirmed cases worldwide, almost 60% of which concentrated in the Americas². The exact number of cases in Brazil is not available, since as from July 16, the Ministry of Health has prioritized notification, investigation and treatment only of the cases with Acute Respiratory Distress Syndrome (ARDS) and of people with risk factors for disease complications: obese individuals; pregnant women; immunocompromised individuals; those with chronic diseases; children under two years of age; and the elderly. Until August 22, there were 5,206 confirmed cases of ARDS due to Influenza A H1N1 in Brazil, with a total of 557 deaths^{3,4}.

In this pandemic, a trend has been observed of a greater number of cases of ARDS and deaths among populations at younger age ranges for Influenza A H1N1 than for seasonal influenza; a significant percentage of those (approximately 45%) had no risk factors for complications³⁻⁵.

Most of the deaths result from severe pulmonary involvement with rapid progression to ARDS and multi-organ failure⁶. Lung injury is caused, in most of the patients, by an effect of the influenza virus infection itself and not by secondary nosocomial infections. Possible mechanisms include direct injury to the respiratory epithelium by the virus and lesion secondary to the exuberant inflammatory response generated by a storm of cytokines and other inflammatory mediators⁷.

The case reported refers to a heart transplant patient, therefore classified in the population at a higher risk of complications due to immunodepression and a small baseline pulmonary function reserve. At baseline, extensive pulmonary involvement by the infection was identified. Thus, the inflammatory response generated was expected to lead to severe ARDS. However, this was not the outcome observed. Despite worsening of the baseline hypoxia and need for non-invasive ventilation, the patient did not develop respiratory failure or other organ failure.

We believe that the fact that the patient was receiving immunosuppressive therapy may have modulated the deleterious effect that an exacerbated inflammatory response would have generated, thus sparing her from a more severe form of Influenza A H1N1 virus infection. Should this finding be observed in similar cases, it will possibly influence the management of the disease, since immunosuppressive therapy may modulate the pulmonary and systemic inflammatory response that significantly contributes to the complications related to the disease.

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