

Viral co-infection with dengue and H1N1 virus in a critical care setting

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Abstract

We describe a 23-year-old man with no history of any other illness contacting H1N1 infection during convalescence from dengue fever. The patient had bilateral pneumonia with renal and hepatic dysfunction. The patient was treated successfully with oseltamivir and noninvasive ventilation along with other supportive measures. Despite multiorgan involvement and severe pulmonary involvement, he had a rapid improvement and did not require invasive ventilation. The possibility of the preceding or concomitant dengue viral infection reducing the severity of H1N1 infection was considered. It may be possible for two viruses to infect the same cell and as such, there may be interaction of the pathologic pathways of the two viruses, leading to change of virulence or altered host response. Such an interaction between the two viruses may be clinically important in the setting of the current H1N1 pandemic and the increased geographic distribution of the dengue virus.

Key words: Co-infection, dengue, H1N1

Introduction

Management can be challenging, in an intensive care setting, in case a patient is afflicted with more than one microbiological infection. It may be possible for two viruses to infect the same cell and as such, there may be interaction of the pathologic pathways of the two viruses, leading to change of virulence or altered host response. We present a case of concomitant infection with dengue and H1N1 virus with an unexpected rapid recovery and milder symptoms of influenza.

Case Report

A 23-year-old man was referred to our institute from a peripheral hospital. The patient had a history of fever, malaise, cough, sore throat, and breathlessness since last 7 days. His

dengue serology was positive for IgM. His platelet count was 14,000/mm³ and was transfused with single donor platelets.

On admission, he was conscious and oriented; had blood pressure of 126/80 mmHg; pulse rate of 102/min; respiratory rate of 26/min; was febrile; and peripheral oxygen saturation was 92% on facemask with oxygen flow rate of 10 L/min. There were bilateral lower limb petechiae. On auscultation of the chest, breath sounds were found to be decreased bilaterally in the lung bases and crackles were present in the mid zones of the lung fields. Clinical examination of other systems was normal.

Investigations revealed—hemoglobin 10.6 gm/dL; total white blood cell count 11,200/mm³; platelets 60,000/mm³; serum sodium 138 mmol/L; potassium 3.7 mmol/L; blood urea 124 mg/dL; and creatinine 2.6 mg/dL. Liver function test showed total bilirubin 2.7 mg/dL with directly reacting fraction at 0.6 mg/dL, serum glutamic oxaloacetic transaminase (SGOT) 2560 IU/L, and serum glutamic pyruvate transaminase (SGPT) 5591 IU/L, and a prothombin time of 32 s (control 13 s). The chest skiagram (AP view) showed bilateral diffuse infiltrates and ultrasonography revealed ascites with bilateral moderate pleural effusion. Arterial blood gas analysis showed a pH of 7.38, PCO₂ 46 mmHg, PO₂ 69.1 mmHg, and standard bicarbonate of 26 mmol/L.

Dengue viral infection was confirmed by dengue serology. Screen for malaria and typhoid was negative. Blood and

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urine samples for microbiological culture were negative. Nasal and pharyngeal swab for H1N1 testing was positive. Serial sputum examination for AFB was negative. Therapy with oral oseltamivir 150 mg twice daily along with azithromycin 200 mg once daily was started. Four units of fresh frozen plasma were transfused.

The next day, the patient's condition deteriorated clinically with an increase in the respiratory rate to 36/min and a fall in oxygen saturation to 76% on facemask with 10 L/min oxygen flow. Chest auscultation revealed bilateral crackles with decreased air entry in the lower zones. He was shifted to the H1N1 intensive care unit (ICU).

Fruusemide 40 mg intravenous daily was started. Central venous pressure-guided fluid therapy (normal saline) was started to maintain central venous pressure between 10 and 12 cm H₂O. Noninvasive ventilation with positive end expiratory pressure of 10 cm and pressure support (PS) of 12 cm was administered. The patient's oxygen saturation improved to 96%-98% and respiratory rate decreased to 14-16/min. Consequently, his liver function tests and renal function tests returned to normal. In the next 2 days, he was afebrile and ventilatory support was decreased to continuous positive airway pressure of 5 cm, and PS of 10 cm with inspired oxygen concentration reduced to 40%.

On day 4, he had a spike of fever and platelet count decreased to 24,000/mm³. The fever resolved with supportive measures and platelet counts increased spontaneously without further platelet transfusion in the next 24 h. The ventilatory support was gradually withdrawn by gradually increasing the period of nonsupported hours in between the non-invasive ventilation (NIV) support and withdrawn completely from ventilator by day 6. He was shifted out of the ICU to isolation ward, kept on observation there and subsequently discharged uneventfully on day 10.

Discussion

Infection of a single host by multiple pathogens may result in competition for host resources. Such an intrahost competition is predicted to shape a variety of pathogen traits, such as virulence, transmissibility, and resource partitioning that could affect epidemiology and virus population dynamics. However, literature is scarce regarding the impact of concomitant infection of dengue and H1N1.

The H1N1 virus replicates in the epithelial cells of the respiratory system.^[1] Deregulation of proinflammatory cytokines from macrophages has been shown to be important in the pathogenesis of acute respiratory distress syndrome (ARDS)

by influenza viruses.^[2] In addition, influenza viruses cause degeneration of infected cells through induction of apoptosis.^[1,3] However, apoptosis is a host defence mechanism and the induced apoptosis of the infected cells limits the continuity of the infection.^[2,3] Infection with H1N12009 is well documented to cause ARDS.^[4,5] The respiratory epithelium is also a target for dengue virus.^[6] As both the infections are known etiologic factors of ARDS, concomitant infection with both was expected to cause severe ARDS in this patient. However, contrary to our expectation, the respiratory involvement was mild enough to be managed with noninvasive ventilation. Moreover, he had a speedy recovery from the respiratory involvement.

ARDS severity depends on release of inflammatory mediators in response to tissue damage or noxious stimuli. ARDS involves stimulation of cellular and humoral immunity in an uncontrolled way, leading to a vicious cycle of tissue damage. cPLA2 (cytosolic phospholipase A2) stimulation is known as a major pathogenic pathway in the development of ARDS and inhibition of the cPLA2 enzyme may be helpful in preventing development of ARDS.^[7] Dengue viruses cause apoptosis in human neuroblastoma cells by stimulating the cPLA2 enzyme.^[8] The respiratory epithelial cell involvement with dengue infection is associated with expression of IL-6 through a NF-κB-dependent pathway, and expression of chemokine RANTES.^[5] Expression of IL-6 and RANTES points to a role of apoptosis. Dengue virus infection also produces a state of immunosuppression, mediated through cytotoxic factor (CF) and suppressor factor produced by T lymphocytes in spleen. CF destroys macrophages and a subpopulation of T lymphocytes, thus producing a nonspecific immunosuppression.^[9]

We offer two possible mechanisms to explain the lower severity of the respiratory involvement and the faster recovery of the patient. First, dengue virus infection may have induced apoptosis in the respiratory epithelial cells, which were infected with the H1N1 virus. Subsequently this limited the H1N1 pneumonia and caused a rapid clearance of the infection. Second, the immunosuppression caused by the dengue viral infection decreased the signaling of the proinflammatory pathways, thereby decreasing the quantum of cellular and humoral proinflammatory mediators required for the continuity of the vicious cycle of inflammation as in ARDS.

During the pandemic of the novel H1N12009 influenza, the outbreaks of dengue virus infections also occurred in many geographic locations, which were experiencing the pandemic of the H1N12009. As both the viruses are circulating in the same community, at the same time, in many locations, there was the likelihood of people being afflicted by concomitant infection with both the viruses. Clinical status in case of concomitant infection with H1N1 and dengue should be

cautiously interpreted. Although the severity of H1N1 may be clinically less obvious because of lesser immune response due to the immune suppression by the dengue virus, both the virus can cause some specific organ damage, which needs to be evaluated timely. Severity of H1N1 in a patient with dengue should not only be clinically evaluated but also by laboratory tests for viral load.

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