**An atypical patient with 2009 influenza (H1N1) infection and multiple organ dysfunctions**

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In this study, we report a case infected with H1N1 influenza virus and developed complications of multiple organ dysfunction (MOD). Also, we describe in this work the clinical course and successful treatment of the patient. We discussed our experience in the diagnosis and treatment of the patient with an atypical disease.

**Key words:** Influenza A, H1N1, Multiple organ dysfunctions.

**INTRODUCTION**

A novel influenza virus originating from swine emerged in North America in April, 2009, and spread worldwide expeditiously. This swine-origin H1N1 influenza virus caused virus detection in 17,410 patients and 115 deaths in 62 countries in the Americas, Europe, Asia and Australasia in June, 2009 (Peiris et al., 2009). Most patients with H1N1 virus infection were self-limited, and had common febrile respiratory illness and symptoms similar to those of seasonal influenza (cough, sore throat, rhinorrhea, headache, and myalgia) (Dawood et al., 2009). Approximately, 38% of cases had vomiting or diarrhea.

However, some patients had more severe symptoms and atypical manifestations, such as multiple organ dysfunction (MOD), which was one of the dangerous medical conditions and hard to manage. Currently, there is little information about how to treat patients with 2009 influenza (H1N1) infection and MOD. Here, we report that an atypical patient with 2009 influenza (H1N1) infection presented with acute respiratory distress syndrome (ARDS), obstructive jaundice, renal insufficiency and coagulopathy and was successfully treated.

**MATERIALS AND METHODS**

A 37-year-old obese man (body mass index, of 31 kg/m\(^2\)) that complained of fever, anorexia, fatigue, diarrhea, and oliguria, and was admitted to Xijing hospital, Xi'an, China on November 9th, 2009 was involved in the study. He denied any significant medical history or regular medication prior to the illness, and any remarkable family history. He complained of cold and fatigue, which started near three weeks ago, and displayed high fever (39.3°C), diarrhea (4 to10 times per day) and shortness of breath. Three days later, his general conditions were worsened by oliguria (400 ml/d) and diffuse bilateral lung infection, which was confirmed by a chest radiograph. He did not respond well to 1 g of cefmenoxime treatment for 10 days before admission.

**RESULTS**

On admission, his vital signs were normal, but with pulse oxygen saturation of 88% (with supplemental oxygen 3 L/min) and oliguria (210 ml/d). Physical examination found sporadic hemorrhagic spots on his arm, and pitting edema on his ankles. His diffused pulmonary infiltration was further demonstrated by repeated chest X-ray (Figure 3C). Laboratory tests indicated that there was no abnormal detection in urine routine, white blood cell counts and haematoglobin, but he had lower platelet counts, prolonged prothromb time, and higher levels of blood D-dimer, serum creatinine, cystatin, urea nitrogen, ferroprotein, and bilirubin (Figures 1 to 3). Furthermore, he displayed higher levels of blood myoglobin (695.7
Figure 1. Effects of H1N1 infection on blood system. The prothrombin time (A), serum D-dimer concentrations (B), peripheral blood platelet (C), and white blood cell counts (D) of the patient were longitudinally examined. In addition, his bone marrow smears were taken for Wright/Giemsa Staining (E). The grey zone in A-D refers to the normal range of each measure.

ng/ml, normal range: 0 to 70 ng/ml) and C reactive protein (CRP, 151 mg/L, normal range: 0-5 mg/L), but lower levels of serum complement C3 (0.81g/L, normal range: 0.9 to 1.8g/L). In addition, he had obstructive jaundice, like cholangiolitis, but he had no obvious biliary tract obstruction in his liver, as determined by ultrasound imaging. Bone marrow aspiration and biopsy revealed erythroid hyperplasia with many premature macrophages (Figure 1E). These results indicate that the patient suffered from MOD. The patient was treated with 3 g of mezlocillin sodium twice per day, supplemented with fluid infusion, nutrition support, and acidosis correction for two days. However, his symptoms deteriorated with lower blood pressure (80/50 mm Hg), and he developed anuria (10 ml/d), hypoxemia, coagulopathy, anaemia, metabolic acidosis, worsening liver function, and heart failure. Based on his conditions, he was treated with continuous renal replacement therapy (CRRT) for nine days (replacement fluid was 2 L/h, 24 h/d for 2 d, and then 10 h/d for 7d), blood plasma replacement therapy (BRT) for two days (2 L/d) to maintain the stability of internal environment. In addition, he was treated intravenously with dopamine (2.17 µg/kg/min) for six days to maintain the blood pressure. He was suspected for H1N1 infection and his pharyngeal swab sample tested positive for H1N1 infection; determined by real-time reverse transcription PCR, which was confirmed by a repeat test at the Xi’an Center for Disease Control and Prevention on Nov. 14. The patient was immediately isolated and treated orally with 150 mg of Oseltamivir twice per day for five days,
Figure 2. Effects of H1N1 infection on renal function. The levels of serum cystatin (A), creatinine (B), urea nitrogen (C) and 24 h urine volume (D) were longitudinally monitored at indicated time points. The grey zone in A-D refers to the normal range of each measure.

intravenously with 10 g of gamma globulin for three days, and $10^6$ U of ulinastatin daily, accompanied by continual treatment with CRRT, liver-protective, and symptomatic therapy. His clinical symptoms and laboratory testing results gradually improved and were near normal by November 27 (Figures 1 and 2; Figure 3A, B, D). He received rehabilitation care for anemia, but he displayed slightly abnormal renal function. He was subjected to renal biopsy on December 1st that showed endocapillary proliferative glomerulonephritis. He was provided with written informed consent for releasing the case report, which was approved by the Institution Research Board of Xijing Hospital.

DISCUSSION

This is an atypical case with 2009 influenza (H1N1) infection. The clinical features of this patient were characterized by early fever (39.3°C, for three days) and diarrhea, complicated by MOD (APACHE score 17). Without initial antiviral therapy, he was tested positive for H1N1 infection four weeks after the onset of symptoms. The patient had dramatically lower platelet counts, and higher levels of serum D-Dimer, unlike other cases with H1N1 infection (Ayala et al., 2009; Dawood et al., 2009; Wiebe et al., 2009). His bone marrow aspiration and biopsy showed erythroid hyperplasia with increased number of premature macrophages. His liver function tests displayed obstructive jaundice (highly increased direct bilirubin), but without obviously biliary tract obstruction on imaging examinations, like cholangiitis. He had acute kidney injury and his renal biopsy showed endocapillary proliferative glomerulonephritis, which was not reported in other reports (Ayala et al., 2009; Dawood et al., 2009; Wiebe et al., 2009). These features indicated that the clinical manifestation of 2009 H1N1 varied and the specific viral test was valuable in any of the suspected patients, even after the presence of clinical symptom for a while. These clinical features also imply that the H1N1 virus may affect multiple organs in some individuals, which deserves further exploration. Our experience emphasizes the importance of a routine and early testing of H1N1 virus for suspected patients with unexplained symptoms during the epidemic season of a special virus, because without early antiviral therapy, the H1N1 virus may spread into many organs, leading to the development of MOD.

We believe that treatment with CRRT, BRT, and high doses of oseltamivir benefits H1N1-infected patients with MOD, although these therapeutic strategies have not been recommended (Rahier et al., 2010). Early CRRT and BRT should eliminate the inflammatory mediators and help in stabilizing the internal environment. These
Figure 3. Effects of H1N1 infection on liver function and chest X-ray examination of the case. The concentrations of urine total bilirubin (A) and direct bilirubin (B) were measured longitudinally at the indicated time points. The grey zone in A-B refers to the normal range of each measure. Chest radiographies were taken for the examination of inflammation in the lung of the patient before (C) and after treatment (D), respectively.

therapeutic strategies are critical for the management of H1N1-infected patients with MOD, because these therapies can promote the recovery of renal, hepatic, pulmonary and zymoplastic function, and help in the clearance of H1N1 virus by oseltamivir. This combined therapy successfully cured the patient and avoided the use of mechanical ventilation in the ICU, similar to other reports (Gordon, 2009; Kidd et al., 2009; Kumar et al., 2009).

REFERENCES