Swine H1N1 Infection in a Renal Transplant Recipient

Gulsum Ozkan,[1] Sukru Ulusoy,[1] Kubra Kaynar,[1] Funda Oztuna,[2] Muammer Cansiz,[1] Nazli Kazaz[3]

Abstract

Influenza pandemics have been observed in several periods throughout history. The first influenza pandemic of the 21st century began in Mexico in 2009 and has spread rapidly all over the world. Swine H1N1 has been officially declared a pandemic by the World Health Organization in June 2009. As has been observed in previous pandemics, pregnant women, adolescents, and immunosuppressed individuals are affected more severely in this pandemic. Despite several reports about the pandemic, there have not been any reports of swine H1N1 infection in individuals who underwent renal transplant. The aim of the current study was to present oseltamivir therapy in a swine H1N1-infected patient who underwent renal transplant 10 months earlier, and was thus under immunosuppressive treatment. To the best of our knowledge, this is the first case report of a swine H1N1 infection in a renal transplant recipient.

Key words: *Swine H1N1, Renal transplant, Oseltamivir*

Introduction

The World Health Organization (WHO) declared the level of swine influenza H1N1 a pandemic alert at phase 5 in April 2009 (1). The prevalence of influenza infections is increased owing to immunosuppressive drug use in patients who received solid-organ transplant and the course of infection is more severe in these patients compared with healthy individuals. Mortality is reduced, especially in immunosuppressed patients, by vaccination or initiation of oseltamivir treatment during the early period after onset of symptoms in case of infection (2). We present an immunosuppressed renal transplant recipient who was effectively treated by early initiated oseltamivir for mortal swine H1N1 infection.

Case report

A 37-year-old man had been on hemodialysis for approximately 16 years owing to chronic renal failure of an unknown cause and received renal transplant from a living donor (his father) 10 months earlier. His creatinine level was around 106.08 μmol/L (1.2 mg/dL) after the transplant, and he did not experience any rejection attacks. The patient was on immunosuppressive treatment consisting of tacrolimus 0.5 mg twice a day, sirolimus 1 mg/d, and prednisolone 7.5 mg/d.

The patient was admitted to our outpatient clinic with complaints of high fever (39ºC), cough, and widespread joint and muscle pain that had started 1 day earlier. At the time of admission, there were no temperature increase, edema, and limited range of motion in his joints on physical examination. His body temperature was 38.5ºC, oropharynx was hyperemic, and the results of a physical examination were normal, except for having an operation scar in the right lower abdominal quadrant.

His laboratory results at the time of admission were as follows: blood urea nitrogen 9.49 μmol/L (26 mg/dL), creatinine 114.92 μmol/L (1.3 mg/dL), hemoglobin 168 g/L (16.8 g/dL), white blood cell count 11.8×10^9/L (11 800/uL), high sensitivity C-reactive protein (hs-CRP) 0.19 mg/L (1.9 mg/dL), procalcitonin 0.00015 ng/L

From the Departments of [1]Nephrology, [2]Chest, [3]Internal Medicine, Karadeniz Technical University, School of Medicine
Address reprint requests to: *Dr. Gülsüm Özkan, Karadeniz Teknik Üniversitesi Tıp Fakültesi, Nefroloji Bilim Dalı, 61080 Trabzon, Turkey*
Phone: *+90 4623775686* ***Fax:*** *+90 462 325 22 70* ***E-mail:*** *gulsumozkan78@hotmail.com*

Experimental and Clinical Transplantation (2010) 4: 318-320

Copyright © Başkent University 2010
Printed in Turkey. All Rights Reserved.

(0.15 ng/mL), *cytomegalovirus* polymerase chain reaction (CMV PCR) negative, and sirolimus level 0.0049 ng/L (4.9 ng/mL). His hs-CRP level was raised to 1.12 mg/L (11.2 mg/dL) and procalcitonin to 0.00995 ng/L (9.95 ng/mL) on the following day. H1N1 infection was considered in the differential diagnosis owing to his symptoms of high fever, cough, myalgia, and immunosuppressive drug use. After a blood sample was drawn for real-time PCR swine H1N1, oral oseltamivir treatment at a dosage of 75 mg twice a day was initiated during the 24th hour, before obtaining the results of real-time PCR. Secondary bacterial pneumonia could not be excluded in the presence of cough (despite the results of a normal physical examination of the lungs and chest radiograph); because of the immunosuppressive status of the host, intravenous moxifloxacin 400 mg/d was added to the treatment. His immunosuppressive drugs were continued. His fever came under control during the 48th hour of the treatment, and H1N1 was found to be positive by real-time PCR. Five-day oseltamivir and 10-day moxifloxacin treatments were planned. Complaints of the patient improved after 2 days of treatment. The patient having hs-CRP level of 0.236 mg/L (2.36 mg/dL), procalcitonin level of 0.00284 ng/L (2.84 ng/mL), and creatinine level of 106.08 μmol/L (1.2 mg/dL) at the end of tenth day, he was discharged with complete clinical remission.

Discussion

Influenza A is an RNA virus belonging to the Orthomyxoviridae family. It has several serotypes classified according to the presence of surface glycoproteins: hemagglutinin (HA) and neuraminidase (NA). In particular, HA (H1, H2, H3) and NA (N1, N2) subtypes lead to infections in humans. These subtypes have caused pandemics during several periods throughout history (3).

Swine H1N1 infection is the first pandemic of the 21st century began in Mexico in the beginning of 2009 and has spread rapidly throughout the world. At the end of April 2009, the WHO has declared the level of swine influenza H1N1 a pandemic alert at phase 5, because it particularly affects young, pregnant, or lactating individuals (1).

Patients with immune deficiency constitute another risk group for the current pandemic. This group includes patients infected with HIV, solid-organ or hemopoietic–stem-cell transplant recipients, those receiving chemotherapy or long-term corticosteroid treatment, and patients with chronic renal failure. Because these patients are susceptible to all infections, they are also susceptible to influenza infections. Moreover, the course of infection is more severe in this patient group (2). The present case received immunosuppressive treatment owing to renal transplant.

The total mortality rate of the H1N1 pandemic is expected to be less than that of previous pandemics. However, vaccination is recommended in high-risk groups and initiation of neuraminidase inhibitors within the first 2 days of symptom onset is important in case of infection (4).

The use of neuraminidase inhibitors has increased since April 2009. Neuraminidase inhibitors, zanamivir, and oseltamivir (oral tablet) have become increasingly popular owing to increased resistance to amantadine and rimantadine. Effective treatment is provided by the administration of both drugs in the early period that is as soon as the initiation of clinical manifestations of the infection (5). We have initiated oseltamivir treatment 24 hours after onset of symptoms and clinical response was observed after 48 hours. Dosage adjustment of oseltamivir is necessary in renal impairment, especially in those with a glomerular filtration rate (GFR) < 30 mL/min. However, in renal transplant patients with GFRs > 30 mL/min, dosage adjustment is not necessary and no drug interactions with immunosuppressant drugs such as cyclosporine, mycophenolate mofetil, and tacrolimus have been reported. Thus, we did not do any dosage adjustment in our patient, and a choice of dosage was made of 75 mg twice a day because the patient had a GFR above 30 mL/min (6).

Immunosuppressive agents were used in patients undergoing organ transplant to avoid rejection; however, they also cause increased susceptibility to infections. Consequently, infections developing in this patient group also may trigger rejection. Critical adjustments are often needed in this patient group and there is often controversy about dosage reduction, cessation, or continuation of immunosuppressives in case of infection. In case of this infection having high

mortality rate, the same dosage of immunosuppressive drugs together with infection treatment was the treatment of choice in the present case considering rejection. The influenza infection was successfully treated without rejection, and the patient was discharged with a creatinine level of 106.08 μmol/L (1.2 mg/dL).

References

1. Tanaka T, Nakajima K, Murashima A, Garcia-Bournissen F, Koren G, Ito S. Safety of neuraminidase inhibitors against novel influenza A (H1N1) in pregnant and breastfeeding women. CMAJ. 2009;181(1-2):55-58.
2. Kunisaki KM, Janoff EN. Influenza in immunosuppressed populations: a review of infection frequency, morbidity, mortality, and vaccine responses. Lancet Infect Dis. 2009;9(8):493-504.
3. Hsieh YC, Wu TZ, Liu DP, Shao PL, Chang LY, Lu CY, et al. Influenza pandemics: past, present and future. J Formos Med Assoc. 2006;105(1):1-6.
4. Donaldson LJ, Rutter PD, Ellis BM, Greaves FE, Mytton OT, Pebody RG, et al. Mortality from pandemic A/H1N1 2009 influenza in England: public health surveillance study. BMJ. 2009;339:b5213.
5. Jefferson T, Jones M, Doshi P, Del Mar C. Neuraminidase inhibitors for preventing and treating influenza in healthy adults: systematic review and meta-analysis. BMJ. 2009;339:b5106. doi: 10.1136/bmj.b5106.
6. Davies BE. Pharmacokinetics of oseltamivir: an oral antiviral for the treatment and prophylaxis of influenza in diverse populations. J Antimicrob Chemother. 2010;65(suppl 2):ii5-ii10.