

# Influenza A/H1N1 Infection in a Renal Transplant Recipient: Early Recognition Prevented Unfavorable Results

## *Bir Renal Transplant Alıcısında Influenza A/H1N1 Enfeksiyonu: Erken Tanı İstenmeyen Sonuçları Önledi*

### ABSTRACT

Influenza A/H1N1 2009 rapidly created a pandemic after it was first reported in April 2009. This virus caused a wave of panic around the world because of the rapidity of transmission and the characteristics of the dying victims, which were apparently healthy young adults. The pandemic caused thousands of laboratory-confirmed cases and many deaths. Despite this high prevalence, few reports of infection and clinical results in renal transplant recipients have been described in the literature. Early recognition and prompt administration of oseltamivir may prevent severe respiratory disease. Here we describe a renal transplant recipient who presented early after symptom onset who was successfully treated with oseltamivir and broad spectrum antibiotics without dire clinical consequences.

**KEY WORDS:** Influenza A/H1N1, Early treatment, Renal transplant recipient, Swine flu

### ÖZ

Influenza A/H1N1 2009, 2009 yılında ilk olguların görülmesinden sonra hızlı şekilde bir pandemi meydana getirmiştir. Bu virüs bulaşma hızı ve özellikle genç sağlıklı erişkinlerde yol açtığı ölümler gibi özellikleri nedeniyle dünya çapında bir panik havasına neden olmuştur. Pandemi binlerce laboratuvar tanımlı olgu ve yüzlerce ölüme neden olmuştur. Yüksek prevalansına rağmen literatürde böbrek transplant hastalarında bu enfeksiyon ve klinik sonuçlarına ilişkin az sayıda bildirim mevcuttur. Erken tanı ve hızlı şekilde oseltamivir uygulaması şiddetli respiratuvar hastalığı önleyebilir. Biz burada H1N1/influenza A enfeksiyonu semptomlarının başlamasından kısa süre sonra başvuran oseltamivir ve geniş spektrumlu antibiyotiklerle tedavisi sonucu çabuk iyileşme gösteren bir böbrek transplant alıcısını sunmaktayız.

**ANAHTAR SÖZCÜKLER:** İnfluenza A/H1N1, Erken tedavi, Renal transplant alıcısı, Domuz gribi

### INTRODUCTION

Influenza A/H1N1 2009 created a pandemic after the first reports of infection on April 2009 (1). Its rapidity of spread and death toll, especially in apparently healthy young adults, caused a wave of panic around the world. The infection spread rapidly throughout Turkey and claimed many lives. The Health Ministry of Turkey initiated a nation-wide vaccination campaign aimed at people at risk. Despite numerous reports in the literature describing influenza A/ H1N1 virus infection in different patient populations, experience in immunosuppressed patients is quite limited to our knowledge. To date, only a few cases have been published

regarding Influenza A/H1N1 infection in renal transplant recipients.

Here we report Influenza A/ H1N1 infection in a renal transplant recipient in which early diagnosis and prompt treatment prevented catastrophic results.

### CASE REPORT

A 55-year-old male who had undergone paid living unrelated renal transplantation in Pakistan 3 years ago presented to the emergency department with a 3-day long complaint of self-reported fever, nausea, vomiting, malaise and flu-like illness (sneezing, runny nose, sore throat and postnasal discharge). The patient had

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returned to Turkey shortly after transplantation and had been followed regularly at outpatient transplantation clinic. He was doing well with a triple immunosuppressive regimen including everolimus 0.75 mg twice daily, tacrolimus 1 mg once a day and prednisone 5 mg once a day. His serum creatinine level was fluctuating between 1.2 and 1.5 mg/dl during follow-up. He was also receiving atenolol, omeprazole, aspirin, and premixed insulin twice daily. He never experienced a rejection episode or underwent a renal biopsy.

At initial assessment he looked anxious, blood pressure was 100/80 mmHg, body temperature was 37.8 C, pulse rate was regular at 84 bpm. The oropharynx was hyperemic but there was no thrush or cryptic tonsillitis. Cardiopulmonary examination revealed normal findings. No lymphadenopathy was noted in cervical and supraclavicular regions. The abdomen was soft and nontender and bowel sounds were normoactive. Biochemistry panel and complete blood count were as follows at admission to nephrology inpatient clinic: blood urea: 35 mg/dl, creatinine: 1.5 mg/dl, uric acid: 6.2 mg/dl, sodium: 137 mEq/L, potassium: 3.6 mEq/L, calcium: 9.6 mg/dl, phosphorus: 2.9 mg/dl, AST: 21, ALT: 19, albumin: 3.9 g/dl, total protein: 7.0 g/dl, c-reactive protein: 40.3, erythrocyte sedimentation rate: 13 mm/h, procalcitonin: 3.2, hemoglobin: 15.6 g/L, white blood cell count:  $13.8 \times 10^3/\text{ml}$ , platelets:  $237 \times 10^3/\text{ml}$ . While the chest X-ray appeared normal, computed tomography of the chest revealed bilateral pleural effusions and ground-glass and nodular opacities in left upper lung lobe (Figure 1).

The patient was hospitalized with concern of a possible H1N1 pandemic influenza A infection. He was commenced on oseltamivir 75 mg twice daily along with piperacilline tazobactam 4.5 gr tid. and placed in respiratory isolation. Throat swab for H1N1 influenza A virus (studied with inhouse real-time

PCR) was found to be positive 3 days after initiation of antiviral treatment. CRP and procalcitonin levels decreased during the course of the hospitalization. His complaints ameliorated and the patient was discharged on the 14<sup>th</sup> day of hospitalization.

## DISCUSSION

Novel Influenza A/H1N1 2009 infection, more commonly known in public as swine flu, was first identified in Mexico on April 2009 and reached pandemic proportions thereafter (1). This virus causes an influenza like illness (ILI) which is defined by centers for Disease Control (CDC) as fever (temperature  $>37.8$  C), and either cough or sore throat in the absence of another known cause (2) A confirmed case is described as ILI with positive test results for the 2009 H1N1 virus by either with real-time reverse transcriptase PCR or viral culture. CDC stopped reporting confirmed or suspected cases through weekly reports but continues to track hospitalization or deaths due to swine flue.

In Turkey, Influenza A/H1N1 2009 quickly became widespread and 627 patients had died as of January 19<sup>th</sup>, 2009. CDC estimated that 41-48 million cases, 183.000-378.000 hospitalizations and 8300-17100 deaths might have occurred due to influenza A/H1N1 pandemic between April 2009 and January 2010 (3). Despite this high prevalence, only two renal transplant recipients with laboratory confirmed influenza A/H1N1 were reported to date (4). This might be due to underreporting or timely vaccination of transplant recipients. Watcharananan et al. reported two renal transplant recipients who developed influenza A/H1N1 2009-associated pneumonia. One of their patients had returned to hemodialysis due to chronic allograft nephropathy but was still on prednisone treatment. The other patient was receiving cyclosporine, mycophenolate mofetil and prednisone. The latter patient required noninvasive mechanical ventilation due to worsening hypoxia and dyspnea. The authors commenced oseltamivir along with broad-spectrum antibiotics early at presentation. Chest CT revealed extensive nodular and ground-glass opacities in both lungs in both patients.

Our patient presented on the second day after the symptoms began, possibly due to heightened awareness and media hype about swine influenza in Turkey at that time. The symptoms at clinical presentation were somewhat mild and nonspecific in nature. He was subfebrile. However, procalcitonin level was moderately high. We believe the timely initiation of antiviral therapy prevented viral and/or superimposed bacterial pneumonia.

Previous studies have shown that inhibition of influenza virus replication as early as possible via administration of antiviral therapy reduces the duration and severity of illness (5). Another recent report also suggested that delayed presentation and initiation of antiviral therapy are responsible partly for some deaths (6). Marfo et al. (7) also reported the benefit of postexposure prophylaxis in a living-related renal transplant



**Figure 1:** Computed tomography of the chest showing bilateral pleural effusions and ground-glass and nodular opacities in left upper lung lobe.

recipient soon after the transplantation operation. In that case the donor had influenza A/H1N1 infection and early administration of oseltamivir prevented development of infection in the recipient who was under intense immunosuppression at that time. Our patient was not vaccinated for with pandemic influenza vaccine.

This case illustrates a very rare experience of novel influenza A/H1N1 2009 infection in a renal transplant recipient. Timely initiation of antiviral treatment effectively prevented respiratory deterioration even under immunosuppressive therapy.

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