

CASE REPORT

46 YEAR OLD FEMALE WITH WORSENING PNEUMONIA

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Abstract

Introduction

First noted in Mexico, the pandemic that started in late March and early April of 2009¹ was caused by the H1N1 influenza A virus that represents a quadruple re-assortment of two swine strains, one human strain, and one avian strain of influenza which had not been previously recognized²⁻⁴. Early documented cases of S-OIV in Mexico reported 2155 cases of severe pneumonia, including 821 hospitalizations and 100 deaths related to rapidly progressive pneumonia, respiratory failure, and acute respiratory distress syndrome. The increased incidence of pneumonia related hospitalizations and death is reminiscent of past influenza pandemics.

Case presentation

This is a case of a 46 year-old Caucasian female admitted to the hospital for worsening pneumonia, hypoxia, and an influenza-like-illness despite outpatient empirical antibiotic treatment from a recent

emergency room visit. Influenza A antigen was subsequently detected from an upper respiratory sample using a nasopharyngeal swab for viral culture and followed by real-time reverse transcriptase (RT)-PCR confirmation of H1N1 influenza A virus⁵. The clinical course, diagnostic studies, and imaging studies will be reviewed in this case presentation.

Conclusion

Patients requiring hospital admission and management for secondary bacterial pneumonia from a primary viral cause, in this case the influenza A (H1N1) virus, should continue to be managed as recommended per CDC guidelines. In patients that respond slowly to treatment with broad-spectrum antibiotics and neuraminidase inhibitor therapy, as demonstrated by this case, may be indicative of a more profound lower respiratory tract inflammatory response to pneumonia. In such patients, it may be necessary to give a longer antibiotic and neuraminidase inhibitor course^{6,7}.

Presentation of case

A forty six year old Caucasian female was admitted to the hospital with hypoxia associated with worsening shortness of breath, non-productive cough, fever, and fatigue. Two days prior to admission the patient went to the emergency room with a five-day history of fever, chills, non-productive cough, headache, fatigue and arthralgias that were not relieved by over the counter cough suppressant and Ibuprofen. A rapid influenza screening using only an oropharyngeal swab was negative in an outpatient clinic prior to the initial emergency room visit. Relevant history indicates that she lives at home with her nine year-old



Image 1: Infiltrate in the right middle lobe and possibly the lingula.

Hematological Studies					
	ER Visit	Admission	1st DAY	2nd DAY	Discharged 8th DAY
WBC	3.94 L	2.86 L	2.10 L	2.94 L	4.87
RBC	4.73	4.71	4.31	4.09 L	3.94 L
Hgb	12.9	12.6	11.5 L	10.9 L	10.5 L
Hct	37.7 L	37.7 L	35.1 L	32.9 L	31.4 L
MCV	80	80	81	80	80
MCH	27.3	26.8 L	26.7 L	26.7 L	26.6 L
MCHC	34.2	33.4	32.8	33.1	33.4
RDW	13.6	13.8	14.6 H	14.0	13.1
Plt Count	122 L	144 L	171	172	321
Neut %	81.4 H				
Lymph %	13.2 L				
Mono %	5.1				
Eos %	0.0				
Baso %	0.3				
Neut #	3.21				
Lymph #	0.52 L				
Mono #	0.20 L				
Eos #	0.00				
Baso #	0.01				
Neutrophils %					
Lymphocytes %					
Monocytes %					
Band Neutrophils					

Serum Chemistry					
	ER Visit	Admission	1st DAY	2nd DAY	Discharged 8th DAY
Sodium	131 L	138 Δ	137	138	143
Potassium	3.4	3.3	3.4	3.2 L	3.8
Chloride	99	101	107	107	107
Carbon Dioxide	20 L	21 L	20 L	20 L	29
Anion Gap	12.0	16.0	10.0	11.0	7.0
BUN	11	11	7	6	4 L
Creatinine	0.7	0.6	0.6	0.5	0.6
BUN/Creatinine Ratio	15.7	18.3	11.6	12.0	6.6
Glucose	144 H	126 H	96	98	106
Calculated Osmolality	273 L	286	281	283	292
Calcium	7.8 L	8.3 L	7.1 L	7.7 L	8.3 L
Ionized Calcium Calc	3.90 L	4.28 L		4.27 L	
Phosphorus				3.4	4.2
Magnesium				2.00	2.34
Iron					
TIBC					
% Saturation					
Unsat Iron Binding					
Ferritin					
Total Bilirubin	0.4	0.3			
AST	30	46 H Δ			
ALT	8	9			
Total Creatine Kinase		945 H			
CK-MB (CK-2)					
Troponin T					
Total Protein	6.7	6.6		5.4 L	
Albumin	3.9	3.5		2.8 L	
Globulin	2.8	3.1		2.6	
Albumin/Globulin Ratio	1.39	1.13			
Alkaline Phosphatase	66	64			

Table 1

son who also had similar symptoms including fever, cough, runny nose and fatigue for less than a week prior to her developing symptoms. Her son's symptoms lasted for two to three days, and resolved spontaneously without any complications or need for antibiotics. She is otherwise healthy and has no significant past medical history. She does not smoke cigarettes, drink alcohol, or use illicit drugs. There is no history of recent travels in or out of the country. All her immunizations are up to date except annual seasonal influenza vaccination. There was no history of wheezing, hemoptysis, night sweats, pleuritic chest pain, nausea, vomiting, diarrhea, weight loss, abdominal pain, exposure to persons with tuberculosis, exposure to animals, pets, or birds, and there were no risk factors for human immunodeficiency virus (HIV) infection. In the Emergency room, her temperature was 39.7°C, blood pressure 124/66, pulse 98, and respiratory rate 20 breaths per minute with 97% oxygen saturation on room air. On physical exam,

she was in mild distress, but able to complete full sentences. Auscultation of her lungs revealed bibasilar crackles, increased over the right base; the remainder of the physical exam was normal. Results of laboratory tests obtained in the emergency room are shown in Table 1. An electrocardiogram showed normal sinus rhythm. Chest X-ray confirmed infiltrates in the right middle lobe (*Image 1.0*). The patient was diagnosed with pneumonia and discharged from the emergency room with a prescription for Levofloxacin 500mg, once daily for seven days.

The patient returned to the emergency room two days later with progressive shortness of breath, a worsening non-productive cough, and fever. She was still taking Levofloxacin. On examination, her temperature was 39°C, blood pressure 100/60 mmHg, pulse 104, a respiratory rate of 22-24 breaths per minute, with 86% oxygen saturation on room air. The patient required 4 Liters of oxygen through a nasal canula to maintain an oxygen saturation of 90%. On examination, the patient appeared acutely ill, with dyspnea during conversation and diffuse crackles over the lungs. Repeat chest x-ray showed worsening of infiltrates in comparison to previous films (*Image 2.0*).

An electrocardiogram revealed a sinus tachycardia at the rate of 104, with normal axes and intervals, without any ST-segment or T-wave abnormalities. Arterial blood gas on room air showed a partial pressure of oxygen 48.7 mmHg, partial pressure of carbon dioxide 29.3, and pH 7.46. Complete blood counts revealed leukopenia with differential count of 78 neutrophils, 7 lymphocytes, 5 monocytes, and 10 bands. Hematologic and chemistry laboratory data are shown in Table 1. Specimens of blood and urine were also sent for bacterial and viral cultures and testing for viral antigens, which were all subsequently negative, including HIV. The patient did not produce any sputum. Urine for Legionella and streptococcal antigen were negative. Mycoplasma antibody was negative by IgM. Influenza screening was repeated using a nasopharyngeal swab and tested positive for influenza A, and subsequently confirmed for swine-origin influenza A (H1N1) virus (S-OIV) using real-time reverse transcriptase (RT)-PCR. A nasal swab culture was also sent to test for Methicillin-resistant *Staphylococcus aureus*. Levofloxacin was discontinued. Intravenous hydration, and broad-spectrum antibiotic coverage with vancomycin, ceftriaxone, azithromycin, and oral oseltamivir was started. The patient was admitted to the intensive care unit and

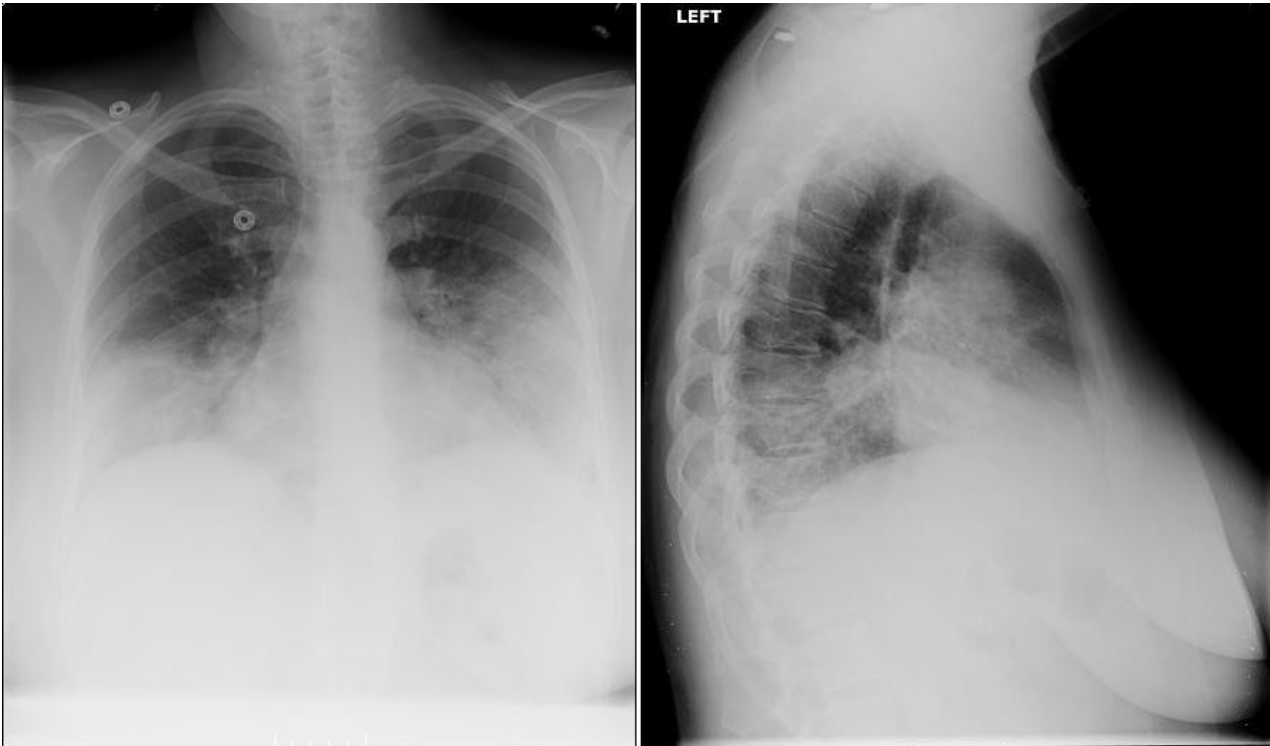


Image 2: Increasing bilateral pulmonary infiltrates.

placed in respiratory isolation.

Forty-eight hours into admission, the patient felt a sense of well-being. Blood pressure stabilized to her base line value of 120-125 mmHg. Her temperature decreased to 37°C, and she remained afebrile for the entire hospital course. The Methicillin-resistant *Staphylococcus aureus* (MRSA) screen was negative and vancomycin was discontinued. Ceftioxone was later discontinued on day five. Despite appearing clinically stable, she continued to require 3-4 liters of oxygen to maintain 90% saturation while in a sitting position. Oxygen saturation dropped to 80% while standing or with minimal activity. Diffuse crackles over the lungs were heard on auscultation. Four consecutive days of chest radiographs (*Image 3.0*), show no worsening or improvements of infiltrates.

Computed tomographic (CT) scan of the chest (*Image 4.0*), confirmed bilateral dense patchy infiltrates with consolidation, and mild diffuse honeycombing. The patient remained in respiratory isolation with continuous oxygen therapy and intravenous Azitromycin, and oral oseltamivir.

On the seventh and eighth day of admission patient showed a gradual improvement of oxygen saturation with 90-95% oxygen saturation on 2 liters of oxygen. All vital signs remained stable. Auscultation of the lungs revealed clearing sounds and milder crackles. A chest radiograph (*Image 5.0*), confirmed decreasing density of bilateral infiltrates. The patient was removed from respiratory isolation and discharged from the hospital with home oxygen therapy of 2 liters, and instructions to take three more days of oral Azithromycin (500 mg once a day) and osel-

tamivir (75 mg twice a day) to complete a total of ten days of antibiotics and neuraminidase inhibitor therapy.

Discussion

The majority of hospitalizations and subsequent documentable diagnoses of the novel swine-origin influenza A (H1N1) virus (S-OIV) per real-time reverse transcriptase (RT)-PCR have been secondary to patients presenting with an influenza-like-illness (fever, head-ache, muscle ache, fatigue, cough, and sore throat) and pneumonia⁹. Pneumonia is the most common complication of influenza and contributes to twenty-five percent of all influenza associated deaths. Uncomplicated cases of secondary bacterial pneumonia can be managed in an outpatient setting with empirical antibiotic coverage, in more severe cases the clinical course of each patient depends on the severity of concurrent infection and systemic manifestations, which ultimately may require prompt hospitalization with indefinite medical management.

Greater than eighty percent of the patients with H1N1 influenza A virus that present with a influenza-like-illness and that subsequently developed secondary bacterial pneumonia requiring hospitalization during this pandemic, ranged between the ages of 5 and 59 years of age¹⁰. This trend is different when compared to past influenza pandemics in which the younger and older age groups were mostly affected. Observation of the age distribution affected with H1N1 influenza A virus during this new pandemic suggests the theory of relative protection for persons who were exposed to the H1N1 strains during childhood before the 1957 pandemic. Our patient's age is 46 years fitting the trend for this pandemic.

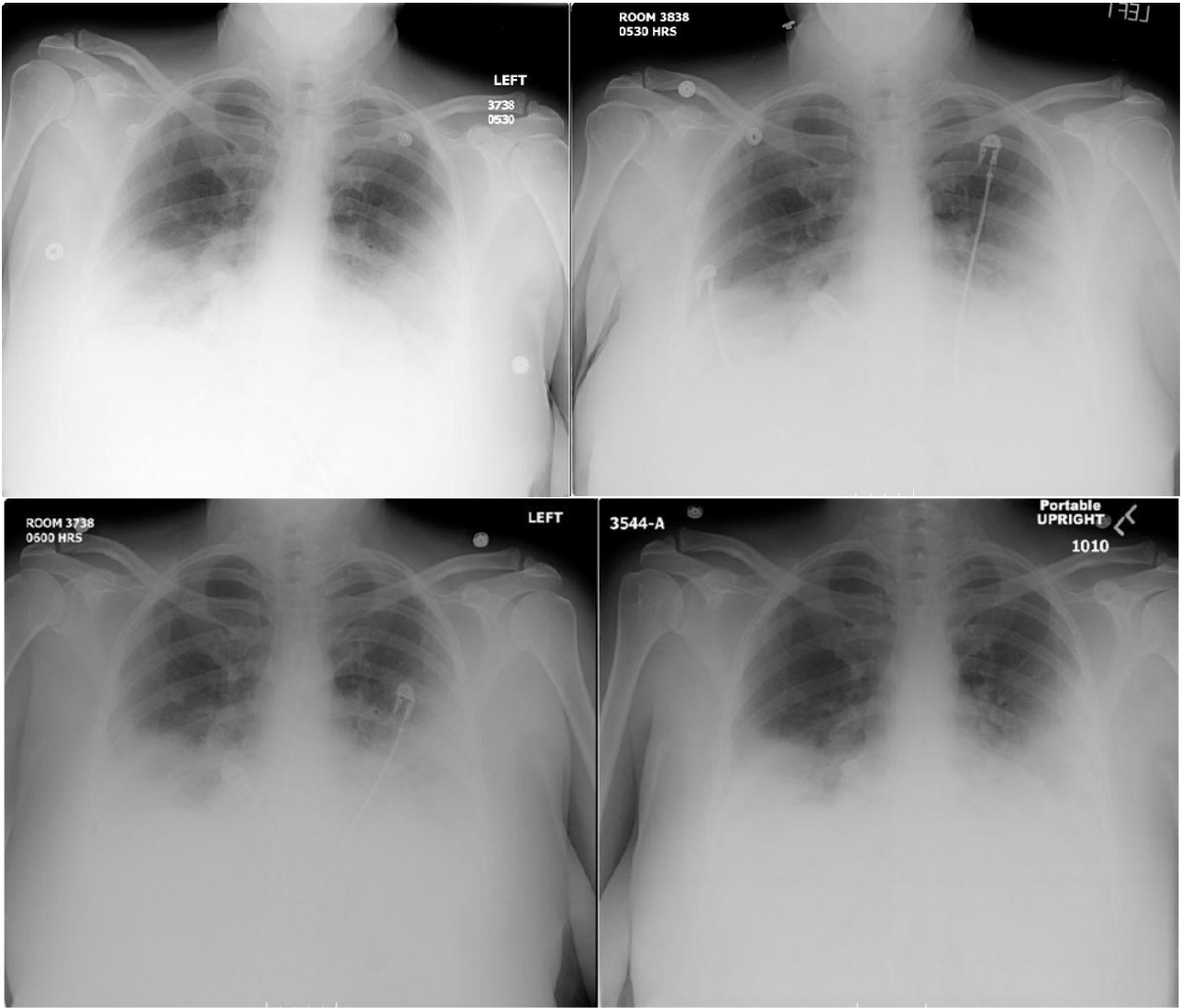


Image 3: Four consecutive chest radiographs without any radiological worsening or improvement of infiltrates

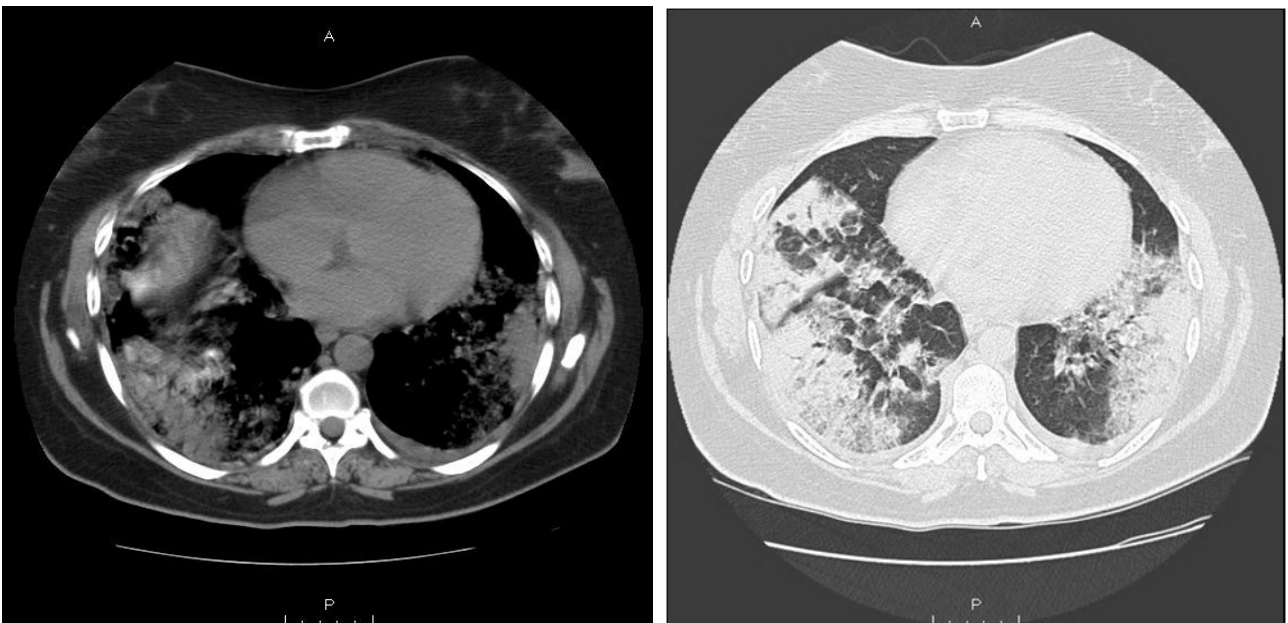


Image 4: Chest CT. Bilateral dense patchy pulmonary infiltrates with consolidation and mild diffuse honeycombing

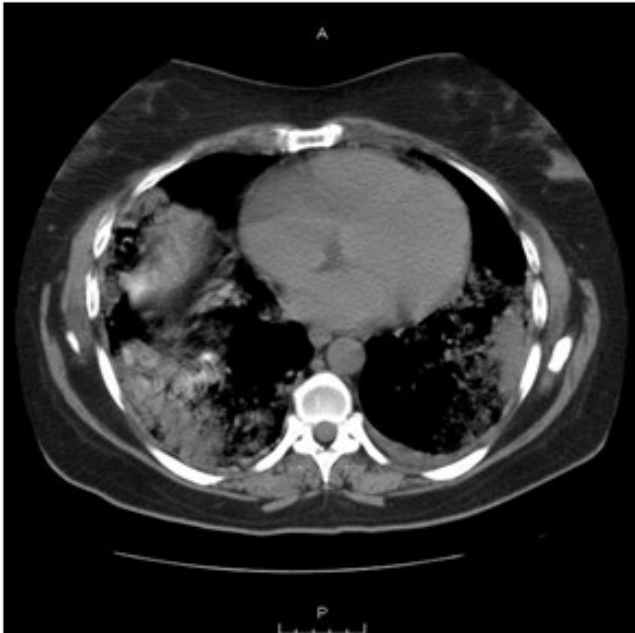


Image 5: Decreasing density of bilateral infiltrates

The rapid spread of the pandemic is due to its transmissibility. It is transmitted from person to person

through exposure to droplets generated by coughing and sneezing, through indirect contact with contaminated fomites, and in some instances, through inhalation of infectious aerosols. This emphasizes the importance of exposure to sick contacts, especially those who have been in contact with others experiencing any influenza-like-illnesses. As our patient's history suggests, her nine year-old son also had influenza- like- symptoms less than a week before she developed symptoms. The Center for Disease Control and Prevention (CDC) now reports the chance of a person with influenza-like-illness symptoms having the H1N1 influenza A during this pandemic is ninety-eight percent⁹. Based on this report, there is a great chance that her son also had the H1N1 influenza A virus.

The actual definitive diagnosis of the swine-origin influenza A (H1N1) virus (S-OIV) is very critical and health care personnel dependent. CDC guidelines state that to establish the diagnosis of H1N1 influenza A, an upper respiratory sample (nasopharyngeal swab, nasal swab, throat swab, combined oropharyngeal/nasopharyngeal swab, or nasal aspirate) should be collected as soon as the start of symptoms and usually no more than 4-5 days later in adults. Sensitivities of rapid diagnostic tests are approximately 50-70% when compared with viral culture or reverse transcription polymerase chain reaction (RT-PCR), which are approximately 90-95%. Therefore, each sample must be sent for RT-PCR confirmation for the official documentable diagnosis of S-OIV by the

CDC⁵. The oropharyngeal swab alone was the reason for initial failure to detect the influenza antigen.

With regards to treatment for swine-origin influenza A (H1N1) virus (S-OIV), the vast majority of strains of pandemic H1N1 influenza A virus circulating in 2009 appeared sensitive in vitro to the neuraminidase inhibitors oseltamavir and zanamivir, but all strains tested have been resistant to amantadine and rimantadine. The United States Centers for Disease Control and Prevention (CDC) suggests for the earliest use (within 48 hours of symptoms starting) of neuraminidase inhibitors in patients with confirmed or suspected pandemic H1N1 influenza A virus infection with five days therapy and prophylaxes for close contacts of up to ten days of therapy⁸.

Neuraminidase inhibitors have been shown to shorten the course of the disease in patients affected with the swine flu, but its role in prophylaxis and decreasing shedding time of the virus has not been proven. Vaccination for S-OIV is now available¹¹. Pneumonia continues to be the most common complication of influenza. Patients with pandemic H1N1 influenza A who develop pneumonia should be treated empirically for community-acquired pneumonia (CAP). In hospitalized patients earliest intervention with broad-spectrum antibiotics and neuraminidase inhibitors continues to be the most essential therapeutic intervention in increasing a favorable prognosis.

In this particular patient, we found it is necessary to continue a longer course of neuraminidase inhibitor along with the empiric antibiotics than that proposed by the CDC for patients that have the novel swine-origin influenza A (H1N1) virus (S-OIV).

Conclusion

In evidence of the recent novel -origin influenza A (H1N1) virus (S-OIV) pandemic, it is predicted that there will be an increase in the rate of pneumonia related hospital admissions in the fall influenza season. Pneumonia continues to be the most common complication of influenza and can present in a variety of mild-to-moderate and moderate-to-severe cases differentiated by primary influenza, secondary bacterial, or mixed viral and bacterial pneumonia, all of which can make for a very challenging medical management. Patients requiring hospital admission and management for secondary bacterial pneumonia from a primary viral cause, as in this case the influenza A (H1N1) virus, should continue to be managed as recommended per CDC guidelines with broad-spectrum antibiotics and early neuraminidase inhibitors. Cases in which a clinically stable patient responds slower to broad-spectrum antibiotics and neuraminidase inhibitor therapy and continues to experience hypoxia without suggestive improvement on

repeat chest radiographs, may be indicative of a more profound lower respiratory tract inflammatory response to pneumonia, such as alveolitis. In such patients, it may be necessary to give a longer antibiotic and neuraminidase inhibitor course than needed for uncomplicated or typical concurrent bacterial infections with a primary viral source¹².

References

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