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Novel Influenza A (H1N1) Viral Infection in Late Pregnancy: Report of a Case

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ABSTRACT

Health care workers, including anesthesia providers, are often exposed to different infectious disease processes. In the operating room, anesthesia providers, nurses, and surgical staff use universal precautions as a standard of practice. The novel influenza A (H1N1) epidemic has heightened concerns because diagnosis is often delayed and transmission can affect those in a close radius to the infected host. The objectives of this report are to describe the intensive care management and outcomes of severe H1N1 viral infection in a patient in the last trimester of pregnancy and to review the epidemiology, management, and outcomes of similar US cases.

Pregnant women have continued to demonstrate increased risks for cardiopulmonary complications related to influenza infections during seasonal influenza epidemics as they have during previous pandemics.[1–9] In addition, the hyperthermia that characterizes influenza infections places fetuses at higher risks for perinatal complications, including preterm births and birth defects.[5,6] Since the current pandemic of novel influenza A (H1N1) or swine-origin influenza began in the United States in April 2009, more than 20 cases of H1N1 have been reported in pregnant women, most of whom were without prior exposure to confirmed or probable cases of the disease or who had no history of recent travel to other pandemic regions, such as Mexico.[7–10] Many of these cases occurred during the third trimester of pregnancy in patients with preexisting asthma and were complicated by abnormal complete blood counts (anemia, leukopenia, leukocytosis, lymphocytosis, thrombocytopenia), pneumonia, and respiratory failure.[7,10] Although the case fatality rate for swine-origin influenza has remained around 1% during the North American pandemic (0.7% in the United States and 1.2% in Mexico), the case fatality rate is increased in pregnancy and in obese patients.[8–11]

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CASE DESCRIPTION

A 22-year-old woman at 35 weeks' gestation presented to a local emergency department (Ochsner Medical Center-Kenner, LA) with a 2-week history of cough, shortness of breath, sinus congestion, and myalgia. The patient also reported a 1-day history of nausea and vomiting but denied diarrhea. She had been in good health throughout her pregnancy and had not traveled to Mexico or been exposed to anyone with confirmed or probable seasonal or novel influenza. Initial vital signs included blood pressure, 94/50 mmHg; heart rate, 124 beats per minute; oral temperature, 98.9°F; and transcutaneous oxygen saturation of 100% in room air. Arterial blood gas analysis demonstrated a pH of 7.45, Pa_{O_2} of 94 mmHg, and oxygen saturation of 98%. Results of a pertinent initial laboratory analysis included a leukocyte count of 6,200 and a normal metabolic panel. Pertinent physical findings included decreased breath sounds bilaterally. The chest radiograph obtained on admission to the obstetric service demonstrated normal heart size, no pulmonary consolidation, and no pleural reaction. However, a chest radiograph that was obtained later demonstrated some degree of peribronchial cuffing in the infrahilar region with localized air bronchograms.

On day 2, the patient's oral temperature was 101°F. A repeat chest radiograph the following day demonstrated bilateral blunting of the costophrenic angles with prominent pulmonary vessels along the left heart border, indicative of pulmonary hypertension (Figure 1). A computed tomographic scan ruled out pulmonary embolism but confirmed bilateral basilar pulmonary consolidation, consistent with pneumonic infiltrates (Figure 2).

On day 4, the patient developed acute respiratory distress and was scheduled for emergent Cesarean delivery under general anesthesia. Vital signs included a heart rate of 102 beats per minute and a transcutaneous oxygen saturation of 94% in room air, prior to preoxygenation for rapid sequence

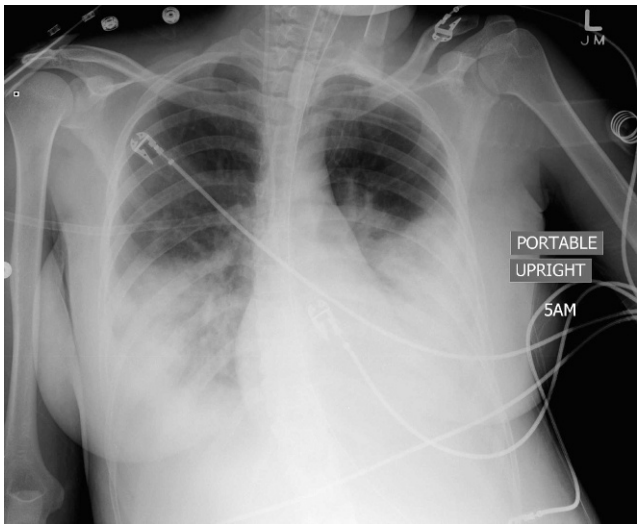

Figure 1. Chest radiograph revealing bilateral blunting of the costophrenic angles with prominent pulmonary vessels along the left heart border, indicative of pulmonary hypertension.

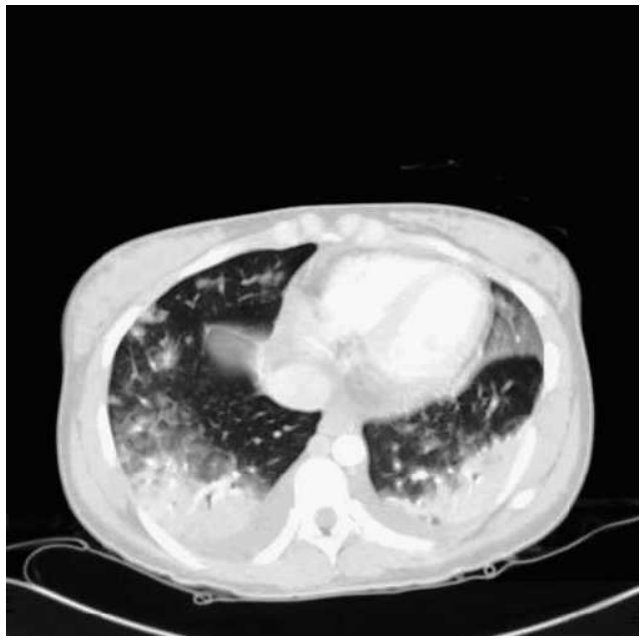

Figure 2. Computed tomographic scan revealing bilateral basilar pulmonary consolidation, consistent with pneumonic infiltrates.

induction and endotracheal intubation. Chest auscultation confirmed proper endotracheal tube placement and demonstrated coarse breath sounds bilaterally.

Following an uneventful delivery, the patient was transferred to the intensive care unit (ICU) for mechanical ventilation. Subsequent real-time reverse transcription-polymerase chain reaction (RT-PCR) analysis of a nasal swab specimen for influenza subtyping confirmed a diagnosis of novel influenza A (H1N1) infection. An infectious disease consultant recommended oral therapy with oseltamivir, 75 mg twice a day for 5 days.

On day 5, the patient's oral temperature increased to 104°F, and she became hemodynamically unstable, requiring inotropic support with intravenous dopamine. Intravenous antibiotic therapy with imipenem, vancomycin, and azithromycin was initiated for presumed pulmonary sepsis. By day 6, the patient had defervesced to 102°F; however, the chest radiograph demonstrated persisting costophrenic consolidation. Subsequent urine, blood, and sputum cultures all had negative findings for bacterial superinfections. The patient improved hemodynamically with intensive care management; intravenous dopamine was titrated off. The patient was weaned from mechanical ventilation on day 16 and transferred to the obstetrical floor the following day. She continued to recover uneventfully and was discharged home with her healthy newborn on day 21.

DISCUSSION

The case presented here of H1N1 that was confirmed by RT-PCR during the third trimester of pregnancy shared several presenting findings of history and physical examination with previously published cases, but the outcomes of the cases ranged from uneventful recovery during outpatient treatment with oral oseltamivir, to successful intensive care for adult respiratory distress syndrome, to death in the ICU from cardiorespiratory failure.[7,10] The shared history findings between this case and others include third trimester pregnancy and a short prodrome of typical febrile, influenza-like illnesses, accompanied by atypical findings of nausea and vomiting (but no diarrhea). Shared physical findings include spiking temperatures and pulmonary congestion. Unique physical findings include air bronchogram effects and pulmonary vascular congestion seen on the chest radiograph that was obtained on admission to the ICU.

With the addition of the case reported here, there have now been more than 20 reported cases of H1N1 virus infections in pregnant women during the third trimester, including 23 confirmed cases and 5 probable cases.[7,10] The detailed clinical characteristics of 7 hospitalized pregnant patients with H1N1 viral infections that were confirmed by RT-PCR are compared in Table 1.[7,10]

According to the US Centers for Disease Control and Prevention (CDC), the case definitions for H1N1 include the following: (1) Confirmed case: an individual with an influenza-like illness (fever with oral temperature of 100°F or greater with a cough or sore throat in the absence of a known cause other than

Table 1. Detailed Clinical Characteristics for 7 Hospitalized Pregnant Patients with Novel Influenza A (H1N1)—United States, April–August 2009[a]

Patient No.	Age, y	Weeks' Gestation	Underlying Conditions	Admission Diagnoses	Abnormal Complete Blood Count Values	Pertinent Chest Radiograph Findings	ICU Admission	Mechanical Ventilation	Antivirals	Length of Stay, Days	Final Outcome
1 (case report)	22	35	None	Viral syndrome, vomiting	Leukocytosis	Peribronchial cuffing, air bronchograms, bilateral basilar consolidation	Yes	Yes	Oseltamivir	10	Full recovery
2	17	NA	None	Viral syndrome	NA	NA	No	No	Oseltamivir	5	Full recovery
3	19	NA	None	Rule out sepsis	Lymphopenia	Not done	No	No	None	2	Full recovery
4	29	NA	None	Pneumonia	Leukocytosis	Bilateral infiltrates	Yes	No	None	9	Full recovery
5	34	NA	None	Asthma	Dehydration	Leucopenia, thrombocytopenia	No	No	None	7	Full recovery
6	42	NA	Asthma, gastrointestinal reflux	Preeclampsia, premature rupture of membranes	None	Not done	No	No	Oseltamivir	4	Full recovery
7	33	35	Mild asthma, psoriasis	Viral syndrome, respiratory distress	NA	Bilateral nodular infiltrates	Yes	Yes	Oseltamivir	15	Died in the ICU, day 15

Abbreviations: ICU, intensive care unit; NA, not available.

[a] Data derived from Refs. 7 and 11.

influenza) and laboratory-confirmed H1N1 virus detected by either real-time RT-PCR or viral culture. (2) Probable case: an individual with influenza-like symptoms who has positive findings for influenza A on rapid antigen screening tests, but negative findings for H1 and H3 proteins by RT-PCR. (3) Suspected case: an individual who does not meet the definition for a confirmed or suspected case but who has influenza-like illness and an epidemiologic link such as exposure to a confirmed or probable case within the past 7 days.[2] (4) Close contact: an individual caring for or living with a person with a confirmed, probable, or suspected case of pandemic H1N1 virus.[8,12] When considering the population in general, the CDC reports that between 39 and 80 million cases have been confirmed between April 2009 and December 2009, with between 7,880 and 16,460 of these cases ending in death.[13] Also of note, the overall hospitalization rates for 2009–2010 have stabilized, and few cases have been confirmed in the week ending January 16, 2010.[13] In addition, almost all of the identified viruses are similar to those chosen for the vaccine.[13]

Diagnostic strategies for H1N1 viral infections include the proper collection of upper respiratory tract specimens (nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, or endotracheal tube aspirates) and the selection of the best rapid screening and confirmatory tests.[8] The CDC recommends rapid influenza antigen tests (RIATs) for screening.[12] The sensitivity and specificity of rapid antigen tests for H1N1 have not been established, but poor sensitivity has been confirmed for seasonal influenza.[12] In April 2009 and again in May 2009, the CDC retested 65 specimens with RIATs that had been previously confirmed positive for either pandemic H1N1 or seasonal influenza A H1N1 or H3N2 by RT-PCR.[12] The study demonstrated that RIATs had only a 40% to 69% sensitivity for detecting other seasonal or H1N1 infection when present and confirmed by RT-PCR.[8,12]

The CDC now recommends that patients with illness compatible with influenza A H1N1 but with negative findings on RIATs be treated empirically based on the level of clinical suspicion, presence of comorbid conditions, severity of illness, and risk for complications, especially during late pregnancy.[8,12] For diagnostic confirmation of novel influenza A (H1N1) viral infections, the CDC recommends either RT-PCR or viral culture.[8] The pandemic strain of H1N1 will test positive for influenza A and negative for H1 and H3 by RT-PCR. Testing may be performed at any state public health laboratory and later reconfirmed at the CDC.[8,12] Although the isolation of H1N1 virus by culture is the ''gold standard'' diagnostic test, the procedure typically is too slow to guide clinical management and can only be conducted in Biosafety Level 3 laboratories.[8,12]

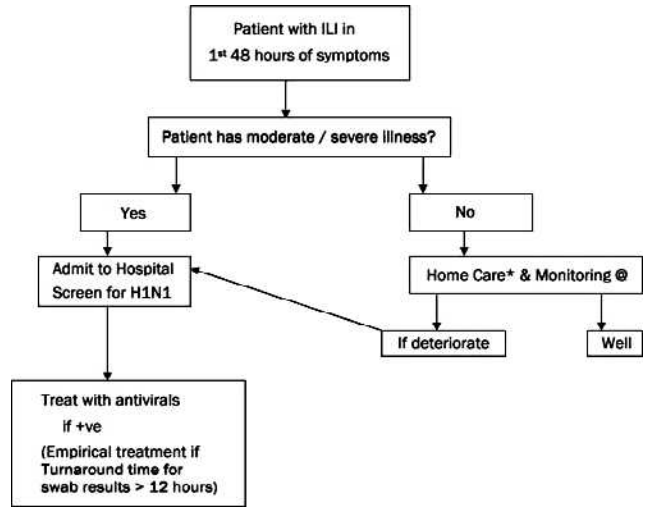

Figure 3. Management strategies for adults with novel influenza A (H1N1) viral infections. (Source: Centers for Disease Control and Prevention. Available at http://h1n1.moh.gov.my/caseManagement.php.)

A management strategy algorithm with antiviral medications for H1N1 viral infections in adults is depicted in Figure 3. Appropriate adult antiviral medications and antiviral combinations include the following: (1) Oseltamivir. Sensitivity testing has shown that pandemic H1N1 influenza A is susceptible to this neuraminidase inhibitor. (2) Zanamivir should be reserved for use in those areas where oseltamivir-resistant H1N1 influenza A virus is endemic or present. (3) Oseltamivir and amantadine/rimantadine. This combination may be used in oseltamivir-resistant individuals when zanamivir is contraindicated (ie, those with asthma or obstructive airway disease). However, H1N1 is resistant to amantadine or rimantadine alone or in a combination which does not include a neuraminidase inhibitor such as oseltamivir or zanamivir.[8,14,15] (4) Peramivir should be considered for intravenous use if the patient cannot tolerate oral medication or if oral medication is deemed contraindicated.[16] Antiviral dosing schedules for adults are compared in Table 2.

For pregnant patients, the most appropriate antiviral and antipyretic medications include oseltamivir and acetaminophen.[14] Oseltamivir (Food and Drug Administration-approved use in Pregnancy Category C) is the drug of choice for pregnant women with confirmed, probable, or suspected cases of H1N1 and/or who have had close contact with someone with a confirmed, probable, or suspected case of the disease.[14,15] Oseltamivir therapy should begin no later than 48 hours after symptom onset in pregnant patients to reduce the risk of serious complications such as pneumonia and respiratory failure.[8,14,15] Treatment should not be withheld while awaiting diagnostic testing.[8,12,14,15] Oseltamivir is preferred

Table 2. Antiviral Dosing Schedules[a]

Agent, Group	Treatment	Chemoprophylaxis
Oseltamivir, adults	75-mg capsule twice per day for 5 days	75-mg capsule once per day
Zanamivir, adults	Two 5-mg inhalations (10 mg total) twice per day	Two 5-mg inhalations (10 mg total) once per day

[a] Available at http://www.cdc.gov/h1n1flu/recommendations.htm.

over zanamivir because its safety in pregnancy has been studied to a greater extent, it exhibits systemic activity, and it is easier to administer orally than zanamivir, which must be administered by inhalation.[15] Limited data to date suggest that oseltamivir is not a major human teratogen, and that both oseltamivir and zanamivir are compatible with breastfeeding.[15] The recommended duration of treatment is 5 days.[16] However, some experts have promoted longer durations and doubling of dosages in patients with severe infections.[16] Also of note, new mothers should be considered as high risk and treated as such until 2 weeks postpartum.[16]

Acetaminophen is an important adjunct to antiviral therapy for novel influenza A (H1N1) during pregnancy because hyperthermia has been associated with fetal damage during pregnancy, including neural tube defects during the first trimester.[5,6] Hyperthermia during the third trimester is a risk factor for preterm delivery and neonatal seizures, cerebral palsy, and neonatal death.[5,6] It should be noted that the use of extracorporeal membrane oxygenation has recently been reported to salvage patients with end-stage adult respiratory distress syndrome resulting from H1N1 and could potentially save lives.[11]

According to CDC guidelines, isolation and personal protection for health care workers caring for patients with H1N1 infections should include the following:[17] (1) Avoid being face-to-face with the sick patient. (2) Clean your hands with soap and water or use an alcohol-based hand rub after you touch the sick patient or handle laundry or used tissues. (3) Talk to your own health care provider about taking antiviral medication to prevent contracting the flu. (4) If you are at high risk of influenza-associated complications, you should not be the designated caretaker, if possible. (5) If close contact with a sick individual is unavoidable, consider wearing a face mask or an N95 disposable respirator. (6) Monitor yourself and your household members for influenza-like symptoms and contact your health care provider if symptoms occur.

The risks of morbidity and mortality from seasonal and pandemic influenza H1N1 are now known to be greater in pregnant than in nonpregnant and postpartum women, especially pregnant women in the third trimester.[1–10] Pregnant patients with H1N1 infections may be anticipated to have underlying comorbidities, especially asthma. They may present with unusual symptoms for influenza-like illnesses, especially vomiting and/or diarrhea, and they may demonstrate significant abnormalities on complete blood counts and chest radiographs.[7–11] Early admission to the ICU for respiratory support with mechanical ventilation and inotropic support with vasopressors may be required. Initiating early antiviral therapy with oral oseltamivir and antipyretic therapy with acetaminophen are recommended within 48 hours of onset of influenza-like illness. Rapid influenza antigen tests are used as screening diagnostic tools; however, they have low sensitivity and should not delay antiviral therapy if they reveal negative findings in the presence of clinical indications. Confirmatory tests include RT-PCR and viral cultures on properly collected upper respiratory tract specimens. Although novel influenza A (H1N1) may not prove as virulent as other pandemic strains, the increased risks of complications and death have been observed to be greater than past influenza pandemics and should be considered when caring for pregnant patients in all trimesters.[1–11] Because pregnant patients are at increased risk of complications from both seasonal and pandemic influenza infections, they should receive the seasonal trivalent influenza vaccine in addition to the monovalent swine-origin influenza vaccine.[18]

Additional cases of novel influenza A (H1N1) in pregnant patients in the third trimester may be anticipated as the pandemic enters the traditional influenza season in the northern hemisphere. It is critical that all health care providers, including anesthesia personnel, use proper preventive measures to avoid infection and appropriately manage those who are affected.[19]

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