

CASE REPORT

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Delay in Diagnosis of Influenza Virus in an Elderly Hospitalized Patient: a Fatal Outcome

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Abstract: Influenza is a well established cause of seasonal hospitalizations and deaths among older persons. However, influenza is frequently underdiagnosed by physicians, because its clinical presentations are often complex, particularly in elderly patients. We report the case of a 78-year-old woman admitted to the emergency department in January 2008 with fever, vomiting, and a history of asthenia and falls in the preceding three days. Diagnosis of influenza at admission was missed. Influenza was diagnosed by direct fluorescent antibody in a sputum specimen four days later, but the evolution was rapidly unfavorable with fatal respiratory distress syndrome. This case illustrates that, during the influenza season, influenza should be suspected in elderly patients admitted to hospital even if they do not present with classical symptoms. Immunofluorescence testing on sputum specimens can provide a rapid diagnosis and merits further evaluation.

Keywords: influenza, hospitalized elderly, sputum, immunofluorescent test

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Introduction

Influenza infection is a well established cause of seasonal hospitalizations and deaths among older persons.¹⁻³ Despite the high disease burden, influenza is frequently underestimated by many admitting clinicians. This underestimation can be explained largely because of the difficulties in clinically identifying influenza in hospitalized patients, especially in elderly patients with comorbidities.³⁻⁶ In this population, the presence of symptoms of pre-existing disease, superposed complications, or atypical manifestations of influenza (symptoms of confusion) may distort the classical symptoms of influenza. Several recent studies have found that elderly patients with influenza are frequently admitted to the hospital with a wide range of diagnoses, including many nonrespiratory diagnoses.^{3,4} We describe an elderly patient admitted to the emergency department with fever and vomiting, and a history of asthenia and falls in the preceding days. Diagnosis of influenza at admission was missed. Influenza was diagnosed by direct fluorescent antibody in a sputum specimen four days later but the evolution was rapidly unfavorable with fatal respiratory distress syndrome.

Case Report

A 78-year-old woman was admitted to the emergency department in January 2008 because of fever and vomiting. In the preceding three days, she had noted asthenia and had fallen at home three times. Her past history included Crohn's disease treated by sulfasalazine and a β -Lactam allergy. She also had congestive heart failure due to valvular disease and hypertension. She had not received influenza vaccine. Physical examination on admission revealed a temperature of 39°C. Her pulse rate was 110 beats per minute and her blood pressure was 150/60 mmHg. She had dyspnea with orthopnea, and her respiratory rate was 30 per minute. On auscultation, there were wheezing, rhonchi, and crepitations at the bases of both lungs. The remainder of the physical examination was unremarkable except for severe functional decline. Laboratory studies showed a white cell count of $14.600 \times 10^9/L$ (with $12.900 \times 10^9/L$ neutrophils), a C-reactive protein level of 154 mg/L and a B-type natriuretic peptide of 770 ng/L. Arterial blood gases on room air were pH 7.34, pO_2 67 mmHg, pCO_2 37 mmHg, and O_2 saturation of 90%. Blood and

urine cultures were negative. A chest x-ray showed bilateral pulmonary infiltrates. It was concluded that the patient had congestive heart failure and acute febrile illness without localizing symptoms. Therapy was initiated with oxygen, diuretics, and intravenous erythromycin.

Over the two next days, the patient remained febrile (38.5°C) despite antibiotic treatment and had abdominal pain. She had no signs of severe sepsis or circulatory failure. She had a blood pressure of 150/70 mmHg, pulse rate of 88 beats per minute, respiratory rate of 22 per minute, and O_2 saturation of 93% on room air. On chest examination, there were persistent rhonchi with cough which produced white sputum. The remainder of the examination was unremarkable. Her white count cell was $8.100 \times 10^9/L$ ($6.900 \times 10^9/L$ neutrophils) and the C-reactive protein level was 275 mg/L. A chest x-ray showed right basal consolidation. Urinary antigen tests for *Streptococcus pneumoniae* and *Legionella pneumophila* serogroup 1 were negative. Abdominal echography was performed and was within normal limits. It was finally concluded that the patient had pneumonia with persistent fever despite antibiotics. Antibiotic cover was extended to include ofloxacin and the patient was admitted the following day to our acute geriatric ward. On admission, her temperature was 38°C and chest examination was the same as described earlier. Sputum for viral examination was collected because the patient had a productive cough, but bacteriologic examination was not performed due to antibiotics. A rapid detection test on sputum by direct fluorescent antibody assay was positive for influenza A in a few hours, with confirmation a few days later by culture. The patient's condition deteriorated on the same day and she succumbed to fatal respiratory distress syndrome.

Discussion

Influenza virus is a leading cause of morbidity and mortality in older persons. Pneumonia caused by either the influenza virus itself or by secondary bacterial infection is the most serious complication affecting patients with influenza.^{1,2,7} The clinical presentation of influenza is often complex in elderly patients. Although some investigators have found that the combination of symptoms of fever, cough, and acute onset have a sensitivity of 78% in older hospitalized patients



during the influenza season,⁸ more recent studies have shown difficulties in clinically diagnosing influenza in hospitalized patients, especially in the elderly.^{3–6,9} Van den Dool et al found that none of the combinations of symptoms had both a positive predictive value and a sensitivity higher than 40% among hospitalized patients.⁶ In a study performed in patients hospitalized with acute pulmonary conditions during four winters, Falsey et al found that more than half the influenza cases identified in their study resulted from hospital screening rather than physician diagnosis.⁹ Moreover, during a winter season, Monmany et al tested for influenza in 136 consecutive adult patients who attended the emergency department with either a classical influenza syndrome or a deterioration of a previous condition or any symptoms with an abrupt onset but no obvious cause, and reported that influenza frequently had an atypical presentation especially in elderly patients, with a high frequency symptoms of confusion and falls.⁴ As a consequence, several authors have suggested that, during the influenza season, physicians should largely test elderly patients admitted to hospital, even if they do not present with classical symptoms on admission.^{3–5}

Diagnosis of influenza might require the use of viral testing methods. Reverse-transcriptase polymerase chain reaction has been shown to be the most sensitive and specific test for influenza but is not routinely accessible to most hospital laboratories and is expensive. Classical diagnostic techniques, such as cell culture or serology testing, require 2 days to 2 weeks for results to be available and thus are not useful for the management of patients. Rapid antigen tests are simple and fast but have poor sensitivity in adults (<40%–60%) compared with reverse-transcriptase polymerase chain reaction and viral culture.^{10,11} Several studies in hospitalized patients have indicated that detection of influenza virus by immunofluorescent testing (fluorescent antibody) can achieve results within hours after specimen submission, with a sensitivity and specificity close to that of reverse-transcriptase polymerase chain reaction and at a lower cost.^{12,13} In most studies, influenza was usually detected in samples from the throat, nose, or nasopharynx. Some studies have indicated that sputum can be useful for the diagnosis of respiratory virus in adult patients.^{14,15} In our patient, detection of influenza virus in sputum was useful and, further, influenza virus was detected seven days after onset of symptoms.

Consistent with our report, several recent studies have found that hospitalized patients, especially the elderly with comorbidities, can have a long duration of viral shedding, beyond 7 days after symptom onset.^{16,17}

Prompt diagnosis of influenza is important to initiate appropriate infection control measures and prevent nosocomial transmission amongst patients. Early diagnosis is also important for therapeutic intervention. Several studies have demonstrated that treatment with oseltamivir within 48 hours after onset of symptoms reduced the incidence of influenza-associated complications and mortality in elderly patients.^{1,2,17,18} Recent studies suggest that antiviral treatment started within 4 days after illness onset might reduce mortality among elderly patients hospitalized with influenza.^{18,19} Other studies have shown that the influenza vaccine was associated with a reduction in influenza-related morbidity and mortality in older persons, although there is a decline in influenza vaccine efficacy in this population.¹ The patient reported here had not received an influenza vaccine.

In summary, our case illustrates that, during the influenza season, influenza should be suspected in elderly patients admitted to hospital even if they do not present with classical symptoms. Early diagnosis is important to initiate appropriate infection control measures and antiviral treatment. In addition, our report suggests that immunofluorescence testing on sputum specimens can provide a rapid diagnosis and merits further evaluation.

Disclosures

Written informed consent for publication of this case could not be obtained despite all reasonable attempts to trace the patient's family. Every effort was made to protect the identity of our patient and there is no reason to believe that any of her relatives would object to publication. The authors report no conflicts of interest in this work.

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