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

Nicole Haber¹, Djamal Khelili¹, Delphine Martineau¹, Siham Dekimeche¹, Carol Szekely¹ and Pierre Lebon²

¹Department of Geriatric Medicine, Hôpital Charles RICHET, Assistance-Publique-Hôpitaux de Paris (AP-HP), Villiers Le Bel, France. ²Department of Virology, Hôpital Cochin-Saint Vincent de Paul, Assistance-Publique-Hôpitaux de Paris (AP-HP), and René Descartes University, Paris, France. Corresponding author email: nicole.haber@crc.aphp.fr

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

Clinical Medicine Insights: Case Reports 2012:5 5–8

doi: 10.4137/CCRep.S8460

This article is available from http://www.la-press.com.

© the author(s), publisher and licensee Libertas Academica Ltd.

This is an open access article. Unrestricted non-commercial use is permitted provided the original work is properly cited.
**Introduction**

Influenza infection is a well established cause of seasonal hospitalizations and deaths among older persons.\(^1\)\(^-\)\(^\text{3}\) 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.\(^3\)\(^-\)\(^\text{6}\) 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.\(^3\)\(^-\)\(^\text{4}\) 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 × 10^9/L (with 12.900 × 10^9/L neutrophils), a C-reactive protein level of 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.\(^1\)\(^-\)\(^\text{2}\)\(^-\)\(^\text{7}\) 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, more recent studies have shown difficulties in clinically diagnosing influenza in hospitalized patients, especially in the elderly. 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. 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. 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. 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.

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. 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. 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. 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.

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. Recent studies suggest that antiviral treatment started within 4 days after illness onset might reduce mortality among elderly patients hospitalized with influenza. 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. 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.

Author(s) have provided signed confirmations to the publisher of their compliance with all applicable legal and ethical obligations in respect to declaration of conflicts of interest, funding, authorship and contributorship, and compliance with ethical requirements in respect to treatment of human and animal test subjects. Author(s) have confirmed that the published article is unique and not under consideration nor...
published by any other publication and that they have consent to reproduce any copyrighted material. The peer reviewers declared no conflicts of interest.

References
1. Rothberg MD, Haessler SD, Brown RB. Complications of viral influenza. *Am J Med.* 2008;121:258–64.
2. Ruf BR, Szucs T. Reducing the burden of influenza-associated complications with antiviral therapy. *Infection.* 2009;37:186–96.
3. Ison MG. Influenza in hospitalized adults: gaining insight into a significant problem. *J Infect Dis.* 2009;200:485–7.
4. Monmany J, Rabella N, Margall P, Domingo P, Gich I, Vazquez G. Unmasking influenza virus infection in patients attended to in the emergency department. *Infection.* 2004;32:89–97.
5. Babcock HM, Merz LR, Fraser VJ. Is influenza an influenza-like illness? Clinical presentation of influenza in hospitalized patients. *Infect Control Hosp Epidemiol.* 2006;27:266–70.
6. Van den Dool C, Hak E, Wallinga J, van Loon AM, Lammers JWJ, Bonten JMM. Symptoms of influenza virus infection in hospitalized patients. *Infect Control Hosp Epidemiol.* 2008;29:314–9.
7. Murata Y, Walsh EE, Falsey AR. Pulmonary complications of interpandemic influenza A in hospitalized adults. *J Infect Dis.* 2007;195:1029–37.
8. Walsh EE, Cox C, Falsey AR. Clinical features of influenza A virus infection in older hospitalized persons. *J Am Geriatr Soc.* 2002;50:1498–503.
9. Falsey AR, Murata Y, Walsh EE. Impact of rapid diagnosis on management of adults hospitalized with influenza. *Arch Intern Med.* 2007;167:354–60.
10. Harper SA, Bradley JS, Englund JA, et al. Seasonal influenza in adults and children- diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of Infectious Diseases Society of America. *Clin Infect Dis.* 2009;48:1003–32.
11. Petric M, Comanor L, Petti CA. Role of the laboratory in diagnosis of influenza during seasonal epidemics and potential pandemics. *J Infect Dis.* 2006;194:S98–110.
12. Barenfanger J, Drake C, Leon N, Mueller T, Troudt T. Clinical and financial benefits of rapid detection of respiratory viruses: an outcomes study. *J Clin Microbiol.* 2000;38:2824–8.
13. Landry ML, Cohen S, Ferguson D. Real-time PCR compared to Binax NOW and cytoxin-immunofluorescence for detection of influenza in hospitalized patients. *J Clin Virol.* 2008;43:148–51.
14. Kimball AM, Foy HM, Cooney MK, Allan ID, Matlock M, Plorde JJ. Isolation of respiratory syncytial and influenza viruses from the sputum of patients hospitalized with pneumonia. *J Infect Dis.*1983;2:181–4.
15. Kok T, Higgins G. Prevalence of respiratory virus and Mycoplasma pneumoniae in sputum samples from unselected adults patients. *Pathology.* 1997;29:300–2.
16. Leekha S, Zitterkopf NL, Espy MJ, Smith TF, Thompson RL, Sampathkumar P. Duration of influenza A virus shedding in hospitalized patients and implications for infection control. *Infect Control Hosp Epidemiol.* 2007;28:1071–6.
17. Lee N, Chan KS, Hui DSC, et al. Viral loads and duration of viral shedding in adults patients hospitalized with influenza. *J Infect Dis.* 2009;200:492–500.
18. Lee N, Choi KW, Chan PKS, et al. Outcomes of adults hospitalised with severe influenza. *Thorax.* 2010;65:510–5.
19. McGeer A, Green KA, Plevnesi A, et al. Antiviral therapy and outcomes of influenza requiring hospitalisation in Ontario, Canada. *Clin Infect Dis.* 2007;45:1568–75.

Publish with Libertas Academica and every scientist working in your field can read your article

"I would like to say that this is the most author-friendly editing process I have experienced in over 150 publications. Thank you most sincerely."

"The communication between your staff and me has been terrific. Whenever progress is made with the manuscript, I receive notice. Quite honestly, I’ve never had such complete communication with a journal."

“LA is different, and hopefully represents a kind of scientific publication machinery that removes the hurdles from free flow of scientific thought.”

Your paper will be:
• Available to your entire community free of charge
• Fairly and quickly peer reviewed
• Yours! You retain copyright

http://www.la-press.com