Low Pathogenic Avian Influenza A (H7N2) Virus Infection in Immunocompromised Adult, New York, USA, 2003

Belinda Ostrowsky,[1] Ada Huang, William Terry,[2] Diane Anton, Barbara Brunagel, Lorraine Traynor, Syed Abid, Geraldine Johnson, Marilyn Kacica, Jacqueline Katz, Lindsay Edwards,[3] Stephen Lindstrom, Alexander Klimov, and Timothy M. Uyeki

In 2003, infection with low pathogenic avian influenza A (H7N2) virus was identified in an immunocompromised man with fever and community-acquired pneumonia in New York, USA. The patient recovered. Although the source of the virus was not identified, this case indicates the usefulness of virus culture for detecting novel influenza A viruses.

Limited numbers of human infections with low pathogenic avian influenza A, subtype H7, viruses have been reported and attributed to recent exposure to infected poultry (*1*–*6*). Such infections generally resulted in clinically mild illness. We report a case of low pathogenic avian influenza (LPAI) A (H7N2) virus infection in an immunocompromised adult.

The Study

On November 3, 2003, a 48-year-old man from the Caribbean sought care at an emergency department in Westchester County, New York, USA, after an episode of near syncopy; a 2–4 week history of feverishness, cough, fatigue, and myalgia; and a 10-pound weight loss over 2 months. He had lived in the United States since 1987 and had no known medical conditions. A month earlier, he had been evaluated at a clinic, and an oral antimicrobial drug was prescribed for possible pneumonia. Eight days before the emergency department admission reported here, he had sought emergency care for unilateral conjunctivitis,

Author affiliations: Westchester County Department of Health, New Rochelle, New York, USA (B. Ostrowsky, A. Huang, W. Terry); Westchester County Department of Laboratories and Research, Valhalla, New York, USA (D. Anton, B. Brunagel, L. Traynor, S. Abid); New York State Department of Health, Albany, New York, USA (G. Johnson, M. Kacica); and Centers for Disease Control and Prevention, Atlanta, Georgia, USA (J. Katz, L. Edwards, S. Lindstrom, A. Klimov, T.M. Uyeki)

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[1]Current affiliation: Montefiore Medical Center of, the University Hospital for The Albert Einstein College of Medicine, Bronx, New York, USA.

[2]Current affiliation: The State University of New York School of Medicine, Buffalo, New York, USA.

[3]Current affiliation: University of Colorado School of Medicine, Denver, Colorado, USA.

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Distinguish the usual severity of infections with LPAI
- Analyze the differential diagnosis for patients presenting with LPAI infection
- Evaluate the epidemiology of LPAI
- Assess other clinical characteristics of LPAI infection

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P. Lynne Stockton, VMD, MS, ELS(D), Technical Writer/Editor, *Emerging Infectious Diseases. Disclosure: P. Lynne Stockton, VMD, MS, ELS(D), has disclosed no relevant financial relationships.*

CME Author

Charles P. Vega, MD, Health Sciences Clinical Professor; Residency Director, Department of Family Medicine, University of California, Irvine. *Disclosure: Charles P. Vega, MD, has disclosed no relevant financial relationships.*

Authors

Disclosures: ***Belinda Ostrowsky, MD, MPH; William Terry, MD, MPH; Diane Anton, MS, M(ASCP); Barbara Brunagel, MS; Lorraine Traynor, BS; Syed Abid, PhD; Geraldine Johnson, MS; Marilyn Kacica, MD, MPH; Stephen Lindstrom, PhD; Alexander Klimov, PhD;*** *and* ***Timothy M. Uyeki, MD, MPH, MPP,*** *have disclosed no relevant financial relationships.* ***Ada Huang, MD,*** *has disclosed the following relevant financial relationships: owns stock, stock options, or bonds from Merck, Pfizer.* ***Jacqueline Katz, PhD,*** *has disclosed the following relevant financial relationships: received grants for clinical research from GlaxoSmithKline for research not related to the current study; received grants for preclinical research from Colby Pharmaceuticals (formerly Juvaris Bio Therapeutics) for research not related to the current study.* ***Lindsay Edwards*** *has disclosed the following relevant financial relationships: spouse owns GlaxoSmithKline stock.*

eye pain, and blurred vision; the diagnosis was corneal abrasion.

Physical examination on November 3, 2003, found that the patient was afebrile, weak, and mildly tachypneic (respiratory rate 18–26 breaths/minute, room air oxygenation saturation 98%) with bibasilar inspiratory rales. Pertinent laboratory findings included mild anemia and thrombocytopenia (hemoglobin 11.9 g/dL, platelets 107 × 10^9/L, leukocytes 8.0 × 10^9 cells/L [52% lymphocytes]), mildly elevated hepatic transaminases (aspartate aminotransferase 116 U/L, alanine aminotransferase 87 U/L), and elevated creatine kinase (1,844 U/L). A chest radiograph showed a right hilar density and left lower lobe infiltrates; computed tomographic scan of the chest and abdomen showed bilateral micronodular opacities with right perihilar infiltrates and lymphadenopathy. The patient was admitted for community-acquired pneumonia and received intravenous gatifloxicin.

A tuberculin skin test was reactive (20-mm induration). HIV ELISA/Western blot test results were positive (HIV test result from 3 years earlier was reportedly negative), and CD4 count was 300 cells/μL. Treatment was switched to rifampin, isoniazid, pyrazinamide, ethambutol, and pyridoxine. Bronchoalveolar lavage (BAL) performed on November 7 yielded influenza A virus by tissue cell culture at the Westchester County Department of Laboratories and Research and was negative for *Pneumocystis* spp., *Legionella* spp., and other bacterial or viral pathogens. A second BAL and biopsy performed later during hospitalization to evaluate adenopathy indicated inflammation without definitive pathology. The lower respiratory tract disease improved after 13 days, and the patient was empirically prescribed tuberculosis treatment (directly observed therapy) and discharged while mycobacterial culture results were pending. After 8 weeks, mycobacterial culture of the BAL specimen was negative for *Mycobacterium tuberculosis* but yielded *M. avium* complex.

The patient lived in an apartment with his wife and 4 children, none of whom were sick during his illness. He denied recent travel and had not traveled outside the United States for 4 years. He worked in a cafeteria as a dishwasher and handled food and garbage until 1 month before hospitalization. He denied any known risk factors for HIV infection.

The influenza A virus isolate was difficult to grow in culture, reacted minimally with antiserum to hemagglutinin H1, and was sent to the Centers for Disease Control and Prevention (CDC) for further characterization. On March 19, 2004, CDC reported that the influenza isolate, designated A/New York/107/2003, was an LPAI A (H7N2), not subtype H1N1, virus.

An epidemiologic investigation was initiated by the Westchester County Department of Health. During 3 interviews (with a Creole interpreter), the patient denied any exposure to live or dead poultry, wild birds, or bird feces. No live poultry markets or poultry were found on the surrounding property or in the neighborhood.

Serum samples obtained during the patient's hospitalization on November 5, 2003, and on April 4, 2004, were tested at CDC by microneutralization assay with the LPAI A (H7N2) virus from the patient. The acute-phase serum sample was negative (titer 10), but the convalescent-phase serum sample was positive (influenza [H7N2] virus neutralizing antibody titer 80), indicating seroconversion and evidence of infection with LPAI A (H7N2) virus. A confirmatory Western blot assay detected H7 hemagglutinin-specific antibody in the convalescent-phase serum sample. Testing of paired serum samples by ELISA demonstrated a 16-fold rise in H7 hemagglutinin-specific IgG. Serum samples collected from the patient's wife and 3 of the children on April 4, 2004, were seronegative for influenza A (H7N2) neutralizing antibodies.

Conclusions

In this immunocompromised man with pneumonia, the contribution of influenza A (H7N2) virus infection to his lower respiratory tract disease is unclear. The diagnosis of influenza A (H7N2) virus infection was not made until long after the patient had been discharged, and no influenza antiviral treatment was administered. The patient's history and clinical findings were consistent with HIV and community-acquired pneumonia with possible clinical response to the antimicrobial drug therapy or improvement of self-limiting viral pneumonia. In patients with HIV infection, *M. avium* complex is often detected as an indolent pathogen, especially associated with disseminated disease in patients with advanced AIDS; clinical resolution usually requires prolonged multidrug treatment (*7*). Isolation of influenza A (H7N2) virus from a BAL specimen and resolution of lower respiratory tract disease during hospitalization suggest that this infection might have contributed to the pulmonary disease. The clinical spectrum of human infection with LPAI viruses, including subtype H7, is generally mild, ranging from conjunctivitis to influenza-like illness (*1*–*6*), although hospitalization of patients with influenza A (H7N2) virus infection has been reported (*6*).

Conjunctival infection with influenza A subtype H7 viruses in persons with conjunctivitis has been confirmed by reverse transcription PCR or virus isolation (*1*–*3*,*5*). The patient initially reported ophthalmologic symptoms. Because conjunctival specimens were not available for virus testing, the role of influenza A (H7N2) virus in the conjunctivitis is unknown. However, intraocular inoculation of mice with the influenza A (H7N2) virus from the patient (A/New York/107/2003) did not result in infection, and the

virus replicated at relatively low levels in murine corneal epithelial cells ex vivo (*8*,*9*). Intranasal inoculation with the LPAI A (H7N2) virus caused respiratory symptoms, elevated mean lung titers, and cytokine increases in mice; among ferrets, the virus replicated efficiently in the upper respiratory tract and was transmissible through direct contact (*8*,*10*).

The source of the patient's infection with influenza A (H7N2) virus was not determined, although exposure to poultry was suspected. A limitation is that the investigations were conducted 5 months after the patient was hospitalized, after the influenza A isolate was identified as an LPAI A (H7N2) virus. LPAI A (H7N2) viruses have been documented among birds in live poultry markets in the northeastern United States, including New York (*11*–*13*). Such viruses have receptor-binding properties consistent with receptors found in the human upper respiratory tract (*10*).

This case of LPAI A (H7N2) virus infection was detected through influenza virus surveillance of specimens submitted from outpatients and hospitalized patients to the Westchester County Department of Laboratories and Research and illustrates the value of virus culture for detection of human infections with novel influenza A viruses, which are nationally notifiable. For the patient reported here, neither seasonal influenza nor zoonotic influenza was suspected. Whether HIV infection might have made the patient more susceptible to lower respiratory tract infection with LPAI A (H7N2) virus is unknown, but a case of pulmonary infection with LPAI A (H9N2) virus in an immunosuppressed adult has been reported (*14*). A serologically confirmed case of LPAI A (H7N2) virus infection in the United States was associated with upper respiratory tract illness (*4*). Although information about the frequency of human infection with LPAI A H7 viruses is limited, 1 study reported antibody detection in 3.8% of exposed poultry workers after an outbreak of LPAI A (H7N3) virus infection among poultry in Italy (*15*). More information is needed to clarify the risk for LPAI A H7 virus infections among immunocompetent and immunocompromised persons.

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Dr Ostrowsky was director of communicable and sexually transmitted diseases at the Westchester County Department of Health when the case reported here was investigated. She is currently director of the antimicrobial stewardship program at Montefiore Medical Center of Albert Einstein College of Medicine. Her research interests include antimicrobial drug resistance, health care–associated infections, and public health.

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Address for correspondence: Belinda Ostrowsky, Montefiore Medical Center, Albert Einstein College of Medicine, 111 E 210 St, Bronx, NY 10467, USA; email: bostrows@montefiore.org