

Letter to the Editor

A successfully treated case of parainfluenza virus 3 pneumonia mimicking influenza pneumonia

Um caso de pneumonia por vírus parainfluenza 3 simulando pneumonia por influenza tratada com sucesso

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To the Editor:

Influenza infection is the most common viral infection causing respiratory illness. Influenza pneumonia is the most severe complication of influenza virus infection, resulting in high mortality.⁽¹⁾ Although seasonal influenza viruses are commonly detected by rapid antigen testing of nasopharyngeal swabs, a swine flu virus (H1N1) is rarely isolated.⁽¹⁾ Therefore, anti-influenza therapy should be started empirically if influenza pneumonia is suspected.

It is known that parainfluenza virus (PIV) caused influenza-like illness during the swine influenza pandemics.⁽²⁾ It has been reported that PIV type 3 (PIV3) can cause pneumonia in immunosuppressed patients, such as adult transplant recipients.⁽³⁾

We report a successfully treated case of PIV3 pneumonia mimicking influenza pneumonia in a 31-year-old female patient with asthma. The patient had high fever (39.5°C), general fatigue, systemic joint pain, and anorexia for two days before being referred to our medical center. She was a current smoker and had a history of smoking (20 pack-years) and of bronchial asthma (no current use of medication). The patient also had poorly controlled diabetes mellitus and a body mass index of 30 kg/m². A chest X-ray revealed diffuse ground-glass opacities in both lungs (Figure 1). Laboratory tests showed severe inflammatory reaction (C-reactive protein = 19.2 mg/dL and ESR = 83 mm/h). She had severe respiratory failure and an SpO₂ of 80% on room air at the first visit, and oxygen therapy was started with noninvasive positive pressure ventilation. Because of the severe respiratory failure, bronchoalveolar lavage was not performed. Although the result of a rapid influenza antigen detection test was negative, she was diagnosed with influenza pneumonia

on the basis of influenza-like symptoms and radiological findings, such as diffuse ground-glass opacities (Figure 2).

The patient was started on empirical treatment with peramivir (600 mg/day) for 5 days (for the influenza infection) combined with a steroid pulse and i.v. erythromycin (1,000 mg/day) for 5 days (for the acute respiratory failure). Her respiratory function gradually improved, and noninvasive positive pressure ventilation was discontinued on day 5. Oral prednisolone was then started (at 80 mg/day), and the dose was tapered, being modified once every three days, as follows: to 40 mg/day on day 6; to 30 mg/day on day 9; to 15 mg/day on day 12; and discontinuation on day 15. The patient was discharged on day 18. Although she tested negative for influenza A and influenza B antibodies, the patient tested

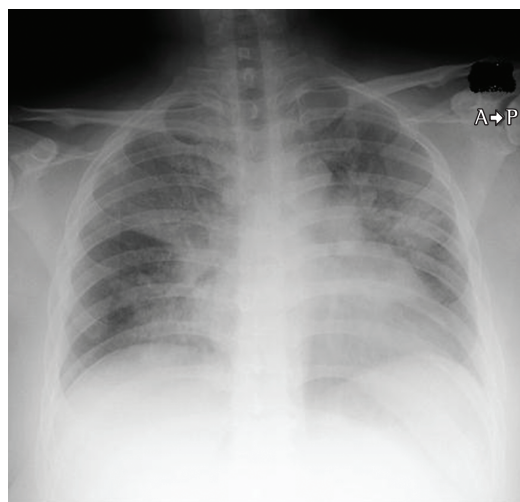


Figure 1 – Chest X-ray showing bilateral shadows predominantly in the hilar region.

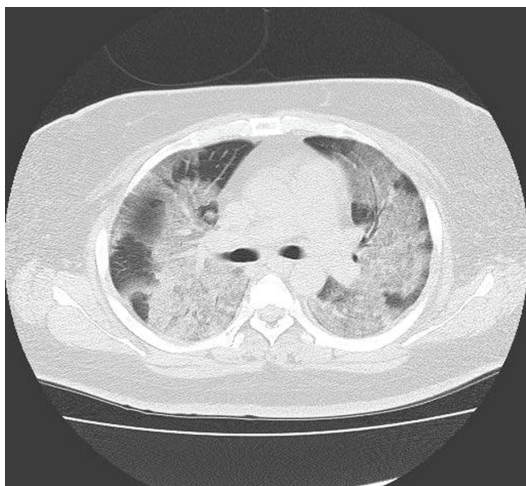


Figure 2 – CT scan of the chest showing bilateral diffuse ground-glass opacities.

positive for PIV3 antibody. A final diagnosis of PIV3 pneumonia was made.

The most common mimics of swine influenza (H1N1) pneumonia are Legionnaires' disease and human PIV3 (HPIV3) pneumonia in adults and pneumonia caused by respiratory syncytial virus or human metapneumovirus in children.⁽⁴⁾ It is known that HPIV types 1–3 are primarily pediatric respiratory pathogens and a common cause of laryngotracheobronchitis (croup) in young children.⁽⁴⁾ In adults, HPIV3 is a recognized cause of community-acquired pneumonia (CAP) in immunosuppressed patients or transplant recipients. However, HPIV3 can also present as a viral CAP in normal hosts.⁽⁵⁾ During an influenza pandemic, clinicians should consider the diagnosis of PIV3 pneumonia if patients present with influenza-like symptoms and negative rapid influenza antigen detection test results.

Although some successfully treated cases have previously been reported,⁽²⁾ the standard treatment for PIV3 pneumonia has yet to be established. We administered a combination of steroid pulse therapy (i.v. erythromycin) and anti-flu medication. As a result, the respiratory function of the patient rapidly improved. It has been reported that macrolides can be effective for severe inflammation, since it is evident that they decrease neutrophil chemotaxis and infiltration into the respiratory epithelium, downregulating adhesion molecule expression and enhancing neutrophil apoptosis.^(6,7) In addition, animal studies have shown that high doses of steroids

are effective in reducing pulmonary lesions and suppressing cytokines, leading to a shutdown in macrophage activation.^(6–8) It is reasonable to assume that, in the present case, erythromycin had an immunomodulatory effect rather than an antimicrobial effect when combined with a high dose of prednisolone.

The plasma level of cytokines such as IL-6 and IL-10 was found to be higher in influenza A (H1N1)-infected patients who died or who had acute respiratory distress syndrome than in patients with less severe disease.⁽⁹⁾ The mechanism of severe pulmonary inflammation is still unclear. Adipokines released by adipocytes could cause an allergic reaction. In addition, a cytokine storm could easily occur in patients with allergic conditions such as bronchial asthma and rheumatic disease.⁽¹⁰⁾ Because she was obese and had a history of bronchial asthma, our patient was at risk of severe pulmonary inflammation.

One limitation of our report is that the plasma levels of cytokines were not determined. Given that inflammatory markers such as C-reactive protein and ESR were very high, we speculate that a cytokine storm occurred in our patient.

In conclusion, physicians should be aware that other pathogens can cause viral CAP mimicking influenza pneumonia during an influenza pandemic. More cases should be investigated in order to establish the standard treatment for viral pneumonia.

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References

1. Itoh Y, Shinya K, Kiso M, Watanabe T, Sakoda Y, Hatta M, et al. In vitro and in vivo characterization of new swine-origin H1N1 influenza viruses. *Nature*. 2009;460(7258):1021-5. PMID:19672242 PMCID:2748827.
2. Cunha BA, Corbett M, Mickail N. Human parainfluenza virus type 3 (HPIV 3) viral community-acquired pneumonia (CAP) mimicking swine influenza (H1N1) during the swine flu pandemic. *Heart Lung*. 2011;40(1):76-80. PMID:20888645. <http://dx.doi.org/10.1016/j.hrtlng.2010.05.060>
3. Whimbey E, Vartivarian SE, Champlin RE, Elting LS, Luna M, Bodey GP. Parainfluenza virus infection in adult bone marrow transplant recipients. *Eur J Clin Microbiol Infect Dis*. 1993;12(9):699-701. PMID:8243487. <http://dx.doi.org/10.1007/BF02009383>
4. Cunha BA, Perez FM, Strollo S. Swine influenza (H1N1): diagnostic dilemmas early in the pandemic. *Scand J Infect Dis*. 2009;41(11-12):900-2. PMID:19922079. <http://dx.doi.org/10.3109/00365540903222465>
5. Marx A, Gary HE Jr, Marston BJ, Erdman DD, Breiman RF, Török TJ, et al. Parainfluenza virus infection among adults hospitalized for lower respiratory tract infection. *Clin Infect Dis*. 1999;29(1):134-40. PMID:10433576. <http://dx.doi.org/10.1086/520142>
6. Amsden GW, Baird IM, Simon S, Treadway G. Efficacy and safety of azithromycin vs levofloxacin in the outpatient treatment of acute bacterial exacerbations of chronic bronchitis. *Chest*. 2003;123(3):772-7. PMID:12628877. <http://dx.doi.org/10.1378/chest.123.3.772>
7. Asai N, Ohkuni Y, Matsunuma R, Iwama K, Otsuka Y, Kawamura Y, et al. A case of novel swine influenza A (H1N1) pneumonia complicated with virus-associated hemophagocytic syndrome. *J Infect Chemother*. 2012. [Epub ahead of print]. <http://dx.doi.org/10.1007/s10156-011-0366-3>
8. Ottolini M, Blanco J, Porter D, Peterson L, Curtis S, Prince G. Combination anti-inflammatory and antiviral therapy of influenza in a cotton rat model. *Pediatr Pulmonol*. 2003;36(4):290-4. PMID:12950040. <http://dx.doi.org/10.1002/ppul.10320>
9. Writing Committee of the WHO Consultation on Clinical Aspects of Pandemic (H1N1) 2009 Influenza, Bautista E, Chotpitayasunondh T, Gao Z, Harper SA, Shaw M, et al. Clinical aspects of pandemic 2009 influenza A (H1N1) virus infection. *N Engl J Med*. 2010;362(18):1708-19. Erratum in: *N Engl J Med*. 2010;362(21):2039. PMID:20445182. <http://dx.doi.org/10.1056/NEJMra1000449>
10. Shore SA, Terry RD, Flynt L, Xu A, Hug C. Adiponectin attenuates allergen-induced airway inflammation and hyperresponsiveness in mice. *J Allergy Clin Immunol*. 2006;118(2):389-95. PMID:16890763. <http://dx.doi.org/10.1016/j.jaci.2006.04.021>