Imaging appearance of swine-origin influenza A (novel 2009 H1N1) pneumonia in an immunocompromised patient

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The Centers for Disease Control (CDC) predicted a resurgence of Swine-origin Influenza A (novel 2009 H1N1) pneumonia, hospitalizations and deaths during the 2009-2010 flu season. Immunocompromised patients are at higher risk to contract it and may present (atypically) with greater morbidity and mortality. We report the first radiographic description of CDC-confirmed swine-origin influenza A (novel 2009 H1N1) in a 32-year-old immunocompromised man. At presentation, chest radiographs demonstrated bilateral, ill-defined nodular airspace opacities. Chest CT showed upper-lobe-predominant, patchy ground-glass opacities with areas of consolidation and a thick-walled cavity.

Case report

A 32-year-old male with a history of pyoderma gangrenosum was undergoing combination immunosuppressive treatment with dexamethasone, mycophenolate, and a TNF-receptor antagonist (infliximab) to achieve disease control when he presented to the emergency room with a three-day history of fever, chills, sweats, dry cough, and progressive dyspnea. He was a nonsmoker with occasional marijuana consumption using a water pipe. He had no history of asthma, no HIV risk-factors, and no recent sick contacts. Physical examination showed mild toxic appearance, mild dyspnea at rest, and moderate diffuse wheezing on lung auscultation. Both lower extremities had classic suppurative, necrotic, ulcerative lesions of pyoderma gangrenosum that were large but improving with aggressive immunosuppression. White blood count was 22K/uL, with 18% bands. Platelets and hematocrit were mildly reduced at 134K/uL and 32%, respectively. Serum sodium was 126 mg/dL. Lactate dehydrogenase was increased to 600 IU/L. Other routine admitting laboratory values were normal. Arterial blood gases on room air were pH-7.42, PaCO2-39, and PaO2-50. His saturation of oxygen by pulse oximetry was 93% on 6 L/min O2 by nasal cannula.

The admission chest radiograph demonstrated new bilateral, ill-defined nodular airspace opacities without pleural effusions (Fig. 1). A chest radiograph taken four weeks earlier was normal. Chest CT performed the following day showed bilateral, upper-lobe-predominant, lobular, ground-glass opacities, some of which followed a bronchovascular distribution. Scattered areas of consolidation and a right-upper-lobe, thick-walled cavity were also present (Fig. 2A-C).

Bronchovascular lavage fluid from the night of admission revealed influenza A hemagglutinin type 1 swine origin (novel 2009 H1N1) by PCR, and this was confirmed by DNA sequencing. Despite discontinuation of immunosuppression and early treatment with oseltamivir, the radiographic infiltrates and hypoxemia progressed, qualifying as acute respiratory distress syndrome (ARDS), and required...
support with continuous positive airway pressure (CPAP) and high FiO2 (70-90%) for ten days. The patient eventually improved and was discharged home after a 30-day hospitalization.

**Discussion**

Clinically, influenza is caused by subtypes of influenza A, B, or C viruses. Influenza A is the most genetically unstable subtype, and the cause of all documented influenza pandemics and epidemics (1). Furthermore, influenza A is the most common type to cause pneumonia (2). The outbreak of the current swine-origin (novel 2009 H1N1) influenza A was first detected in Mexico in late March 2009. Fewer than four months later, the World Health Organization raised its pandemic level to phase 6, the highest level, defined as widespread community transmission on at least two continents, based on the extent of international spread and not the severity of disease (3). The unique reassortment of gene segments that make up this strain had not been previously documented; however, the individual genes have been circulating for years. Previous exposure to these genes may explain the milder disease that is often present in older individuals. Swine influenza genes compose the largest portion of this viral strain. Furthermore, one of the swine influenza gene segments identified in the current strain is believed to be from the strain that caused the 1918 influenza pandemic (1).

Influenza A typically causes an upper-respiratory-tract infection in otherwise healthy individuals and only rarely causes pneumonia. Initial published reports from Mexico described a severe respiratory illness in 18 patients, with a median age of 38 years. Sixty-seven percent of
Chest CT findings of influenza A pneumonia in immunocompetent patients include predominantly diffuse or patchy ground-glass opacities mixed with smaller areas of consolidation, typically bilateral and without associated pleural effusion (5). Lobar consolidation has also been reported (6).

In immunocompromised patients, most descriptions of viral pneumonia have been reported in stem-cell transplant patients. In general, radiographic appearances of all types of viral pneumonias are quite similar and include small, poorly defined, centrilobular nodules; patchy bilateral areas of peribronchial ground-glass opacity; and consolidation. Air-trapping, septal and bronchial wall-thickening, and tree-in-bud opacities may also be present. With influenza A pneumonias, cases typically occur as seasonal outbreaks or, as in the current setting, during pandemics (2). Influenza A typically presents with patchy or diffuse ground-glass opacities or consolidation, but small centrilobular nodules are less common. As in healthy patients, lobar consolidation has been described (7).

The predominant radiographic findings in our case are typical of influenza A viral pneumonia in immunocompromised patients. Our case also demonstrated at least one cavitary lesion. Cavitary lesions are rarely associated with viral pneumonia. One report of H5N1 avian influenza A found thick-walled cavitary lesions in a small number of patients, similar to our case. Many individuals in that case series developed severe, rapidly progressive influenza pneumonia, with 85 deaths out of the 178 total infections (8). Given the paucity of data regarding cavity lung lesions in viral pneumonia, it is difficult to form any strong conclusions regarding the etiology of the cavity in our patient. However, our finding, in conjunction with the report of cavitary lesion in the H5N1 avian strain, raises the possibility that cavitation may be a feature of certain strains of influenza A pneumonia and/or may predict serious disease. Although cavitary pulmonary lesions have been rarely described in pyoderma gangreno-

Figure 2B and C. 32-year-old male with swine-origin (H1N1) influenza A. Additional selected slices from the same CT.

patients required mechanical ventilation, and the mortality rate was 38.9% (4). In contrast, currently in the U.S., the CDC speculates that complications are similar to that of seasonal influenza in both healthy and immunocompromised people.
sum, the presence of a recent normal chest radiograph and the development of a cavitary lesion in the acute phase of influenza pneumonia suggests that this cavity is likely a part of the swine-flu disease spectrum (6).

Generally, our findings for swine-origin H1N1 influenza A pneumonia in an immunocompromised patient were as expected for influenza pneumonia in the clinical setting of immune deficiency, with the exception of cavitary lesions. While there is not yet enough data, it remains possible that cavitation may be a distinguishing feature of this novel strain of influenza A, or it may signify life-threatening disease similar to that reported in the H5N1 avian influenza. Given the fact that immunocompromised patients often present atypically and are at higher risk for infection and complications, this description may be especially valuable [9].

References
1. Garten RJ, Davis CT, Russell CA, et al. Antigenic and genetic characteristics of swine-origin 2009 A/H1N1 influenza viruses circulating in humans. Science 2009;325:197-201 [PubMed]
2. Kanne JP, Godwin JD, Franquet T, Escuissato DL, Muller NL. Viral pneumonia after hematopoietic stem cell transplantation: high-resolution CT findings. J Thorac Imaging 2007;22:292-299 [PubMed]
3. Outbreak of swine-origin influenza A (H1N1) virus infection - Mexico, March-April 2009. MMWR Morb Mortal Wkly Rep 2009;58:467-470 [PubMed]
4. Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, et al. Pneumonia and Respiratory Failure from Swine-Origin Influenza A (H1N1) in Mexico. N Engl J Med 2009 [PubMed]
5. Kim EA, Lee KS, Primack SL, et al. Viral pneumonias in adults: radiologic and pathologic findings. Radiographics 2002;22 Spec No:S137-149 [PubMed]
6. Tanaka N, Matsumoto T, Kuramitsu T, et al. High resolution CT findings in community-acquired pneumonia. J Comput Assist Tomogr 1996;20:600-608 [PubMed]
7. Scott JD, Englund JA, Myerson D, Geballe AP. Influenza A pneumonia presenting as progressive focal infiltrates in a stem cell transplant recipient. J Clin Virol 2004;31:96-99 [PubMed]
8. Qureshi NR, Hien TT, Farrar J, Gleeson FV. The radiologic manifestations of H5N1 avian influenza. J Thorac Imaging 2006;21:259-264 [PubMed]
9. Update: influenza activity--United States, April-August 2009. MMWR Morb Mortal Wkly Rep 2009;58:1009-1012 [PubMed]