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CORRESPONDENCE

Secondary bacterial pneumonia due to *Staphylococcus aureus* complicating 2009 influenza A (H1N1) viral infection

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In April 2009, a novel influenza virus (2009 influenza A [H1N1] virus) was first reported in humans [1]. This was followed by case series of patients with severe 2009 influenza A (H1N1) viral infection [2–5]. Although secondary bacterial pneumonia due to *Staphylococcus aureus* was a major cause of death in patients with influenza during prior pandemics [6], it has not been well characterized during the current pandemic [2–5]. We therefore describe two patients with early onset secondary bacterial pneumonia due to *S. aureus* that occurred as a complication of 2009 H1N1 viral infection.

Patients seen at Cooper University Hospital (Camden, NJ, USA) during a 3-month period (1 June 2009 through 31 August 2009) with confirmed 2009 influenza A (H1N1) viral infection complicated by early onset secondary bacterial pneumonia due to *S. aureus* were included in our case report. Patients were considered to have confirmed 2009 H1N1 viral infection if 2009 influenza A (H1N1) virus was detected by real-time reverse transcription-polymerase chain reaction (RT-PCR) from a nasopharyngeal swab sample. *S. aureus* pneumonia was defined as a clinical diagnosis of pneumonia plus one of the following microbiological criteria: (1) growth of *S. aureus* from blood cultures, or (2) growth of *S. aureus* at a threshold of 10,000 colony forming units/mL from a quantitative bronchoalveolar lavage culture. We also performed a review of the PubMed database through 31 August 2009 to search for additional cases of early onset secondary bacterial pneumonia due to *S. aureus* that occurred as a complication of 2009 H1N1 viral infection.

Nine patients with confirmed 2009 influenza A (H1N1) viral infection were admitted to our institution over a 3-month period (1 June 2009 through 31 August 2009). Three (33%) patients with confirmed 2009 influenza A (H1N1) viral infection developed respiratory failure, and two (22%) of these patients (described below) presented with early onset secondary bacterial pneumonia due to *S. aureus*.

Patient 1 A 59-year-old female with diabetes mellitus, hypertension, hyperlipidemia, and coronary artery disease presented in late July 2009 with 1 week of nonproductive cough, fever, chills, vomiting, myalgias, and dyspnea. She had recently traveled to California where she was in close contact with a family member who had confirmed 2009 influenza A (H1N1) viral infection. At the time of hospital admission, her temperature was 100.3°F, heart rate 116 beats/min, blood pressure 93/71 mmHg, and oxygen saturation of 83% while breathing room air. Her body mass index was 41.5. She required intubation, mechanical ventilation, and vasopressor support. Laboratory examination showed a peripheral leukocyte count of 9,700 cells/mm^3 with 84% polymorphonuclear forms and a serum creatinine of 3.4 mg/dL. Influenza A/B antigen on a nasopharyngeal swab specimen was negative. A nasopharyngeal swab sample submitted for 2009 influenza A (H1N1) virus analysis by RT-PCR was subsequently reported as positive. Gram stain of a tracheobronchial aspirate showed 4+ Gram positive cocci in clusters. Bacterial culture of a tracheobronchial aspirate and one of two sets of blood cultures

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from admission subsequently grew oxacillin susceptible *S. aureus* (MSSA). Chest radiograph revealed right lower lung field opacity and computed tomography of the chest showed right middle lobe and right lower lobe consolidation consistent with pneumonia. She was empirically treated with cefotaxime, levofloxacin, rifampin, vancomycin, and oseltamivir. The antibiotic regimen was subsequently changed to nafcillin following return of blood culture results. She received oseltamivir (150 mg orally every 12 h) for 5 days and nafcillin for 4 weeks. She had difficulty weaning off of mechanical ventilation due to development of acute respiratory distress syndrome, and her hospital course was complicated by vascular catheter associated bloodstream infection. She was ultimately discharged on hospital day #53.

Patient 2 A 23-year-old female with asthma, who was 24 weeks pregnant, presented in late June 2009 with 1 week of cough and fever. On admission, her temperature was 101.7°F. Influenza A/B antigen via nasopharyngeal swab was negative. Her clinical status worsened on hospital day #3. Her temperature was 103°F, heart rate 137 beats/min, blood pressure 106/52 mmHg, respiratory rate of 47 breaths/min, and oxygen saturation of 90% while breathing with a non rebreather mask. Laboratory examination showed a peripheral leukocyte count of 10,400 cells/mm^3 with 83% polymorphonuclear forms and 15% band forms. Blood cultures drawn prior to antibiotic therapy subsequently grew MSSA in one of two sets. A respiratory tract sample could not be obtained for culture. A nasopharyngeal swab sample submitted for 2009 influenza A (H1N1) virus analysis by real-time RT-PCR was subsequently reported as positive. Chest radiograph revealed extensive right upper and lower lung field opacities and left lower lung field opacity consistent with pneumonia (Fig. 1). She required mechanical ventilation and vasopressor support. She was initially treated empirically with ceftriaxone, azithromycin, vancomycin, and clindamycin. The antibiotic regimen was subsequently changed to cefazolin following return of blood culture results. She received 4 weeks of antibiotic therapy active against MSSA. She did not receive oseltamivir because of inability to take medications enterally due to ileus. She delivered a pre-term infant at 28 weeks gestation via vaginal delivery. She had difficulty weaning off of mechanical ventilation due to development of acute respiratory distress syndrome, and her hospital course was complicated by acute renal failure requiring hemodialyis, vascular catheter associated blood stream infection, and ventilator associated pneumonia. She was ultimately discharged on hospital day #64.

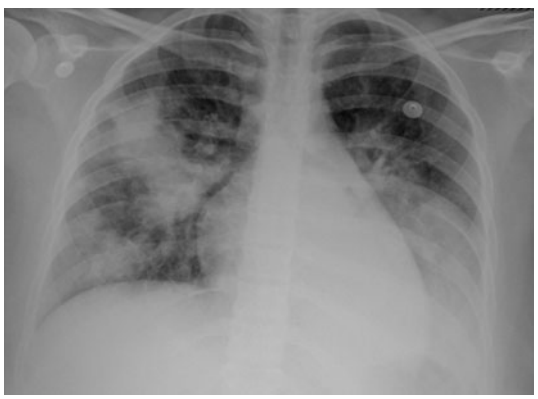

Fig. 1 Chest radiograph from patient #2, showing right upper/lower lung field opacities and left lower lung field opacity consistent with pneumonia

We performed a review of the PubMed database through 31 August 2009 and found one possible case of secondary bacterial pneumonia due to *S. aureus* complicating 2009 H1N1 viral infection. In this report, four cases of confirmed 2009 influenza A (H1N1) viral infection complicated by pneumonia were described [7]. In one of these cases, an endotracheal aspirate grew MSSA and *Escherichia coli*; however, since quantitative respiratory cultures were not performed and blood cultures were negative, it was unclear if the growth of *S. aureus* represented colonization or infection [7]. No additional cases were found in other reported series. Of 26 hospitalized patients reported with confirmed 2009 influenza A (H1N1) viral infection in California, 15 had radiographic evidence of pneumonia; however, none had microbiologic evidence of secondary bacterial infection [2]. In another case series, none of ten critically ill patients hospitalized in Michigan with confirmed 2009 H1N1 viral infection complicated by pneumonia had evidence of bacterial infection based on culture of blood and bronchoalveolar lavage (BAL) fluid [3]. Of 22 hospitalized patients with confirmed 2009 H1N1 viral infection in the United States, 11 had radiologically confirmed pneumonia; but none had microbiologically confirmed secondary bacterial infection [4]. In a case series of 18 patients in Mexico with confirmed 2009 influenza A (H1N1) viral infection complicated by pneumonia, all bacterial cultures submitted were negative [5].

In this report, we describe two patients with 2009 influenza A (H1N1) viral infection complicated by secondary bacterial pneumonia due to *S. aureus*. To our knowledge, these are among the first cases reported thus far of early onset secondary *S. aureus* pneumonia complicating 2009 influenza A (H1N1) viral infection. Given the early onset of *S. aureus* infection in these patients, these episodes would not be considered nosocomial complications but rather directly attributable to the influenza A (H1N1) infection.

Primary influenza pneumonia, secondary bacterial pneumonia, or a combination of both viral and bacterial

infection are all potential etiologies of pneumonia complicating influenza infection. Data suggest that the majority of deaths from the 1918–1919 influenza pandemic were likely due to secondary bacterial pneumonia precipitated by an interaction between the influenza virus and bacterial pathogens colonizing the respiratory tract [6]. Influenza virus has been shown to cause desquamative tracheobronchitis and bronchiolitis extending to the alveolar ducts and alveoli, which may allow for secondary spread of large numbers of colonizing bacteria along the denuded epithelial lining and subsequent secondary bacterial pneumonia [6]. Although primary influenza pneumonia has been reported in prior influenza epidemics and pandemics, the incidence appears to have been low [6, 8].

Streptococcus pneumoniae and *Streptococcus pyogenes* were the predominant causes of secondary bacterial pneumonia in the 1918–1919 influenza pandemic; however, subsequent influenza pandemics in 1957–1958 and 1968–1969 showed an increase in the proportion of cases of secondary bacterial pneumonia caused by *S. aureus* [6, 8–10]. The emergence of pneumonia caused by community-associated methicillin-resistant *S. aureus* (CA-MRSA) during the 2003–2004 and subsequent influenza seasons has further altered the microbiological spectrum of secondary bacterial pneumonia in the setting of influenza [11, 12].

In conclusion, we describe a case report of two patients with 2009 influenza A (H1N1) viral infection complicated by early onset of secondary bacterial pneumonia due to *S. aureus*. Although the 22% incidence of serious complicating staphylococcal infection in our report is based on a relatively small number of cases, this may be a harbinger of what clinicians might expect as we encounter wave two of the pandemic in the upcoming 2009–2010 influenza season. High suspicion, appropriate diagnostic studies, and potential empiric treatment for secondary bacterial pneumonia caused by *S. aureus*, including CA-MRSA, and for other community acquired pneumonia pathogens, including *S. pneumoniae* and *S. pyogenes*, needs to be considered in patients with pneumonia in the setting of 2009 influenza A (H1N1) viral infection.

Conflicts of interest statement None.

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