

# A case of swine flu superinfected with carbapenem resistant *Klebsiella*

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## ABSTRACT

Swine flu is caused by antigenic shift of influenza A virus with clinical features similar to seasonal influenza virus. Majority of the morbidity and mortality due to swine flu are attributable to pneumonia and the acute respiratory distress syndrome (ARDS). Bacterial superinfection can occur, though it is rare in adults. Here we report a case of swine flu superinfected with carbapenem resistant *Klebsiella*, which is often coined as *Klebsiella* 'superbug'.

**Key words:** Swine flu, Bacterial superinfection, Carbapenem resistant *Klebsiella*

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## INTRODUCTION

Swine flu is primarily a respiratory disease caused by a reassortant virus. Though it is usually species specific (pigs), occasionally it crosses species barrier and infects humans.<sup>1</sup> First isolation of swine influenza virus from a human was done in 1974.<sup>2</sup> In the past, though cases of person to person transmission have been reported, it resulted in small outbreaks only.<sup>2</sup> Then in March and April 2009, there was an outbreak of swine H1N1 influenza A virus in Mexico with subsequent cases being detected later in several other countries including United States and India<sup>3</sup> (so called 2009 flu pandemic). The signs and symptoms of swine flu caused by H1N1 influenza A virus are similar to those in seasonal influenza virus.<sup>4</sup> However, secondary bacterial pneumonia may complicate viral pneumonia, especially in pediatric age group.<sup>4</sup> But among adults, bacterial coinfection is a rarity.<sup>4</sup> Here, we report a case of swine flu superinfected with carbapenem resistant *Klebsiella*.

## CASE REPORT

A 65 years old female patient presented to us with history of abrupt onset high grade fever along with chill, headache, dry cough, sore throat, myalgia, malaise and anorexia of one week duration. The patient was disoriented, dehydrated and tachypneic. The cough was

nonproductive and nonpurulent. There was no history of diarrhea or vomiting. Neck rigidity was absent. There was diminished movement of right side of chest. Also, there was impaired resonance on percussion. On auscultation of right side of chest, bronchophony and tubular breath sounds were found especially in the mid portion. On routine investigations, neutrophilic leukocytosis (total white blood cell [WBC] count 13,400 /cu mm with 84% neutrophil) and moderate anemia (hemoglobin 8.95 g/dL) were found. Liver function test (LFT) showed elevated SGPT (serum glutamic pyruvic transaminase- 3706.0 U/L) level. Chest x-ray PA (posteroanterior) view showed homogenous opacity involving right middle lobe of lung with no mediastinal shift. Initially she was diagnosed as a case of viral hepatitis with encephalopathy and chest infection and treated symptomatically with empirical antibiotics (co-amoxiclav 1.2 g and metronidazole 500 mg, both thrice daily intravenously) and adequate hydration.

However on the very next day, the real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) swine flu panel was done on throat swab specimen and it showed a positive result for swine flu (as per report from National Institute of Cholera and Enteric Diseases [NICED], Kolkata). Subsequently, neuraminidase inhibitor oseltamivir 75 mg twice daily through Ryle's tube (patient was disoriented) was started without any delay. For initial couple

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of days, the patient responded with reduced total leukocyte count (12,200 /cu mm) and SGPT level (402.8 U/L). On 5<sup>th</sup> day of admission, the patient became unconscious, dyspneic with peripheral desaturation (oxygen saturation of peripheral arterial blood [SpO<sub>2</sub>] <85%) and crepitations throughout both lung fields. Arterial blood gas analysis showed mild respiratory alkalosis (pH) with PaO<sub>2</sub> (partial pressure of oxygen in blood) of 55 mm Hg. The patient was immediately intubated and put on mechanical ventilator on volume control mode (with tidal volume 6 ml/kg of predicted body weight and positive end expiratory pressure [PEEP] of 10 cm H<sub>2</sub>O maintaining plateau airway pressure below 30 cm H<sub>2</sub>O). Antibiotic regimes were changed to linezolid (600 mg twice daily intravenously) and ceftazidime (2 g thrice daily intravenously). Chest x-ray PA view revealed diffuse, bilateral, interstitial and alveolar infiltrates. Steroids (hydrocortisone 100 mg twice daily on intravenous route and budesonide respules 0.5 mg/2 ml, 4 times a day through nebulisation) and bronchodilator (salbutamol respules 5 mg/2.5 ml, 4 times a day through nebulisation) were added. With these measures, vital hemodynamic parameters (pulse, respiratory rate, non-invasive blood pressure and oxygen saturation) became stable. Acute respiratory distress syndrome (ARDS) was suspected. Graveness of the situation was explained to patient party. Suction material from endotracheal tube was sent for bacteriological culture and sensitivity maintaining adequate sterility. Next day, the culture and sensitivity reports were received. The VITEK® 2 Advanced Expert System™ (AES) phenotypically identified the organism as *Klebsiella* spp. with ESBL (extended spectrum beta lactamase) + Carbapenemase (Metallo- or KPC i.e., *Klebsiella pneumoniae* Carbapenemase) resistance mechanism sensitive only to colistin (minimal inhibitory concentration [MIC] <0.5 mcg/ml) and intermediate sensitivity to tigecycline (MIC 4 mcg/ml). Then, the patient was started on tigecycline (100 mg bolus followed by 50 mg every 12 hours through intravenous route). The rRT-PCR was repeated on throat swab specimen and it was negative for swine flu virus (as per report from NICED). In spite of the treatment, the patient gradually developed hypoxia followed by type I respiratory failure. Over next two days, she developed shock and azotemia. Vasopressor was added (noradrenaline infusion started initially at 12 mcg/min and later titrated as per blood pressure). The patient experienced a rapid and progressive downhill course over the next four days by developing multi organ dysfunction syndrome. Subsequently, the patient died on the thirteenth day of admission.

## DISCUSSION

Influenza occurs in seasonal epidemics affecting mainly those with extremes of ages (<6 months or >65 years) or

with comorbid medical illness. About 80% of influenza deaths and most severe disease are attributable to H3N2 strains of influenza A.<sup>5</sup> In early months of 2009, a novel H1N1 influenza A virus descendent of the 1918 pandemic strain, appeared in Mexico.<sup>3</sup> It was sufficiently different from previously circulating seasonal H1N1 viruses to qualify as an antigenic shift and its resultant spread around the world has been classified as 2009 flu pandemic. This new strain of H1N1 influenza A virus is known as pandemic H1N1 or pH1N1, novel H1N1, SOIV (swine origin influenza virus) or swine flu.

Influenza epidemics due to seasonal strain used to occur as a result of minor changes in the antigenic characteristics of the hemagglutinin and neuraminidase glycoproteins of the influenza viruses (antigenic drift).<sup>6</sup> Morbidity and mortality associated with seasonal influenza outbreaks are significant, especially in older patients.<sup>5</sup> However, influenza pandemics like that of swine flu, occur less frequently due to major changes of surface glycoproteins of the viruses (antigenic shift). Groups at risk of getting affected with swine flu include those with underlying cardio-pulmonary disease, having immunosuppression, pregnancy, lactation, diabetes, obesity or neurological disabilities.<sup>7</sup> The clinical features of uncomplicated influenza are that of other respiratory viral infections.

Majority of the morbidity and mortality due to swine flu are attributable to pneumonia and the acute respiratory distress syndrome (ARDS).<sup>8</sup> Pneumonia may be primary viral or mixed viral and secondary bacterial. Those progressing to ARDS have the worst prognosis.<sup>8</sup> Secondary bacterial infection is much more prevalent in swine flu affected patients than their seasonal counterpart. A study on lung specimens from 77 fatal cases of pH1N1 infection found 29% prevalence of bacterial superinfection and *Pneumococcus*, *Staphylococcus aureus*, and *Streptococcus pyogenes* being the commonest.<sup>4</sup>

However, *Klebsiella* superinfection in a swine flu patient is a rare finding. To the best of our present knowledge, it is the first case report of swine flu superinfected with carbapenem resistant *Klebsiella*. Carbapenemase producing bacteria are often referred to as 'superbugs' because infections caused by them are difficult to treat. Sometimes, such bacteria are sensitive to polymyxins or tigecycline<sup>9</sup> (in our case, it was sensitive to colistin and intermediately sensitive to tigecycline). In 2009, a Swedish national travelling India, developed UTI (urinary tract infection) caused by carbapenem resistant *Klebsiella* sensitive to tigecycline and colistin. After genotypic analysis of the isolate, a new strain was found which is known today as NDM-1 or New Delhi metallo-beta-lactamase-1.<sup>10</sup> Unfortunately in our case, genotypic analysis could not be done.

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### Authors Contribution:

**RH & MSM** – Prepared the initial draft. **RH, MBM, SC, KG** – Contributed to the manuscript. **RH** – Reviewed and helped in final preparation of the manuscript.

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