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CASE REPORT

Coinfection with *Mycobacterium tuberculosis* and pandemic H1N1 influenza A virus in a patient with lung cancer

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Streptococcus pneumoniae, *Haemophilus influenzae*, and *Staphylococcus aureus* were responsible for bacterial coinfection during previous or 2009 influenza pandemic and were associated with a higher risk of influenza-related morbidity and mortality. Despite tuberculosis (TB) is still a growing problem worldwide, *Mycobacterial tuberculosis* is rarely a copathogen with influenza. We hereby report a cancer patient with TB and pandemic H1N1 influenza A virus coinfection. Physicians should be aware that TB may present as a coinfection in an immunocompromised patient with 2009 influenza A (H1N1) infection, especially in TB endemic area.

Introduction

Although the emergence and subsequent globally spread of the 2009 pandemic influenza A (H1N1) has gained worldwide concern, tuberculosis (TB) remains another serious public health issue. According to the estimation of World Health Organization, there were 13.7 million TB cases globally with 9.27 million new cases and 1.76 million deaths

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from TB in 2007.[1] In Taiwan, there were 14,265 newly diagnosed TB cases with an incidence of 62 cases per 100,000 population and a TB mortality rate of 3.3 deaths per 100,000 population in 2008.[2] Moreover, the high prevalence of multidrug-resistant TB and the presence of extensively drug-resistant TB in Taiwan is another potentially devastating threat to TB control.[3]

During previous influenza pandemic, most deaths caused by influenza A virus infection were accompanied by concurrent bacterial pneumonia.[4,5] In 2009, study of autopsy specimens from 77 fatal cases of confirmed pandemic influenza A (H1N1) showed that 22 (29%) had concurrent bacterial infection, and 10 of them were caused by *Streptococcus pneumoniae*.[6] However, the knowledge about coinfection with *Mycobacterium tuberculosis* (MTB) and pandemic H1N1 influenza virus is still limited.[7] We hereby report a case with TB and pandemic H1N1 Influenza A virus coinfection.

Case report

A 63-year-old man presented with fever and shortness of breath on September 13, 2009. No headache, productive cough, myalgia, vomiting, or diarrhea was complained. He had a history of squamous cell lung cancer noted in 2007 and was currently treated with chemotherapy and radiotherapy. Dilated cardiomyopathy and coronary artery disease were also diagnosed in 2009. The patient denied a history of travel and animal contact, but he reported that his daughter was diagnosed to have influenza A on September 14, 2009. His body mass index was 26.8 kg/m^2 and, vital signs were temperature of 39°C, pulse rate of 96/min, respiratory rate of 26/min, and blood pressure of 116/74 mmHg. Physical examinations were unremarkable except for bilateral coarse crackle and diffuse wheezes on chest auscultation. The results of laboratory tests were as below: white blood cell, 4,610 cell/mm^3 (neutrophil, 82.4%; lymphocyte, 11.1%); hematocrit, 31.1%; platelet count, 152,000 cell/mm^3; serum creatinine, 1.3 mg/dL; and C-reactive protein, 3.86 mg/dL (normal $<$ 0.8 mg/dL). Chest radiography and computed tomography showed a mass lesion at the right paratracheal region, a new developed consolidation lesion with air bronchogram over the right middle lobe, right pleural effusion, and increased infiltration bilaterally (Fig. 1). No malignant cells were found in the aspirated pleural effusion. Serological tests for anti-*Mycoplasma pneumoniae* IgM (Savyon Diagnostics Ltd., Ashdod, Israel), Binax NOW *S pneumoniae* urinary antigen test (Binax Inc., Portland, ME, USA), and *Legionella* urinary antigen test for serogroup 1 (Binax Inc.) were all negative. The influenza rapid test (QuickVue Influenza A + B test; Biomerieux, San Diego, CA, USA) for a nasopharyngeal swab sample was positive for influenza A. An in-house real-time reverse transcriptase polymerase chain reaction from nasopharyngeal swab sample was also positive for 2009 pandemic influenza A (H1N1). He then received a 5-day course of oseltamivir (75 mg twice daily). The sputum culture yielded *S pneumoniae*, although the quality of the sputum specimen was not acceptable (polymorphonuclear cells, 10—25 cells per low-power field and epithelial cell count, 10—25 cells per low-power field). Cefuroxime (250 mg every 12 hours) was also prescribed for suspected coinfection of bacterial pneumonia. The patient received antimicrobial treatment for 7 days and was discharged uneventful. However, one sputum specimen collected during hospitalization was acid-fast smear negative but grew MTB, which were susceptible to all anti-TB agents tested. The patient then received anti-TB treatment (isoniazid, rifampin, ethambutol, and pyrazinamide) since October 9, 2009. Two sputum samples collected during outpatient clinic visits also grew MTB.

Discussion

Previous studies showed that *S pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and group A *Streptococcus*

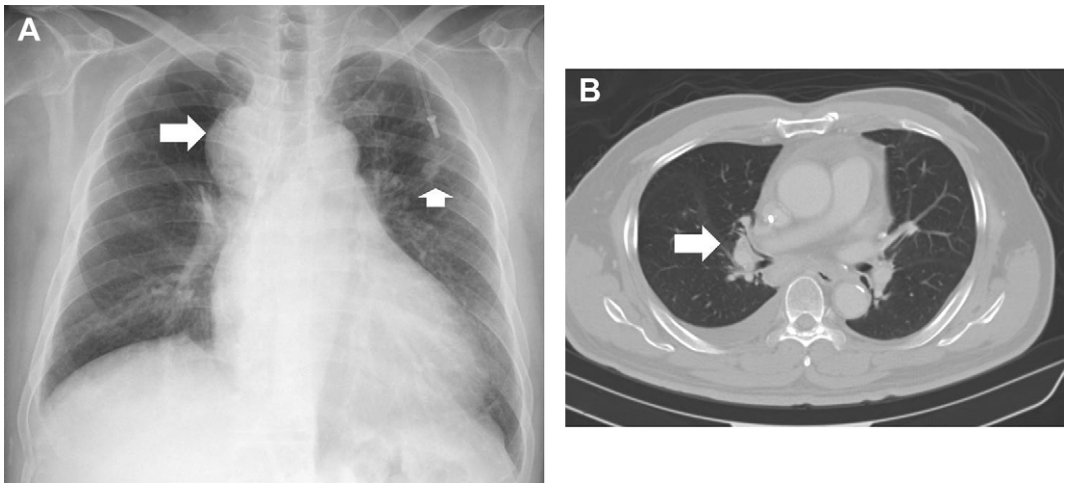

Figure 1. (A) Chest radiography showing a mass lesion (lung cancer, arrow) at the right paratracheal region, a calcified nodular lesion (arrow head) over the left upper lobe, increased infiltration over the bilateral lung, and pleural effusion in the right lung and (B) chest computed tomography demonstrating a new developed consolidation lesion with air bronchogram (arrow) over the right middle lobe and right pleural effusion in a patient with lung cancer who had coinfection with *Mycobacterium tuberculosis* and 2009 influenza A (H1N1) virus.

were responsible for bacterial coinfection during previous or 2009 influenza pandemic,[4–6] but active TB coinfection was only reported in seven fatal pandemic H1N1 influenza infection cases in South Africa.[7] This is the first case with laboratory-confirmed coinfection with pandemic H1N1 influenza virus and MTB in an immununocompromised patient in Taiwan, an area with a high incidence of TB. Although sputum culture was positive for *S pneumoniae* in this patient, the poor quality of the sputum specimen and negative urinary pneumococcal antigen testing excluded the possibility of coinfection with *S pneumonaie*.

It should be noted that persons with risk factors for severe complications from pandemic 2009 influenza A infection, such as chronic lung disease and immunosuppression,[8] also appear to be at risk of TB. In the present report, the immunocompromised status from his lung cancer would have contributed both to the development of TB and to the onset of influenza. Furthermore, early diagnosis of TB is crucial for patients that receiving immunosuppressive treatments, such as cancer chemotherapy and immunomodulatory agents, because delay in diagnosis may contribute to morbidity and mortality. Therefore, MTB should also be considered as one of the important copathogens with pandemic H1N1 influenza A infection to avoid delay diagnosis in the area with a high prevalence of TB.

Previous studies showed that bacterial coinfection was associated with a higher risk of influenza-related morbidity and mortality.[4–6] Likewise, active TB coinfection might also be associated with a higher morbidity and mortality in patients with influenza. TB was associated in 10% of the 2009 influenza A (H1N1) fatality cases in South Africa, and even higher (19%) in deceased pregnant women.[7] It is difficult to determine a cause and effect relationship between TB coinfection and mortality based on the rare occurrences of TB coinfection with influenza A, further epidemiology study is need to clarify the role of TB coinfection in contribution to severe complications.

In conclusion, physicians should be aware that TB may present as a coinfection in an immunocompromised patient with 2009 influenza A (H1N1) infection, especially in TB endemic area.

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