

# CASE REPORT

## HEMOPTYSIS IN CHILDREN WITH PANDEMIC INFLUENZA H1N1 2009 INFECTION

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**Abstract.** Three patients were admitted to Hat Yai Hospital, Songkhla Thailand with hemoptysis. They were previously healthy children aged 6, 13, and 14 years old who had attended schools in which outbreaks of influenza had occurred. They all had a history of fever, rhinorrhea, and severe cough accompanied by hemoptysis. Two developed hemoptysis on Day 3 and the third on Day 6 of illness, with one of them displaying massive hemoptysis. Chest radiographs were compatible with viral pneumonia in two cases and the third case was unremarkable. Coagulation profiles in the severe case were carried out and were normal. All the patients responded very well to treatment with oseltamivir and did not require intubation. Their subsequent nasopharyngeal swabs were positive for human pandemic influenza A H1N1 by real-time reverse transcription-polymerase chain reaction (RT-PCR), and their sputum for acid-fast bacilli and tuberculin skin tests were negative.

### INTRODUCTION

A novel pandemic influenza A H1N1 virus emerged from Mexico in March 2009. The first two cases were reported in Thailand on May 12, 2009. There were no further reported cases of influenza A H1N1 in Thailand until June 12, 2009 when outbreaks occurred in several schools in Bangkok. The schools had 7 to 20 cases each (Chieocharnsin *et al*, 2009). Since then, more than 20,000 confirmed cases have been reported in Thailand. Of those, there were 153 deaths (Department of Disease Control, Thailand, 2009). Presentation

of influenza virus infection varies from asymptomatic infection to serious illness that may include exacerbation of other underlying conditions and severe viral pneumonia with multi-organ failure (WHO, 2009). Hemoptysis is an unusual of seasonal influenza virus infection. Here, we describe three cases of hemoptysis in children with pandemic influenza H1N1 2009 infection admitted to Hat Yai Hospital, Songkhla Thailand, during the peak of the influenza outbreak in southern part of Thailand between July and August, 2009.

### CASE REPORT

#### Case 1

A previously healthy Thai boy age 13 years, presented to the hospital with a history of low grade fever, rhinorrhea and

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severe productive cough. He was treated as an outpatient with roxithromycin. On day 3 of illness, his fever had improved but he still had persistent cough and developed bloody sputum (3-5 ml of fresh blood with and without mucus). On the 7<sup>th</sup> day of illness, he was admitted to hospital due to unimproved severe cough, hemoptysis and vomiting.

On admission, the patient appeared acutely ill but without clinical signs of respiratory distress. His temperature was 36.5°C, his blood pressure was 100/60 mmHg, his pulse rate was 80 beats/minute, his respiratory rate was 24 breaths/minute, and his oxygen saturation was 98% on room air. A physical examination of his chest had good air movement bilaterally with no adventitious sounds. The chest radiograph was unremarkable. His complete blood count revealed normal hematocrit (40%), a white blood cell count of 7,200 cells/mm<sup>3</sup> with a differential of 52% segmented neutrophils and 44% lymphocytes, and a platelet count of 312x10<sup>3</sup>/mm<sup>3</sup>. Due to the outbreak of pandemic influenza H1N1 in his school, he was started on oseltamivir treatment on the first day of admission and treatment was continued with roxithromycin. During hospitalization, he improved and was discharged on oseltamivir on the third day after admission. His subsequent nasopharyngeal swab was positive for pandemic influenza A H1N1 by real-time RT-PCR. His sputum for acid-fast bacilli and tuberculin skin test were negative.

## Case 2

A 14-year-old girl was referred from a district hospital with a history of massive hemoptysis. She developed high grade fever, rhinorrhea, and colored sputum for 2 days. On the third day of illness, she developed cough with a large amount, approximately 300-400 ml, of fresh blood just prior to her admission to the district hospital

where she soon again had hemoptysis of 200 ml. At the district hospital her temperature was 39.0°C, her blood pressure was 122/75 mmHg, her heart rate was 118 beats per minute, her respiratory rate was 30 breaths per minute, and her oxygen saturation was 94% on room air. She had received a normal saline infusion and oxygen therapy by cannula before being transferred. She had no history of underlying diseases.

She was transferred to our intensive care unit and had respiratory monitoring with stand-by for emergency intubation and ventilation support. She was slightly pale, without dyspnea, or cyanosis and afebrile (36.6°C). Her blood pressure was 109/72 mmHg, her pulse rate was 100 beats/minute, her respiratory rate was 28 breaths/minute, and her oxygen saturation was 95% on room air. On physical examination her lung, had fine crackles bilaterally. A chest radiograph showed a reticulonodular infiltration of the perihilar regions, mild blunting of the left costophrenic angle which could have been due to effusion or pleural thickening and her trachea and main bronchus appeared normal. (Fig 1) Her complete blood count showed anemia with a hematocrit of 28%, a white blood cell count of 10,200 cells/mm<sup>3</sup> and a differential of 75% segmented neutrophils and 21% lymphocytes, and a platelet count of 205x10<sup>3</sup>/mm<sup>3</sup>. Her prothrombin time was 13.8 seconds (control = 12.7, INR 1.10) and her partial thromboplastin time was 26.3 seconds (control = 26.3 seconds).

She had a history of contact with friends positive for pandemic influenza A H1N1 virus infection. The patient was started on oseltamivir treatment within the first hour upon admission. Two hours after admission, she had hemoptysis of a further 200 ml of fresh blood and her oxygen saturation on room air dropped to 93% but her vital signs remained stable. Her respiratory status was observed closely. Serial hematocrits



Fig 1-The chest x-ray of the second patient showed reticulonodular infiltration at the perihilar region, mild blunting of the left costophrenic angle.

remained between 28% and 30% and did not require replacement of blood or blood products. Sixteen hours after treatment, she coughed up a small amount of old clotted blood. On the second day of admission, she was weaned off nasal cannula oxygen and was discharged on the fourth day after admission. Her subsequent nasopharyngeal swab was positive for pandemic influenza A H1N1 by real time RT-PCR and her sputum for acid-fast bacilli and tuberculin skin test were negative.

### Case 3

A 6-year-old boy was admitted on the sixth day of illness with a history of fever and hemoptysis. He had previously been healthy and came to the hospital with high

grade fever, rhinorrhea, and productive cough with clear sputum. He was treated with amoxicillin but his symptoms did not improve. He still had fever and persistent severe cough with a small volume of fresh blood in the sputum (approximately 10 ml), followed by vomiting.

On admission, his a temperature was 38.0°C, his blood pressure was 90/60 mmHg, his heart rate was 118 beats per minute, his respiratory rate was 32 breaths per minute, and his oxygen saturation was 97% on room air. Upon initial physical examination, he displayed mild dyspnea but his chest showed good air movement bilaterally with no adventitious sounds. Chest radiograph showed increased density of the right lower lung field with air bronchograms, suspicious for right lower lung bronchopneumonia.

His complete blood count showed a hematocrit of 39%, white blood cell count of 22,200 cells/mm<sup>3</sup> and a differential of 85% segmented neutrophils and 13% lymphocytes, and a platelet count of 259x10<sup>3</sup>/mm<sup>3</sup>, CRP of 12 mg/l.

Due to the pandemic influenza A H1N1 outbreak in his school, he was started on oseltamivir treatment within 2 hours of admission and continued on amoxicillin due to his elevated white blood cell count. Two hours after admission, he again had hemoptysis with fresh blood. After 24 hours treatment, his fever and hemoptysis had subsided. He was discharged after 2 days. His subsequent nasopharyngeal swab was positive for pandemic influenza A H1N1 by real time RT-PCR and his sputum for acid-fast bacilli and tuberculin skin test were negative.

### DISCUSSION

There have been previous reports of hemoptysis associated with influenza virus infection in children, who without exception displayed abnormal coagulation (Davidson

*et al*, 1973; Bond and Vyas, 2001). Another report described severe hemoptysis associated with viral tracheitis in a 51-year-old woman, which was subsequently exacerbated by anticoagulant treatment (Lewis *et al*, 1982). Recently, there was a report of a 47-year-old female with pandemic influenza H1N1 who presented with hemoptysis and was diagnosed with real time RT-PCR (Kapelusznik *et al*, 2009).

During the outbreak of pandemic influenza A H1N1 in southern Thailand, we had three cases of previously healthy children who developed influenza-like illness (ILI) presenting with hemoptysis and were subsequently diagnosed with having pandemic influenza A H1N1 infection. The second case had massive hemoptysis without coagulation abnormalities. Unfortunately, the coagulation profiles for the first and third case were not been carried out because of their hemoptysis was mild. None of the patients required intubation even in the case of massive hemoptysis and all improved very well after treatment with oseltamivir. Even though virus infection has not been mentioned as a probable cause of hemoptysis in children (Boat, 1998; Nevin, 2007), due to pandemic influenza A H1N1 infection, when the clinical signs and history are suggestive for ILI, a viral etiology, such as influenza, should be considered in the differential diagnosis of hemoptysis, especially in healthy children. In these cases, bloody sputum was one of the indicators of disease progression which would necessitate an urgent review of patient management (WHO, 2009).

According to a recent study, in ferrets and mice comparing novel pandemic H1N1 influenza virus and contemporary H1N1 influenza virus (A/Brisbane/2007/H1N1) in terms of pathogenicity and transmissibility (Maines *et al*, 2009; Munster *et al*, 2009), the novel H1N1 virus had the ability to more efficiently replicate in both the upper and

lower respiratory tract than the seasonal H1N1 influenza virus. Pandemic influenza viruses can be recovered from the nasal turbinates, trachea and lungs while with seasonal influenza virus it is detected exclusively on the nasal turbinates. Although ILI symptoms are mild to moderate when a patient is infected with the novel pandemic virus, the symptoms observed in ferrets proved to be more severe and caused necrotizing rhinitis, tracheitis, bronchitis and bronchiolitis. Thus, due to its higher replication efficiency, the pandemic influenza A virus 2009 can develop more severe and prolonged cough, causing traumatic bleeding, with bloody sputum and hemoptysis in some patients, such as children and immune-deficient individuals.

In conclusion, during an outbreak of the novel pandemic H1N1 influenza virus, patients with extraordinary symptoms such as severe cough, blood streaked sputum and hemoptysis may occur.

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