Spontaneous pneumomediastinum in a child due to 2009 pandemic influenza A (H1N1) virus

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The 2009 pandemic influenza A (H1N1) virus spread throughout the world and caused different clinical situations. Here, we report a 4.5-year-old boy with spontaneous pneumomediastinum (SPM) complicating pneumonia associated with H1N1 virus. SPM could be associated with bronchial obstruction or necrotizing pneumonia, and the prognosis of patients with SPM associated with necrosis is worse than of patients with SPM associated with bronchial obstruction.

Key words: children, complication, influenza, influenza A (H1N1) virus, pneumonia, spontaneous pneumomediastinum.

The epidemiology of the 2009 pandemic influenza A (H1N1) virus infection to date indicates that children and young adults have had the highest attack rates. A wide clinical spectrum of disease ranging from non-febrile, mild upper respiratory tract illness or febrile influenza-like illness to severe or even fatal complications, including rapidly progressive pneumonia, has been described[1]. Approximately 10-30% of hospitalized patients in some countries have required admission to intensive care units[2]. Critically ill patients include those who experienced rapidly progressive lower respiratory tract disease, respiratory failure and acute respiratory distress syndrome with refractory hypoxemia. Other severe complications have included secondary invasive bacterial infection, septic shock, renal failure, multiple organ dysfunction, myocarditis, encephalitis, and worsening of underlying chronic disease conditions such as asthma, chronic obstructive pulmonary disease or congestive cardiac failure[3].

Spontaneous pneumomediastinum (SPM) is a rare and usually benign entity seen most commonly in children with asthma. It implies a spontaneous alveolar rupture leading to the presence of mediastinal air without a pneumothorax and excludes those related to trauma, ventilation or iatrogenic barotraumas[4].

We report a child with unexpected SPM complicating pneumonia associated with nosocomial 2009 pandemic influenza A (H1N1) virus under treatment for bilateral retinoblastoma. To the best of our knowledge, this is the first report of SPM developed in an immunocompromised child due to nosocomial 2009 pandemic influenza A (H1N1) virus.

Case Report

A 4.5-year-old boy was referred to our pediatric infectious diseases department and pediatric intensive care unit (PICU) from our pediatric oncology department with a history of sudden onset of dyspnea and cough, which started a few hours before presentation. He had been admitted to our pediatric oncology department to receive chemotherapy for retinoblastoma three weeks before.

His physical examination showed severe dyspnea and cyanosis. His respiratory rate was 52 breaths per minute and he had an oxygen saturation of 84% on room air. He had marked flaring of the alae nasi and subcostal and intercostal retraction. On auscultation, bilateral rales and insufficient vesicular sounds

were heard. On cardiac examination, he was tachycardic with regular rhythm without murmurs, rubs or gallops. His blood pressure was 105/72 mmHg and body temperature was 37.3°C. The remainder of the physical examination was unremarkable.

We transferred the patient from pediatric oncology clinic to PICU for severe respiratory distress syndrome. His white cell count was 23,400/mm^3 (total neutrophil count: 20,124/mm^3 and total lymphocyte count: 2,808/mm^3) and C-reactive protein (CRP) was 1.9 mg/dl. The arterial blood gas showed hypoxia (pH: 7.4, pCO_2: 40.2 mmHg and pO_2: 56.3 mmHg) and the biochemical examination was normal. There were infiltrations bilaterally but especially on the left side on chest X-ray. We took nasopharyngeal and oropharyngeal-swab specimens for 2009 pandemic influenza A (H1N1) virus, and we started oseltamivir (90 mg/day), ganciclovir, meropenem, teicoplanin, and co-trimoxazole with oxygen via high flow nonrebreathing oxygen mask.

In the PICU, on the 5th day of follow-up, his respiratory distress increased. A check of his chest X-ray revealed suspected pneumomediastinum and a computed tomography (CT) scan was performed, which revealed bilateral necrotizing pneumonic infiltrations and mediastinal emphysema (Fig. 1). There was no pneumothorax and no extension to the retroperitoneum. We decided to follow without mediastinal tube since he could maintain values of blood gases within normal limits.

The patient's sample was positive for 2009 pandemic influenza A (H1N1) virus by real-time polymerase chain reaction (PCR). We preferred to follow him under oxygen supplementation without positive pressure ventilation due to fear of over collection of air in the mediastinum or addition of new air leaks. However, on the 7th day of PICU admission, acute respiratory failure developed and conventional mechanical ventilation (MV) was administered at a rate of 30/minute, inspiration time 1.2 second, peak inspiratory pressure 36 cmH_2O, positive end-expiratory pressure 14 cmH_2O, and FiO_2 100%. However, since the patient's PO_2/FiO_2 was 55 and oxygenation index was 46 under conventional MV, we switched to high frequency oscillatory

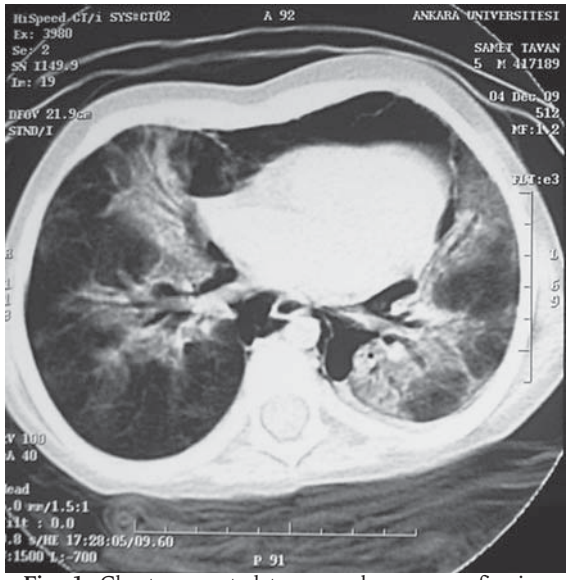

Fig. 1. Chest computed tomography scan confirming mediastinal emphysema and necrotizing pneumonic consolidation.

MV. His pneumomediastinum increased during MV and crepitus appeared due to subcutaneous air retention on the neck and the upper sides of the chest. Then, two mediastinal chest tubes were inserted, and mediastinal air collection decreased. We delivered in the prone position because of uncorrected severe hypoxemia due to acute respiratory distress syndrome based on the 2009 pandemic influenza A (H1N1) virus.

No bacteria were cultured in the patient's tracheal aspirates or blood and urinary samples. Cytomegalovirus was negative in blood samples. *Pneumocystis jiroveci* was negative in tracheal aspirate. Despite those treatment modalities, he died on the 11th day of PICU admission because of acute respiratory distress syndrome and multiple organ dysfunction syndrome due to 2009 pandemic influenza A (H1N1) infection. This report was approved by our Institutional Review Board.

Discussion

In contrast to seasonal H1N1 viruses, the 2009 pandemic influenza A (H1N1) virus disproportionately affects children and young adults, and the presentation can be severe. The most frequent serious complications of influenza are pulmonary and include primary viral pneumonia, secondary bacterial

pneumonia, pneumonia attributable to unusual pathogens, and exacerbations of chronic underlying pulmonary diseases[3]. Primary viral pneumonia is the main cause of intensive care unit admission in 2009 pandemic influenza A (H1N1) virus- infected patients, with developing severe respiratory failure, which is associated with a relatively high case fatality[5]. In our patient, the symptoms started suddenly and his clinical progress worsened rapidly because of the complicated pneumonia associated with the occurrence of SPM due to 2009 pandemic influenza A (H1N1) virus.

Pneumomediastinum or mediastinal emphysema is defined as the presence of air in the mediastinum. SPM occurs in cases of mediastinal leaks that are not caused by trauma (i.e., endotracheal or endoesophageal procedures, MV, cardiac catheterization, or thoracic surgery in patients without underlying lung disease). In most cases, the pathogenesis of SPM is due to excess pressure causing distention and the eventual rupture of a pulmonary alveolus surrounding bronchioles and pulmonary vessels. The air spreads into the mediastinum by traversing the hilum along the peribronchovascular sheaths. Additionally, SPM can complicate pulmonary emphysema, with air drainage through the interstitium to the hilum, mediastinum, neck, and skin[6].

Pneumonias complicated by SPM are most notably *Pneumocystis jiroveci* and *Mycoplasma pneumoniae* pneumonias[7,8]. SPM subsequent to seasonal influenza is relatively rare, even though a patient with influenza virus bronchiolitis complicated by SPM was described by Tutor et al.[9]. Hasegawa et al.[10] reported two occurrences of SPM complicating pneumonia in Japanese children infected with the 2009 pandemic influenza A (H1N1) virus. One of those children was previously healthy and the other had a history of allergic rhinitis. Both of them showed signs of bronchospasm and the developmental mechanism of SPM was associated with bronchial obstruction. Both were treated with continuous inhalation of a bronchodilator and intravenous prednisolone, as well as antiviral therapy. Their outcomes were good and they recovered within four days[10]. In children, SPM is observed most commonly in status asthmaticus, bronchiolitis or bronchitis, like those Japanese patients infected with the 2009 pandemic influenza A (H1N1) virus. However, there were no signs of bronchospasm due to bronchial obstruction on physical examination in our patient and the chest CT scan showed parenchymal necrosis. Therefore, we suspect that in our patient SPM was caused by necrotizing pneumonia.

Spontaneous pneumomediastinum usually follows a benign and self-limiting course, and the usual treatment required is bed rest, oxygen therapy, reassurance, and analgesics. It should be remembered, however, that potentially life-threatening complications might arise. These conditions - tension pneumomediastinum, single or bilateral simple pneumothorax or tension pneumothorax and increased pressure in the pulmonary interstitium - make respiration difficult. In most of these patients, it appears that the pneumomediastinum resolves over a period of one week, and they rarely experience any sequelae related to this problem[4,6]. In our patient, acute respiratory failure developed refractory to conventional MV because of the SPM. Despite successful insertion of two mediastinal chest tubes and high frequency oscillatory MV, his hypoxic status did not change. Unfortunately, the patient could not be saved despite the early diagnosis, prompt initiation of antiviral treatment and supportive respiratory approach to SPM.

In conclusion, SPM may rarely be the symptom of 2009 pandemic influenza A (H1N1) virus infection. This condition could be associated with bronchial obstruction or necrotizing pneumonia, and the prognosis of the patients with SPM associated with necrosis is worse than that of SPM associated with bronchial obstruction.

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