PULMONARY FINDINGS OF AVIAN INFLUENZA A (H5N1) PNEUMONIA OF A FAMILY CLUSTER IN KAMPHAENGPHET OUTBREAK.

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ABSTRACT

Until now, avian influenza pneumonia is very hot issue and life threatening disease in Kamphaengphet, in Thailand and in Asian countries. Recent outbreak of avian influenza A (H5N1) in rural areas of Kamphaengphet Province and human infection with this virus were occurred in September 2004 (second outbreak in Thailand).

The object of this report was to show the epidemiology, clinical features and pattern of pulmonary findings that could be found in avian influenza pneumonia, which might be helpful for future diagnosis and comparison of this disease with the next outbreaks.

We reviewed the pulmonary findings of a family cluster of three involved patients. Two confirmed cases were mother and aunt. They have been confirmed as cause by H5N1 strain by viral study. The mother was dead but the aunt has been survived. One probable case was the index girl. She was the first fatal case and was under investigation for H5N1 on admission due to initial diagnosis was dengue hemorrhagic shock syndrome. However, her retrospective diagnosis was presumed by a history of exposure to infected household chickens, and clinical features that corresponding to cardinal features of previously reported cases, and her mother's death from severe H5N1 pneumonia after having close contact with her.

In fact, the mother had no history of exposure to poultry, so we believe that the avian influenza H5N1 virus was probably transmitted directly from the infected girl to the mother after unprotected bedside care. No additional cases were identified among contacts.

The radiographs of these three involved patients were abnormal on admission. All pulmonary findings were air space patterns, including unilateral and bilateral lesions, patchy infiltration and lobar consolidations.

INTRODUCTION

Avian influenza is an infected disease of birds, cause by type A strain of the influenza virus. The disease which was first identified in Italy more than 100 years ago and had been occurred worldwide with some influenza virus subtypes.[1] First documented avian influenza (H5N1) infection of human occurred in Hong Kong in 1997. The 1997 outbreak of influenza A (H5N1) in Hong Kong established that highly pathogenic avian influenza viruses can infected human directly with resulting in severe respiratory illness that was fatal in 6 of 18 patients.[1,2,3,4,5,6] This outbreak ended abruptly after the culling of poultry.[1]

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However the later current outbreaks presented challenges because of the large geographic areas and large numbers of affected poultry.[7]

In late 2003 and early 2004, there were reports of large outbreaks of highly pathogenic avian influenza A (H5N1) and more widespread among poultry farms in Asian countries-Cambodia, Indonesia, Japan, Laos, South Korea, China, Vietnam and Thailand.[3,5,6,7] Direct infection of human with H5N1 related to these poultry outbreaks (avian to human spread) were confirmed in Thailand and Vietnam.[3,5,8] As of November 11, 2004, H5N1 infected at least 44 human cases, of which 32 were fatal.[4,8,9]

First outbreaks in Thailand in early 2004, the disease were found in a community of chicken farms in Ayuthaya and Pathum Thani Provinces. The causative agent was identified as H5N1 influenza virus. Human cases were recognized in Sukhothai, Kanchanaburi and Suphan Buri Provinces.[10,17,18]

H5N1 avian influenza usually has limited capacity to infect humans because of host barrier to infection. However, the H5N1 infected human cases were confirmed and reported at least five occasions since 1997.[7] In most of the human cases were thought to have resulted from exposure to infected poultry and the man to man transmission has not been clearly detected.[10] But to date, there have been several recent studies of possible limited person to person transmission. Such event occurred in 1997 in Hong Kong, two health care workers who had taken care of the patients were later found to have antibodies to hemagglutinin H5N1 and one developed respiratory illness.[3,4,8,15] Two family clusters in Vietnam in 2004 were also considered to be compatible with possible limited person to person transmission.[3,6,12]

The reported symptoms of avian influenza infection in humans have ranged from asymptomatic infection to typical influenza-like symptoms (e.g., fever, cough, sore throat, and muscle aches), conjunctivitis, fatal pneumonitis, acute respiratory distress, other life-threatening complications and multiple organ failure. Lymphopenia, thrombocytopenia and positive chest radiographs were observed among patient with severe infection.[2,3,5,6,7,8,9,13,14,16,17,18]

CASE REPORTS

Patient 1

The patient 1 was a first fatal case in Kamphaengphet Province and was under investigation for avian influenza H5N1 infection.

A 11 year old girl (index case) who lived with her aunt in area with abnormal poultry deaths in the village of Kamphaengphet Province. She had significant history of exposure to sick and dying household chickens for 3-4 days before the onset of illness. She presented to a clinic with symptoms of fever, cough, sore throat and dyspnea on September 2, 2004. Few days later she was admitted to the District Hospital with progressive respiratory illness on September 7, 2004. The initial diagnosis was dengue hemorrhagic fever. Because of progressive worsening, she was transferred to pediatric department of Kamphaengphet Hospital on September 8, 2004 (day 7 of her illness). She developed progressive respiratory distress, hypoxia and shock, leading to rapid dead for only three hours later after admission in spite of aggressive support, including intubation and mechanical ventilation, broad-spectrum antibiotics and fluid resuscitation. Initial diagnosis was dengue shock syndrome, pneumonia or septicemia.

A serum sample was negative for antibody to dengue virus and inadequate residual serum sample to test for hemaglutinin H5.

Chest radiography revealed right lower lobe consolidation and left lower lobe patchy infiltration (Fig. 1A-B)

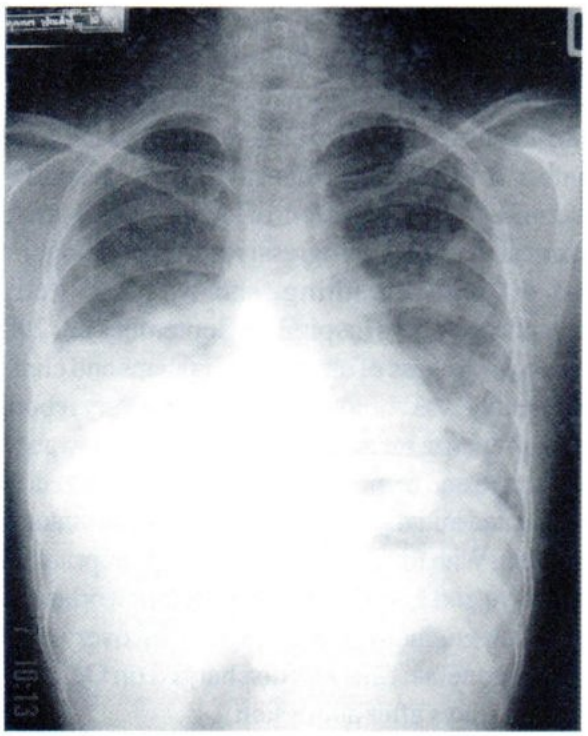

Fig.1A On day 6

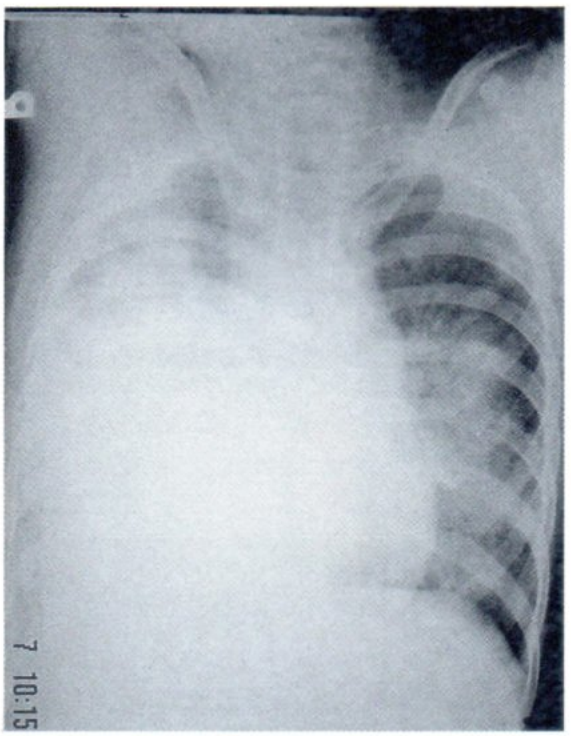

Fig.1B 9 hours later

Fig.1A-B Chest radiographs of patient 1 (index girl) on day 6 of her illness, revealed rapid progressive right lower lobe consolidation with left lower lobe patchy infiltration and air bronchogram. AP view (Fig.1A), 9 hours later (Fig.1B)

Patient 2

The index girl's mother was 26-year-old woman, who lived in Nonthaburi Province. She came to visit and provided unprotected bedside care for her hospitalized daughter (patient 1) during the last 2 days of her daughter's life, before the girl died. She sat on the bed, wiped secretions, hugged and kissed her daughter all the times. She developed flu-like symptoms three days later on September 11, 2004, and still stayed in her daughter's village for one night and returning to her home in the following morning.

On September 17, 2004, she was admitted to her own provincial hospital with severe pneumonia and progressive respiratory failure. She died on September 20, 2004.

Testing for hemaglutinin H5 was positive for reverse transcriptase polymerase chain reaction (RT -PCR) of autopsy lung tissue.

Chest radiography revealed bilateral lower lobe consolidations.[8] (Fig. 2)

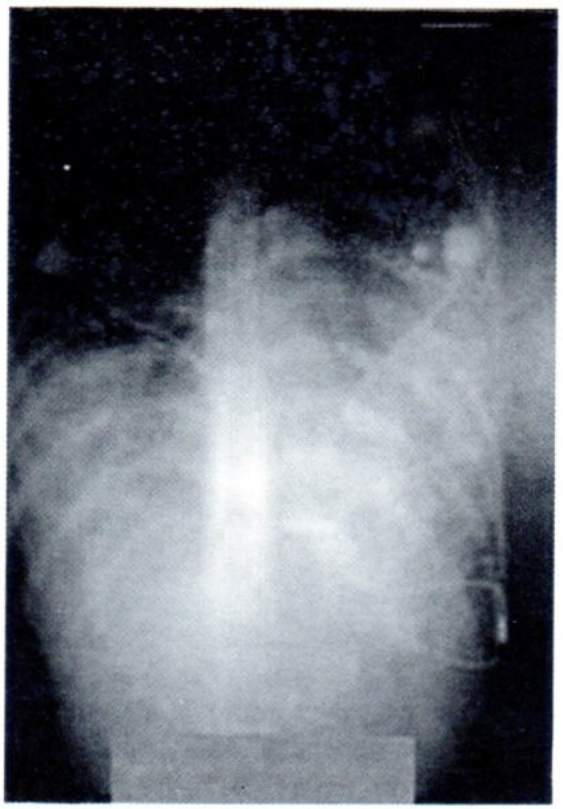

Fig.2 Chest radiograph of patient 2 (index girl's mother) on day 9 of her illness, revealed bilateral lower lobe consolidations and air bronchogram.[8]

Patient 3

A 32 year old index girl's aunt lived with her niece (patient 1). She provided unprotected bedside care on day 6 of her niece's illness. 9 days later (September 16, 2004), she began the onset of respiratory tract infection with symptom of fever, myalgia and chill. According to rapid progressive severe pneumonitis and difficult breathing, she was admitted to Kamphaengphet Hospital on September 23, 2004. Due to awareness of attending clinicians and clinical feature that was compatible with previously reported avian influenza infection, so oropharyngeal swab was performed and respiratory specimens was tested. She was treated initially with oseltamivir and instituted full isolation. With rapid diagnosis, earlier prompt antiviral treatment and good team of health care workers, her condition gradually improved, fully recovery and no major sequelae. She was discharged on October 7, 2004, 14 days after admission.

Testing for hemaglutinin H5 was positive for reverse transcriptase polymerase chain reaction (RT -PCR) of oropharyngeal swab. Culture of respiratory and blood specimens did not show bacterial pathogens.

Chest radiography revealed left lower lobe consolidation. (Fig. 3 A-H)

Table1 Clinical Features of the Family Cluster of Avian Influenza (H5N1)

Patient	Age (yr)	Date of onset	Date of admission	Chest Radiograph	Antiviral treatment	Respiratory Isolation	Viral study	Outcome
Girl	11	Sept. 2	Sept. 7	Bilateral lower-lobe consolidation	No	No	Inadequate sample	Died Sept. 8
Mother	26	Sept. 11	Sept. 17	Bilateral lower-lobe consolidation	No	No	Positive (RT-PCR of lung tissue)	Died Sept. 20
Aunt	32	Sept. 16	Sept. 23	Left lower-lobe consolidation	Yes	Yes	Positive (RT-PCR of oropharyngeal swab)	Survived; discharged Oct. 7

Source: Adapted from Unchusak K. et al., 2005.[8]

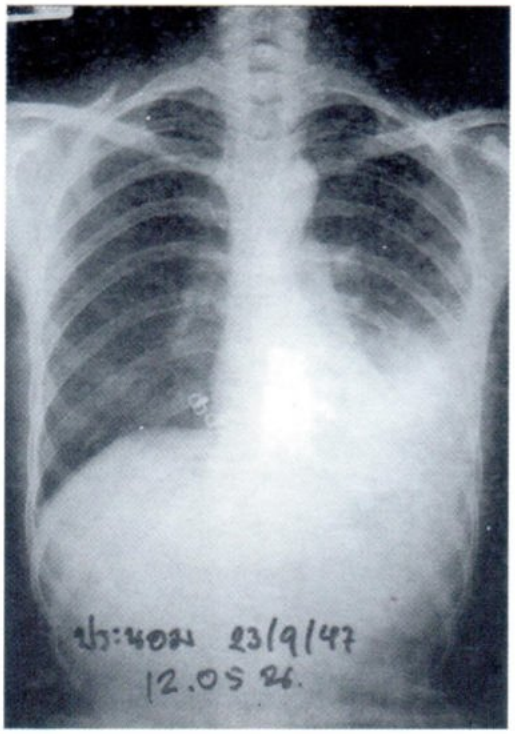

Fig.3A On admission, Sep. 23, 2004

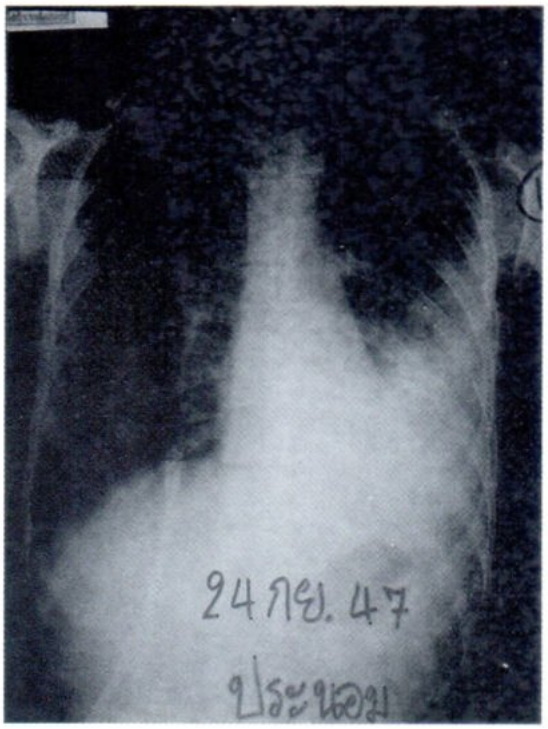

Fig.3B On day 2, Sep. 24, 2004

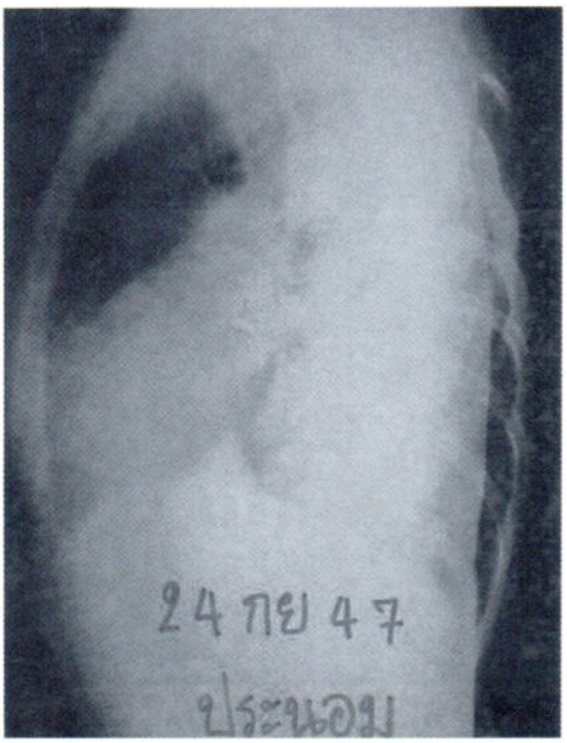

Fig.3C On day 2, Sep. 24, 2004

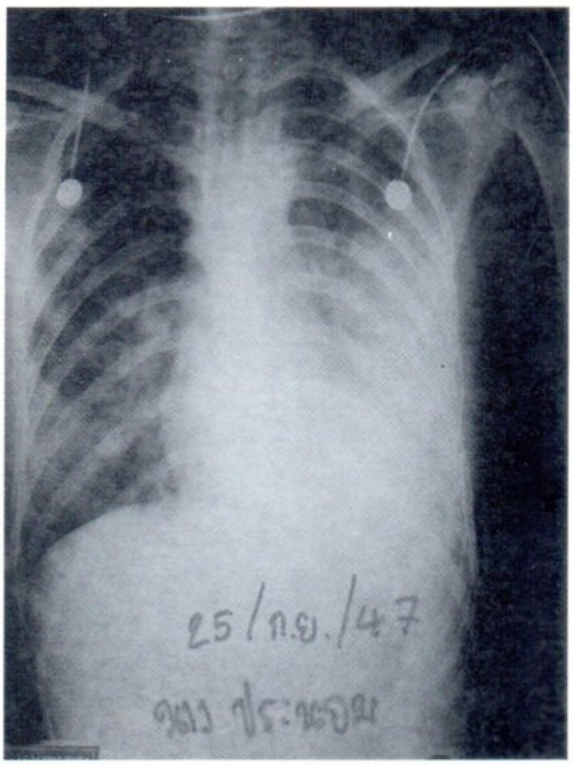

Fig.3D On day 3, Sep. 25, 2004

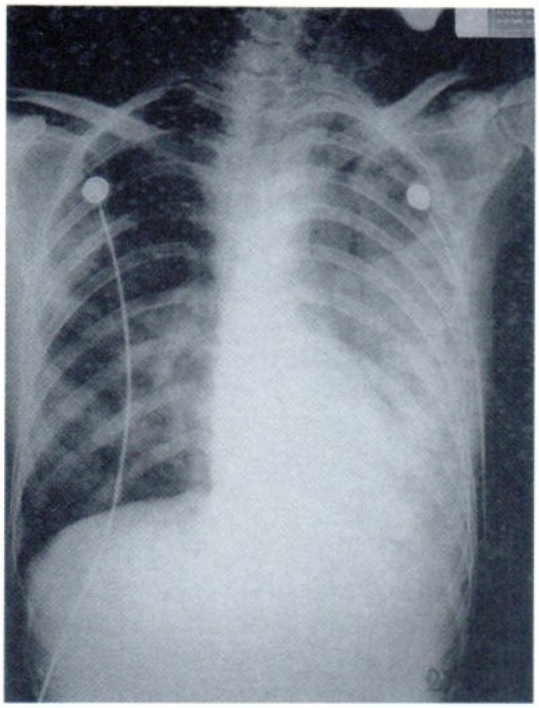

Fig.3E On day 5, Sep. 27, 2004

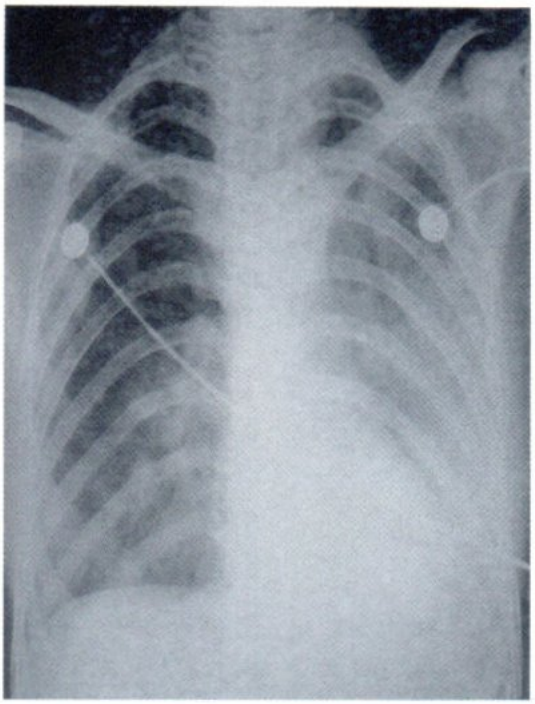

Fig.3F On day 7, Sep. 29, 2004

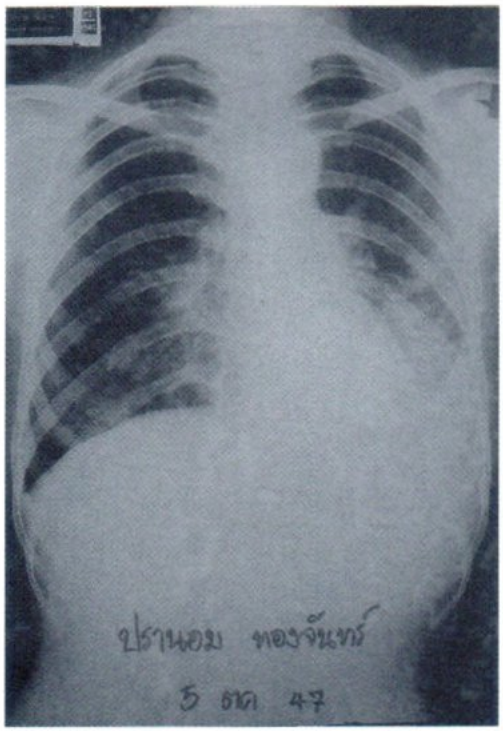

Fig.3G On day 13, Oct. 5, 2004

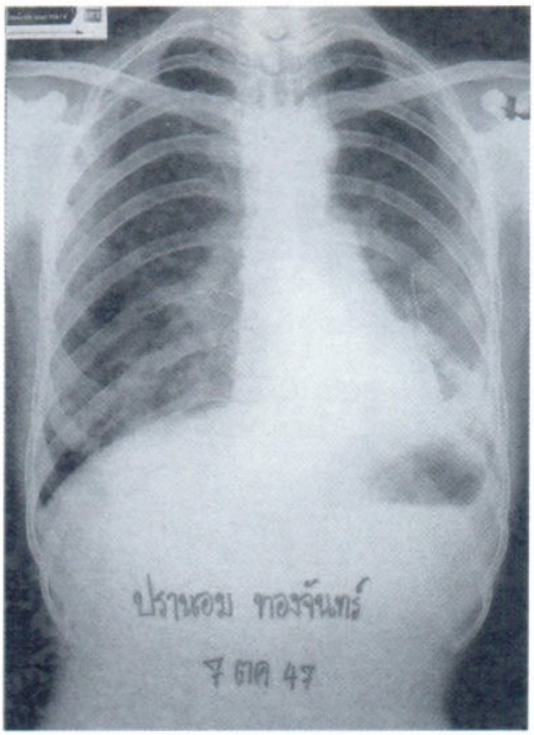

Fig.3H On discharge, Oct. 7, 2004

Fig.3 A-H Serial chest radiographs of patient 3 (index girl's aunt) demonstrated left lower lobe consolidation with gradual improvement and nearly complete clearing on the day of discharge.

DISCUSSION

In Kamphaengphet Hospital, since September 8 to November 22, 2004, there were 72 patients who presented with influenza like illness and pneumonia, and had history of poultry exposure or lived in areas of abnormal poultry death. There were one probable index case and two confirmed cases.

All of our three patients presented with influenza like symptoms, severe respiratory illness, lymphopenia and abnormal chest radiographs on admission that corresponding with signs and symptoms of previously reported human cases.

The diagnosis of the index girl (patient 1) could not be confirmed by viral study, but to be presumed by (1) history of exposure to infected household chickens, (2) clinical features of influenza like symptoms and fatal pneumonitis, correspond to the cardinal features of previously reported human cases. And (3) the death from H5N1 avian flu pneumonia of the mother despite of absence poultry exposure, 12 days after her daughter died of the disease, has raised support that this virus also cause the disease in the girl.

The mother and aunt had no exposure to poultry within the accepted incubation period (2-10 days). So we believe that the disease in the mother and aunt probably resulted from human to human transmission during the prolonged face-to-face unprotected bedside care for the infected girl.[3,8,14] However, it was limited within a family. No other household members, other family contacts, exposed neighbors or exposed health care workers were later found to be ill within14 days, but still continued closed active surveillance.[8,14]

Only the aunt has been survived, due to awareness, rapid diagnosis and earlier prompt antiviral treatment. Early detection and appropriated management of the illness are essential, since treatment with antiviral agents is likely to be beneficial only when it is started early in the course of the illness.[16]

We classified chest radiograph findings as normal, interstitial infiltration and air space pattern by using standard criteria. The pulmonary findings of our three involved patients were air space patterns with unilateral and bilateral lobar consolidations, mimic usual features of bacterial pneumonia.

Our study has been supported by several previous studies in Hong Kong, Thailand and Vietnam. At the beginning of 2004, clinical features of 5 Thai fatal confirmed cases and 10 Vietnamese cases have been reported.[6,7,17,18] All Thai patient had apparent pneumonia progressing to respiratory failure. Their chest radiograph changes were observed with patchy infiltration in four and interstitial infiltration in one.[17,18] Chest radiographs of 10 Vietnamese infected avian influenza pneumonia were reviewed by Tran Tinh Hien et al., the radiographic findings were categorized with attention to unilateral or bilateral changes, focal, lobar and patchy consolidations, air space infiltrates, air bronchogram, similar findings of our report.[6]

12 confirmed cases from January to March 2004 in Thailand were reported by Chotpitayasunondh T. Et al. Two patients had interstitial infiltration and 10 patients had patchy lobar infiltration in a variety patterns (single lobe, multiple lobes, unilateral or bilateral distributions).[5]

A family cluster in Hong Kong in the beginning of 2003, infected boy and his father had characteristic respiratory illness of avian influenza pneumonia, and chest radiographs appear to have left lingular lobe consolidation and right lower lobe consolidation, respectively.[11]

According to few infected human cases were collected since the large outbreaks in Hong Kong in 1997, and limited information about pulmonary finding details, so unable to specify the characteristic pulmonary findings of avian influenza pneumonia.

However, almost of our reviewed cases were air space pattern. We hope that our report may be helpful for future diagnosis, in comparison with findings to another and next outbreaks, finally initiate the investigation team to concern and learn about patterns of pulmonary features.

De Jong MD et al. report an additional a Vietnamese family cluster of two fatal confirmed cases who presented with atypical symptoms by severe diarrhea followed by rapid progressive coma, convulsion and acute encephalitis but no apparent of respiratory illness and primarily negative chest x-ray findings, suggested that the clinical spectrum of influenza H5N1 is wider than previously thought and clinical surveillance should focus not only on respiratory illness but also on clusters of unexplained deaths or severe illness of any kind.[12,16]

CONCLUSION

Avian influenza is an infected disease of birds and poultry.

Directed infection of human has been clearly confirmed but not often in frequency, carrying a high risk of death.

Clinical experience with avian H5N1 disease in human is limited. However certain helpful features are, direct exposure to ill poultry with flu-like symptoms, progressive respiratory illness, lymphopenia and abnormal chest radiographs.

The majority of abnormal chest radiographs were air space patterns.

Atypical symptoms without primarily respiratory illness were reported in Vietnam.

Sustained human to human transmission of H5N1 has not yet been confirmed. However, influenza viruses are genetically variable and transmissibility is difficult to be predicted. Therefore, the health care workers and the contacts should continue to take measures to protect themselves with the assumption that, human to human transmission can occur.

Due to increasing evidence of infected human cases, progressive more virulence and high mortality, so clinicians must remain alert and continued monitoring about the disease.

Good preparation for future outbreaks, early detection in order to initiate optimal antiviral therapy, information shared and infection-control measures for both animal and humans are very important.

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