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Out of the East – Emerging infections

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INTRODUCTION

Two new infections with pandemic potential have emerged from Asia in the new millennium. Severe Acute respiratory syndrome (SARS) originated from southern China and rapidly spread to many countries in early 2003 with over 8000 cases worldwide.[1] Human infection due to a highly pathogenic avian influenza A (H5N1) virus was first described in a mini-outbreak from Hong Kong in 1997. Since 2003, there were many reports of the infection in wide birds and domestic poultry in many countries. Since then, more than 150 human cases and 80 deaths have been reported.[2] Both infections are of animal origins and the viruses have jumped the species barrier. Children infected with SARS usually developed mild disease,[3] but the reported mortality for children infected with avian flu was more than 50%.[4] Early and proper isolation of infected individuals along with strict public health measures are important in controlling these infections.[5]

SARS IN CHILDREN: CLINICAL PRESENTATION, DIAGNOSIS AND TREATMENT

The outbreak of SARS started in late 2002 in southern China and the infection rapidly spread to many parts of the world within 3 months.[1] Young children tend to have milder disease while older adolescents may have more serious illness similar to those in adults.[3] Almost all pediatric cases got infected by exposure to infected adults. The incubation period is between 5–10 days. Children usually presented with fever and symptoms of upper respiratory tract infection. The initial radiograph is usually normal while early thoracic computer tomography may show poorly defined, ground glass opacifications of the lung in the subpleural areas.[6] The typical laboratory findings are lymphopenia, thrombocytopenia and elevation of liver enzymes. The non-specific clinical and laboratory findings are no different from children with pneumonia due to other rival etiologies.[3] SARS is caused by a newly identified coronavirus which is genetically very similar to strains of coronavirus isolated in wild animals sold in the markets in the Guangdong province of China.[7] The most reliable rapid early diagnosis is by reverse-transcription-polymerase chain reaction to detect the virus in respiratory secretions.

The treatment of SARS in pediatric patients is supportive as the majority of patients will recover uneventfully.[8] Currently, there is no known effective treatment for SARS. Although a variety of anti-virals along with steroids have been used during the outbreak in 2003, proper clinical trials are needed to evaluate these treatment strategies.[9] Although the majority of pediatric patients will recover uneventfully, 40% of patients may have residual radiological abnormality and impaired peak oxygen consumption and lower oxygen uptake efficiency at 15 months follow-up.[10]

HUMAN INFECTION WITH AVIAN INFLUENZA

Avian influenza is a common infectious disease affecting many wild birds and domestic poultry. The first outbreak of human disease of avian influenza occurred in 1997 with 18 cases and 6 deaths.[11] Since late 2003, there have been many reports of outbreaks of avian influenza (H5N1) in many countries in Asia, Europe, and Africa. Up till February 2006, there have been more than 150 human cases and 80

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deaths.[2] Unlike SARS, human disease of avian influenza has a high mortality in both adults and children.[4] The current knowledge of the epidemiology and pathophysiology of avian flu in humans is rather incomplete and further clinical and epidemiological research is needed.

EPIDEMIOLOGY

Before the outbreak of human infection of avian influenza started in Hong Kong in 1997, there were reports of outbreaks of fatal avian influenza in chicken farms in Hong Kong.[12] Subsequent molecular analyses revealed that the H5N1 virus isolated from humans showed >91% sequence homology to the avian isolates.[13] This suggests a direct chicken to human cross-species transmission of the virus without involving an intermediate host as "mixing vessels". The majority of human cases were confirmed to have contact or consumption of diseased birds. Probable person to person transmission was documented in two family members who took care of an infected girl.[14] Serological studies of exposed health care workers suggested that human to human transmission was inefficient and extensive surveys in Vietnam and Thailand did not reveal any evidence of asymptomatic infections among contacts.[15,16]

CLINICAL PRESENTATION AND DIAGNOSIS

The clinical presentation of human H5N1 infections is primarily based on reports of hospitalized patients. The incubation period of avian influenza A (H5N1) has been reported to be 2–8 days.[4] Most cases have been previously healthy children or adults presented with fever and respiratory symptoms. The disease usually progressed rapidly within the first week to respiratory failure.[4,11] Radiological changes include multifocal or patchy infiltrates and segmental or lobar consolidation. Many patients would progress to multiorgan failure resulting in death in the second week. Laboratory studies usually revealed lymphopenia, thrombocytopenia and elevated aminotransferase levels. Increased risk of mortality has reported to be associated with marked lymphopenia.[17] Laboratory diagnosis can be made by viral isolation or the detection of H5-specific RNA by molecular method.

PATHOGENESIS AND MANAGEMENT OF AVIAN INFLUENZA

The exact mechanism responsible for the severity of H5N1 disease in humans is not known. It is believed that H5N1 virus would activate multiple pathways of innate immunity resulting in elevated levels of various cytokines and chemokines.[18] With such uncontrolled cytokine storm, severe pneumonia and multi-organ damages will develop. Postmortum examination revealed diffuse alveolar inflammation with interstitial lympo-plasmacytic infiltration and scattered histiocytes showing reactive hemophagocytic activity. Similar reactive hemophagocytic activity was also noted in the bone marrow and the spleen but the precise mechanisms resulting in the cytokine driven hemophagocytic syndrome remain to be explored.[18]

The optimal treatment for human H5N1 infections is still unclear. Because of the severity of this infection, patients suspected or proven to have H5N1 influenza should be hospitalized in facilities with strict isolation. They should be started on neuraminidase inhibitor while waiting for confirmatory testing.[4] The exact dosage and duration of treatment are not known.

CONCLUSION

The successful control of the SARS outbreak has highlighted the importance of public health measures in controlling a newly emerged infection. Both SARS and avian flu are infections that have jumped the species barrier. The natural reservoir of the SARS coronavirues appears to be palm civet and raccon dog. A national band in slaughtering and human consumption of these animals was highly successful in preventing re-emergence of SARS. The control of avian flu will be a lot more difficult, if not impossible, as the natural reservoirs are many species of birds and domestic poultry. To complicate the issue, many species of birds can carry the virus without any apparent signs of illness. If mutation of the virus occurs resulting in efficient human to human transmission, a pandemic resulting in significant global mortality is highly likely. There is an urgent need for effective monitoring of outbreak and carriage of avian flu in wild birds and domestic poultry. Development of effective immunization and anti-virals are necessary to control outbreak at the source. Proper isolation of infected cases and border control will be necessary to minimize the impact when large outbreaks of human cases do occur.

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