Case Report

A Succesful Treatment of Avian Influenza İnfection in Turkey

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Summary

Avian influenza is a disease characterized with severe pneumonia caused by virus influenza A. Birds and poultry are vectors for spread of this disease. It is diagnosed by clinical evidence and reverse transcription-polymerase chain reaction. Here, we discuss the treatment procedures of a child diagnosed as avian influenza.

Key words: avian influenza, treatment.

Introduction

The avian influenza virus, a member of the orthomyxoviridea family, is classified according to the antigenic features (hemaglutinin and neuraminidase subtypes) of its A type surface glycoprotein [1, 2]. The H5N1 strain is the vector in birds and poultry that has spread to many countries. It was isolated for the first time in the south of China in 1996, then in Hong Kong in 1997 and later in Africa, Europe, Asia and America [3]. By May 2006, 291 cases had been reported, with 172 deaths [4]. The first human cases were reported in Hong Kong between 1997 and 1998; there were 18 cases and 6 deaths [5].

We present one of 21 cases reported in 8 Turkish provinces in January 2006 [6]. This patient was hospitalized in our pediatric infectious diseases clinic and was discharged in good health after prolonged intensive care. The case report discusses treatment, including the use of M-enriched immunoglobulin and noninvasive ventilation.

Case Report

This 4.5-year old boy, weight 20 kg, lived in the east of Turkey in the town of Doğubeyazıt of the Province of Ağrı. About 20 days before admission, he had developed a severe productive cough, high fever and fatigue. After 2 days in hospital, he was discharged, but was readmitted a few days later and transferred to our hospital because of his worsening respiratory status, when areas of consolidation were detected in the left lung on plain chest X-ray.

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The family did not keep poultry, but had eaten a cooked chicken obtained from a neighbor 20 days previously. There had been some deaths among the neighbor's chickens; it was not known whether the child had had contact with any dead birds. The child had had a chest infection a year previously, which did not require hospitalization. The child had been vaccinated (pertussis, diphtheria, tetanus, tuberculosis, mumps, rubella, rubeola and hepatitis B). He was not given Flu vaccine.

On examination, the boy was in respiratory distress, with alar breathing, and a fever of 38.6°C (axillary). There was bronchial breathing over the right lung on auscultation and crackles in the right lung base, and there was tachycardia of 152 min^{-1}. Plain chest X-ray showed bilateral consolidation as did the lung tomography (Fig. 1). He was admitted to the pediatric infectious diseases clinic with a presumptive diagnosis of avian flu. Bronchoscopy showed no foreign body, and bronchoalveolar lavage was performed. Samples of bronchoalveolar fluid were sent to the Refik Saydam Hygiene Center in Ankara, Turkey and the UK Influenza Reference Laboratories in London. In both centers, the reverse transcription–polymerase chain reaction (RT–PCR) for H5N1 was positive. RT–PCR H5N1 samples taken from the boy's parents were negative. No virus could be cultured from blood, urine, stools or bronchoalveolar fluid. Leukocytosis was present (25 000 μl^{-1}).

The boy's respiration problems increased, and his PaO_2 was 43 mmHg on the third day; he was transported to our intensive care unit (ICU) for isolation and further management. Electrocardiogram, oxygen saturation (SpO_2), noninvasive blood pressure and urine output were monitored in the

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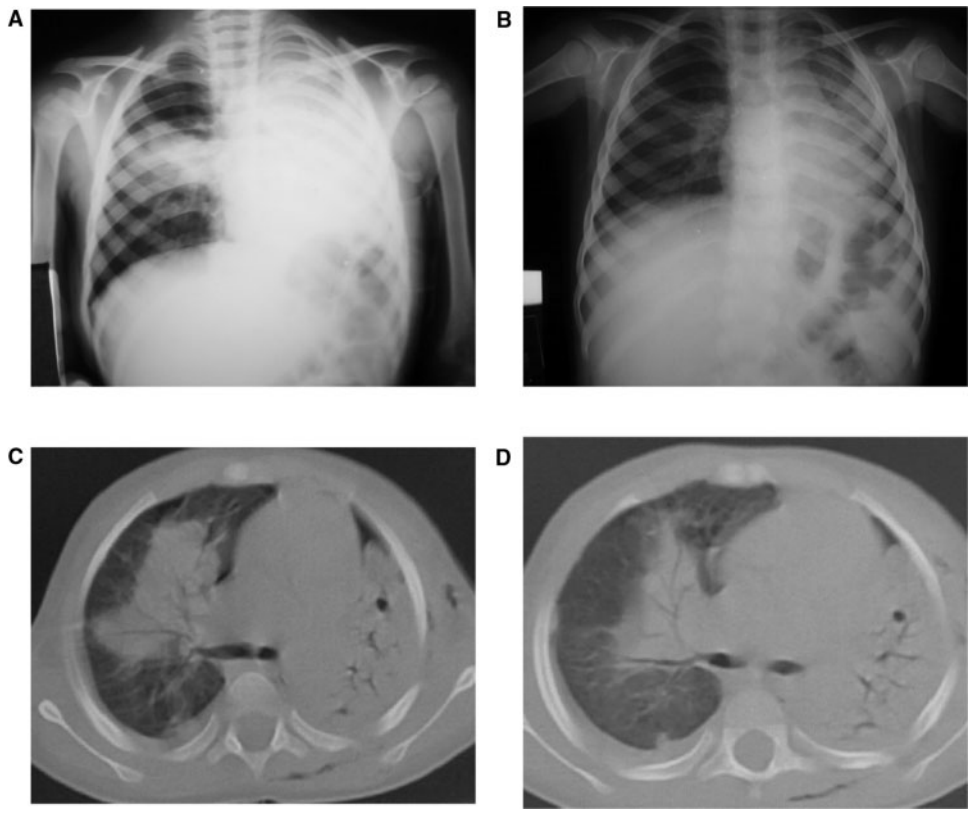

FIG. 1. (**A**) Chest radiogram of case at hospitalization; left all lung consolidated, right middle zone consolidated (**B**). Chest radiogram 1 year later (**C** and **D**). Computerized tomography of case at hospitalization; pneumonic consolidation at left lung paranchimal consolidation and minimal fluid at anterior segment of right upper lobe and superior segment of inferior lobe.

ICU. Oseltamivir (Tamiflu®75 mg, Roche, Hertfordshire, UK) prophylaxis was given to the parents and the attending health team. Noninvasive ventilation was instituted (pressure support 15 mmHg, PEEP 5–6 cmH_2O, Trigger sensitivity 8, plateau pressure $\leq$25 cmH_2O (T-Bird*, Ventilator Series, Bird Product Corp., USA) because of decreasing PaO_2 and SpO_2. Noninvasive ventilation was continued intermittently for 13 days, monitored by SpO_2 and arterial blood gas analyses. Respiratory physiotherapy and postural drainage were given.

In addition to antibiotic therapy and intensive care, M-enriched immunoglobulin (Pentaglobin®, Biotest, Dreieich, Germany) was given by infusion for 3 days, 100 ml day^{-1} (1 ml solution contains: human plasma protein of which immunoglobulin is 50 mg; Immunoglobulin M 6 mg, Immunoglobulin A 6 mg and Immunoglobulin G 36 mg). Fever was initially treated by cooling, and then by paracetamol. Intravenous fluids were given and parenteral nutrition was also prescribed for the initial 10 days. On the 11th day of his hospitalization, a pneumothorax was treated by continuous suction. After a further 4 days, the lung had re-expanded and the drain was removed. At 15 days, the boy was transferred to the pediatric infectious diseases clinic. Antibiotic treatment was continued and he was discharged on day 34 after hospital admission. At 1 year, chest X-ray showed much improvement (Fig. 1B) and complete clinical improvement was observed. Laboratory tests were normal.

Discussion

Influenza viruses of the Orthomyxoviridae family have A, B and C types in a single chain envelope. Type C causes a mild illness; types A and B are capable of causing epidemics. H5N1, first isolated in geese in 1996, is capable of transmitting to migrating waterfowl, chickens, wild birds, wild migratory birds, poultry and domestic turkeys [3]. One gram of infected bird feces can infect 1–10 million birds, which accounts for the rapidity of transmission [1]. Viruses are classified according to the two surface

glycoproteins, hemagglutinin and neuraminidase; the H5N1 virus has 16 of the former and 9 of the latter subtypes [2, 7, 8]. However, there are also atypical forms [9].

The H5N1 virus was first seen in Turkey in two children on 3 January 2006 in the Doğubeyazıt district of Ağrı Province, appearing as fulminant atypical pneumonia [10]. There was a total of 21 cases in the following epidemic, of which 4 died [1, 11]. Most of the patients in east Turkey were <16 years of age. An important factor in the outbreak was the severe weather, during which many domestic birds were kept living indoors with humans, as in other provinces of Turkey in this epidemic [11].

Avian influenza generally presents with respiratory symptoms and others such as fever, headache, myalgia, stomachache, nausea, vomiting, cough, sputum, sore throat, rhinorrhea and dyspnea [1, 12]. Deaths in nearby poultry should also suggest the diagnosis. Our case had typical symptoms except for the lack of gastrointestinal symptoms. Leucopenia, increased aminotransferases, pulmonary infiltrations and severe respiratory distress were also present [1, 12]. The PaO_2/FiO_2 ratio was <200. Although cardiac failure and renal dysfunction are described, neither of these was seen in our case [1].

The boy was transferred to intensive care for treatment of his respiratory failure, and isolated in a negative pressure room. High-efficiency masks (NIOSH-certified-N-95 or equivalent), glasses and special clothes were used during nursing at the bedside [12]. The recommended Oseltamivir prophylaxis was given to the parents and the medical team for 7 days [12]. Noninvasive ventilation is commonly used in acute respiratory failure in pediatric patients [13–16]. However, a pneumothorax developed. Oxygenation during ventilation was not a problem.

The diagnosis of avian influenza is defined by the World Health Organization (WHO) [17]. It can be identified by viral culture, the PCR, rapid antigen testing and immunoflourescant methods [1]. In our case, RT-PCR testing of bronchoalveolar lavage material was positive.

In 2002–03 in Asia severe acute respiratory syndrome (SARS-CoV) concomittant atipic pneumonia caused by coronavirus and looks like avian influenza that is a viral infection [18, 19]. SARS-CoV and avian influenza viruses were isolated in recent years and rapidly spread. Clinic and labaratory findings and treatment principles of each two disease are similar [18, 19].

Two types of agents are important in the treatment and prophylaxis of avian influenza: M_2 inhibitors (amantadine and rimantadine) and neuraminidase inhibitors (oseltamivir and zanamivir). We treated our patient with oseltamivir; it was continued for 9 days, with two daily doses of 50 mg. Oseltamivir is the treatment choice for older children and adults [20]. Nosocomial infection was controlled with broad spectrum antibiotherapy. Clinical features, treatment methods and used drugs for treatment were similar to the cases diagnosed as avian influenza [21–23]. In addition, we used M-enriched immunoglobulin. A study of 12 cases showed that M-enriched immunoglobulin treatment promotes radiological healing and reduces the need for oxygen in steroid-resistant acute respiratory distress syndrome [24]. We used it as it is beneficial in sepsis and septic shock, in order to supply immunological support, control infection and reduce oxygen requirement [24–26]. It was successful in reducing oxygen requirements temperature. Immunglobulin treatment used for SARS-CoV seems to improve upon treatment, so more studies are needed to provide evidence [27]. In our opinion, M-enriched immunoglobulin treatment for avian influenza also needs more controlled trials studies. Vaccination against influenza has been available for two decades, although there is not yet any for the H5N1 virus [28].

In conclusion, we describe a case of avian H5N1 subtype influenza caused by the A-type virus, which caused severe respiratory symptoms. In the treatment of avian influenza, prevention from complications and treatment of developed complications are important. We used noninvasive ventilation successfully in our patient, a child, and believe it is to be preferred. We believe that antibiotic prophylaxis against nosocomial infections is also important.

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