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A Case of Pneumonia Due to Co-Infection with Two Different Viruses

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ABSTRACT:

A case of pneumonia due to co-infection with two different viruses

Objective: Community acquired pneumonia is one of the leading causes of death worldwide, especially for small children. There is a wide range of etiological agents varying according to age. As conventional culture methods require longer test times for viral and atypical pathogens, nucleic acid tests with higher sensitivity and specificity are advantageous for rapid detection. Due to detection of several different agents in the same sample, multiplex polymerase chain reaction poliymerase chain reaction test offers rapid diagnosis.

Case: In this paper, a 4-year-old boy was presented with a severe course of pneumonia/pleural effusion. The presence of the co-infection of H1N1 virus and human metapneumovirus has been demonstrated by poliymerase chain reaction methods.

Conclusion: This case highlights the importance of detection of viral causes in the etiology of pneumonia, especially with poliymerase chain reaction to avoid unnecessary antibiotic use.

Keywords: Human metapneumovirus, Influenza A (H1N1), Multiplex poliymerase chain reaction, Pneumonia

ÖZET:

İki farklı virusun ko-infeksiyonu nedeniyle gelişen bir pnömoni vakası

Amaç: Toplumda kazanılmış pnömoni, tüm dünyada özellikle küçük çocuklarda, ölümlerin en sık nedenlerinden birisidir. Etiyolojide yaşa göre değişen çok çeşitli etkenler bulunmaktadır. Konvansiyonel kültür yöntemleri, viral ve atipik patojenler için uzun zaman gerektirdiğinden, nükleik asid testleri yüksek sensivite ve spesifite özelliklerine ek olarak hızlı tanı avantajı sağlamaktadır. Aynı örnekte çeşitli farklı etkenleri tespit edebilmesi nedeniyle multipleks polimeraz zincir reaksiyonu metodu ile hızlı teşhis sağlanmaktadır.

Olgu: Bu yazıda 4 yaşında bir erkek çocukta ağır seyirli bir pnömoni/plevral effüzyon olgusu sunulmuştur. Hastada etken olarak H1N1 virüsü ve human metapnömovirusun eşzamanlı varlığı polimeraz zincir reaksiyonu metodları ile ortaya konmuştur.

Sonuç: Bu vaka, pnömoni etyolojisinde viral nedenlerin araştırılmasının, özellikle polimeraz zincir reaksiyonu ile gereksiz antibiyotik kullanımından kaçınılmasının önemini vurgulamaktadır.

Anahtar kelimeler: Human metapnömovirus, Influenza A (H1N1), Multipleks polimeraz zincir reaksiyonu, Pnömoni

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INTRODUCTION

Community acquired pneumonia (CAP) is one of the leading causes of death worldwide, especially in the first two years of life (1). The common etiologic agents of CAP vary according to the age. A wide range of etiological agents are responsible for the pneumonia. In pediatrics, Streptococcus pneumoniae and Haemophilus influenzae are the most commonly detected bacterial organisms between 2-59 months of age (2). After clinical diagnosis of CAP, empiric antibiotic therapy is the mainstay of treatment. Several viruses and their combinations can cause infection. Up to 60% of the patients are associated with respiratory virus infections, so unnecessary and ineffective antibiotic treatment may often be used (3).

Sputum culture is used for the determination of etiology. But the diagnostic specimen may be influenced by the way of collection, transport, rapid processing and correct use of cytological criteria (4). As conventional culture methods require longer test times for viral and atypical pathogens, nucleic acid tests with high sensitivity and specificity are advantageous for rapid detection. In addition to detection of several different agents in the same sample, multiplex PCR offers rapid diagnosis (5).

The clinical impact of combined infections has not been fully evaluated. In this paper, we report a case of pneumonia caused by the co-infection of two different viruses.

CASE REPORT

A 4-year-old, previously healthy child was admitted to our hospital with complaints of fever, cough, dyspnea and chest pain lasting for 3 days with intercostal and suprasternal retractions. He was refusing the intake of food and liquids. On his medical history, all the vaccinations were completed according to age except influenza. On physical examination, he appeared ill and had difficulty in breathing. His body temperature was 39.2°C, heart rate was 108 beats per minute, respiratory rate was 42 breaths per minute, blood pressure was 90/65 mm Hg, and oxygen saturation (SpO2) on room air was 92 mmHg. Auscultation of lungs revealed inspiratory crackles in both lung fields and diminished breath sounds on the lower part of right lung. A chest radiograph showed right middle lobe consolidation and left lobe retrocardiac small consolidation. Also right pleural effusion was also noticeable (Figure-1). The results of laboratory tests revealed as hemoglobin level 12 mg/dl, white blood cells $6.2x10^9$/l (neutrophils 52.9%, lymphocytes 36.9%, monocytes 8.8%, and eosinophils 0.2%), platelet count $183X10^3$/l and C-reactive protein 0.4 mg/L (N:<0.5 mg/L). Antibiotic therapy (ceftriaxone sodium 100mg/kg/day), oxygen and intravenous liquid supplementation were started for presumed bacterial pneumonia in the department of pediatrics at hospital. During the next 48 hours, his respiratory status worsened. Despite prompt resolution of fever, general condition did not improve and retractions increased, with Sp02 remaining 93% and rising to 95% with oxygen supplementation. A chest X-ray obtained at third day of admission showed progression in right pleural effusion and left retrocardiac consolidation (Figure-2). A computed tomography (CT) scan on the fifth day of admission demonstrated massive right pleural effusion causing long compression. The CT scan also revealed minimal left pleural effusion (Figure-3a,b). The chest tube thoracostomy-assisted drainage was performed by pediatric surgeons. Pleural fluid was clear, cell count was $233/mm^3$ (lymphocytes), and lactate

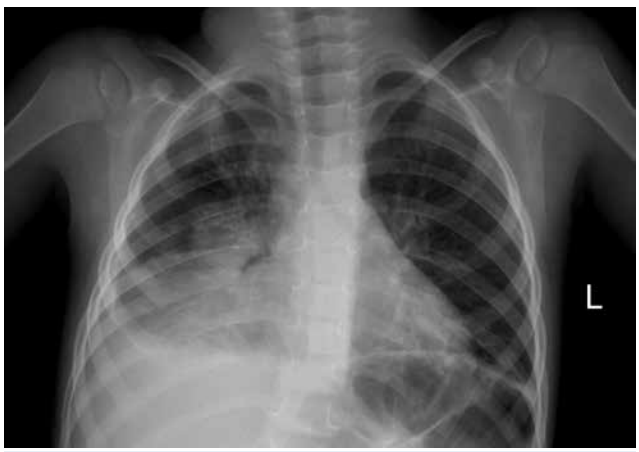


Figure-1: Chest radiograph shows wide consolidation in middle and lower zone of right lung. Also there is small consolidation in left lung lower zone. Note there is accompanying right pleural effusion.

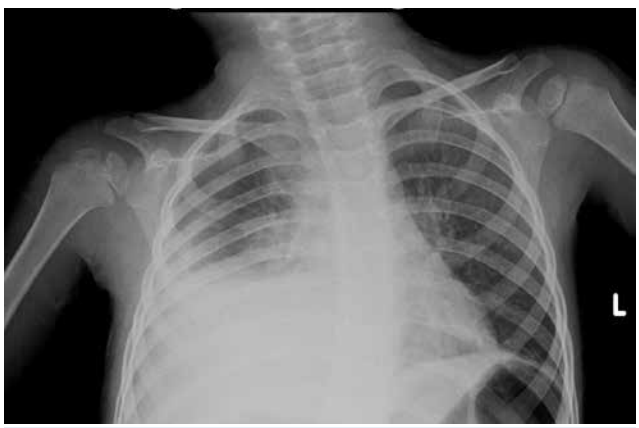
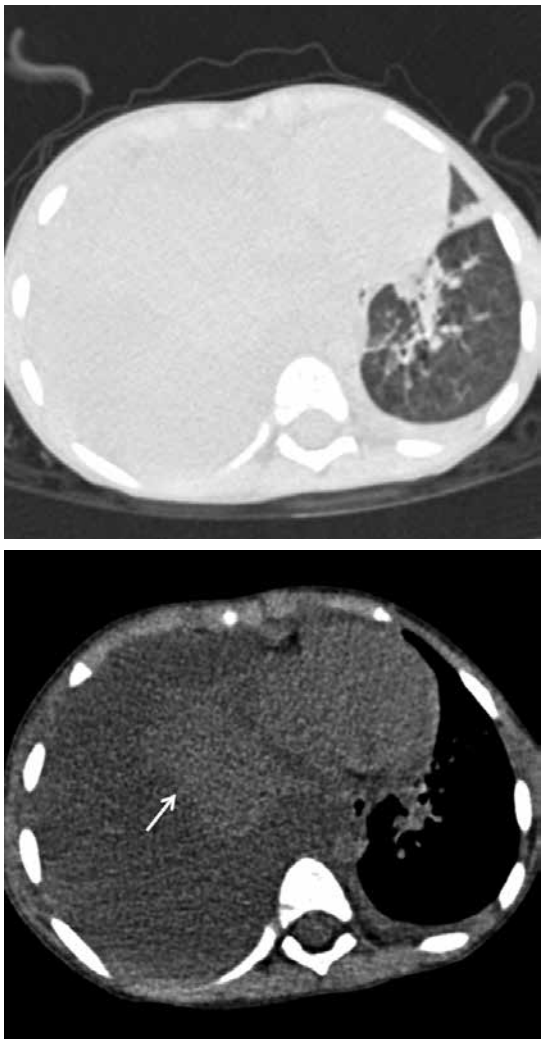


Figure-2: Chest radiograph obtained on the third day following admission shows increase in right pleural effusion. Consolidation in right lung is masked by pleural effusion. Left lung retrocardiac consolidation increased over time.



b)

a)

Figure-3: CT image a) with mediastinum window settings reveals massive right pleural effusion that compressed right lung (arrow). Note the high pressure of the pleural effusion that shifts heart to left. Also there is small left pleural effusion. b) with lung window settings reveals left lower lobe consolidation and linear atelectasis in lingular segment.

dehydrogenase (LDH): 47 U/L, pleural fluid/serum LDH ratio: <0.6, pleural fluid/serum protein ratio: <0.5, and pH and glucose were in normal ranges. Pleural fluid analysis indicated parapneumonic pleural effusion. The Gram stain was negative for microorganisms. Cultures of blood, pleural fluid, urine and sputum specimens did not show growth of any pathogenic organisms. Rapid antigen test was found negative for influenza. Nasopharyngeal swab result was positive for human metapneumovirus and Influenza A (H1N1) by polymerase chain reaction (PCR) testing and negative for other pathogens. Antiviral treatment was started with oseltamivir (45 mg twice a day) and was continued for 5 days. Antibiotic therapy was discontinued after PCR test result. Soon after the drainage, the general condition improved immediately and he was discharged from the hospital after a week.

DISCUSSION

Human metapneumovirus (HMPV), first identified in 2001- a RNA virus of Paramyxovirus family- is a leading cause of upper and lower respiratory tract infections in children in spring and winter months as in our patient had the infection in January (6). Although researches have confirmed the prevalence of HMPV world wide, data from Turkey remained limited. Cough, wheezing, rhonchi, and dyspnea are the major manifestations. The clinical features of the illness caused by HMPV infection range from a mild upper respiratory tract infection to life-threatening severe bronchiolitis and pneumonia. Epidemiologic studies have demonstrated that a greater number of children infected with HMPV are diagnosed as having pneumonia (7). Radiographic abnormalities include diffuse findings, such as perihilar infiltrates and alveolar disease, and focal findings, including bronchopneumonic changes, lobar pneumonia, and effusion (8). Bacterial superinfection can occur. HMPV was initially identified in cell culture, but viral cultures take up to 10 to 14 days and are, therefore, not useful clinically. Currently, the gold standard for diagnosis is PCR testing. In many clinical laboratories HMPV has been incorporated into multiplex diagnostic PCR assays used to simultaneously evaluate for multiple respiratory pathogens. There is no approved antiviral drug therapy against MPV.

Influenza viruses are RNA viruses from orthomyxovirus family. Human infection and effective human-to human transmission has been achieved by only 3 hemagglutinins and 2 neuraminidases in 3 combinations: H1N1, H2N2, and H3N2 (8). The peak incidence of infection occurs earlier in the pediatric population. Influenza virus is transmitted primarily by large particle droplets, although

contaminated surfaces can also spread disease. The incubation period is 1 to 4 days (mean, 2 days) (8,9). Upper respiratory tract infection (URI), laryngotracheitis (croup), bronchiolitis, and pneumonia are all possible presentations of influenza in the younger children. Parapneumonic effusion and empyema are common complications. Accurate and rapid diagnosis of influenza infection can allow prompt initiation of antiviral therapy simultaneously, limiting antibiotic use (9). Rapid antigen testing is the most commonly used method in the laboratory diagnosis of influenza infection. But the major disadvantage of rapid tests is their low and highly variable sensitivity, ranging from 20% to 90%. On the other hand, molecular methods of detection are replacing viral culture as the gold standard in the diagnosis of many viral infections, including influenza. PCR- based assays offer superior sensitivity that are available in many laboratories. In our patient, rapid antigen test was negative but PCR-based influenza assay was positive for Influenza A (H1N1). The administration of active antiviral therapy early in the course of disease has been found to shorten symptom duration and prevent the spread of virus. However, treatment should optimally be initiated within 48 hours of symptoms. It may also be beneficial in hospitalized patients and in those with severe disease, even when started later in the disease course (10). We were able to begin the treatment with oral oseltamivir two days after the hospitalization according to laboratory confirmation. Co-infection of HMPV with other respiratory pathogens varies in different clinical trials. In a study, Bosis et al. (11) evaluated nasopharyngeal swabs of the 42 HMPV-positive samples, and 6 were also positive for influenza viruses. Çiçek et. al. (12) in a study, detected respiratory viruses and influenza A virus subtypes using multiplex PCR. Cebey-López et al. (13) published a paper on viral co-infections in pediatric patients hospitalized with lower tract acute respiratory infections. Studies also have found HMPV co-infection with bacterial pathogens like Streptococcus pneumonia, Mycoplasma pneumonia, and Chlamydia pneumonia (14). However, the interaction of HMPV with other etiological agents is unclear. Clinical outcome of co-infections of multiple viruses from combined infections remains unpredictable and challenging (15).

This case highlights the importance of detection of viral etiologies especially with PCR to avoid unnecessary antibiotic use.

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