Coronaviruses OC43 and 229E lower respiratory tract co-infections: a clinical report of two cases

Maria Eboriadou[1], Katerina Haidopoulou[2], Panagiota Xanthou[1], Anna Papa[3]

[1]2nd Paediatric Department, Medical School, Aristotle University, Thessaloniki, Greece
[2]4th Paediatric Department, Medical School, Aristotle University, Thessaloniki, Greece
[3]A' Department of Microbiology, Medical School, Aristotle University, Thessaloniki, Greece

Submitted: 31 July 2007
Accepted: 14 December 2007

Arch Med Sci 2008; 4, 1: 88–90

Corresponding author:
Katerina Haidopoulou, MD, PhD
Lectures in Paediatrics
Paediatric Pulmonology
4th Paediatric Department
Medical School
Aristotle University of Thessaloniki
Thessaloniki, Greece
Phone: +30 2310 823888
Fax: +30 2310 823888
E-mail: haidoka@med.auth.gr

Abstract

We report two cases of hospitalized children with human coronavirus (HCoV) co-infection. The first patient was a 6-month female infant admitted for acute bronchiolitis with serologically confirmed respiratory syncytial virus (RSV) infection, while the second one was a 7-year old boy with serologically confirmed *Mycoplasma pneumoniae* infection. HCoV-OC43 and HCoV-229E were detected in nasopharyngeal aspirate samples of the patients respectively using reverse transcriptase-polymerase chain reaction (RT-PCR). Both children recovered uneventfully. HCoV-229E and HCoV-OC43 usually cause upper respiratory infections; however, rarely, they are associated with lower respiratory tract infection. We discuss their possible role as a co-infectious agent in lower respiratory tract infection.

Key words: coronavirus, respiratory syncytial virus, *Mycoplasma pneumoniae*, lower respiratory tract infection.

Introduction

Human coronaviruses (HCoV) 229E in serogroup 1 and OC43 in serogroup 2 are the second most important cause of the common cold after rhinoviruses [1]. Infections by coronaviruses are usually limited to the upper airways and are clinically indistinguishable from other upper respiratory infections caused by numerous other viruses. The clinical manifestations of coronavirus infections are essentially those of the so-called 'common cold', that need little or at most symptomatic treatment [2]. In some cases, however, lower respiratory infection can occur, causing bronchitis, bronchiolitis and even pneumonia. In a recent epidemiological study on coronaviruses among children with acute respiratory tract infection in Greece it was found that during a 12-month period (2003-2004) 2.5% (5/200 patients) of children presented a coronavirus infection (HCoV-NL63, HCoV-229E and HCoV-OC43), while during the winter months of 2005-2006 the respective percentage was 4.5% (2/44 patients) (HCoV-229E and HCoV-OC43) [3]. In this study we describe the clinical presentation of two of the above-mentioned cases of 2006 in which HCoV-OC43 and HCoV-229E were detected. Nasopharyngeal swab specimens were collected on the day of admission from a 6-month infant and a 7.5-year old child who were hospitalized for lower tract respiratory infection. Specimens were tested by reverse transcriptase-polymerase chain reaction (RT-PCR) [3].

Case reports

Patient 1

A 6-month old female infant was hospitalized in January 2006 because of shortness of breath on the day of admission. She presented with a history of four days of fever, cough and difficulties in feeding. The patient had an uneventful medical history. She was born at 38 weeks' gestation by unassisted vaginal delivery, with a birth weight of 3.140 kg.

On admission, she was noticed to have respiratory distress with insucking of chest. The respiratory rate was 66/min, the heart rate was 160/min and oxygen saturation in room air was 92%. Her blood pressure was normal and she had fever (axillary temperature 38.8°C). Auscultation of her chest revealed diffuse crepitations and prominent wheezing. Examination of the abdomen and of the cardiovascular and neurological systems was unremarkable.

The laboratory findings on admission are summarized in Table I. Chest radiograph (CXR) revealed focal consolidation of the right medial lobe. Blood cultures were negative. Serological tests for parainfluenza virus, influenza A and B viruses, and adenovirus were negative. Serological assays revealed increased levels of RSV IgM antibody titres, indicating a recent infection. HCoV-OC43 was detected in nasopharyngeal aspirate by RT-PCR.

The infant was treated with nebulized bronchodilators (salbutamol 2.5 mg and ipratropium 250 mg PRN) and IV amoxicillin-clavulanic acid (90 mg/kg/24 hours). Oxygen saturation was maintained at 95 to 100% with 2-3 l/min oxygen via nasal cannula.

Symptoms gradually subsided and supplemental oxygen was discontinued after 3 days. She was discharged on day 6 with the diagnosis of acute RSV bronchiolitis with HCoV-OC43 co-infection.

Patient 2

A 7.5-year old boy was hospitalized in February 2006 because of lower respiratory tract infection. He presented with a history of five days of fever and cough. The patient had an uneventful medical history.

Physical examination revealed mild tachypnoea and fine diffuse crackles on lung auscultation. The respiratory rate was 35/min, the heart rate was 110/min and oxygen saturation in room air was 95%. His blood pressure was normal and he had fever (axillary temperature 40.5°C). Examination of the abdomen and of the cardiovascular and neurological systems was unremarkable.

The laboratory and microbiological findings on admission are summarized in Table I. Chest radiograph (CXR) revealed diffuse hilar opacities. Blood cultures were negative. Serological assays revealed raised *M. pneumoniae* IgM antibody titres, indicating a recent infection. Serological tests for RSV, parainfluenza virus, influenza A and B viruses, and adenovirus were negative. HCoV-229E was detected in nasopharyngeal aspirate using RT-PCR. The boy was treated with nebulized salbutamol 5 mg PRN and IV clarithromycin (30 mg/kg/24 hours).

Symptoms gradually subsided and he did not require supplemental oxygen. He was discharged after 4 days with the diagnosis of *M. pneumoniae* infection with HCoV-229E co-infection.

Table I. Laboratory findings of the two cases

Parameters	Reference values	Case 1	Case 2
White blood cells (/mm^3)	3,600-9,600	19,950	20,600
Granulocytes (%)	42.2-75	80.3	83.1
Lymphocytes (%)	20.5-51.1	16.3	11.6
Monocytes (%)	1.7-9	3.4	5.3
Haematocrit (%)	40-52	34.9	36.2
Haemoglobin (g/dl)	12-16	11.6	12.4
Platelets (/mm^3)	140,000-440,000	544,000	390,000
Erythrocyte sedimentation rate (mm/h)	0-20	35	98
C-reactive protein (mg/dl)	<0.35	1.11	10.8
Procalcitonin (ng/dl)	<0.5	0.35	0.89
Urea (mg/dl)	10-50	20	16
Creatinine (mg/dl)	0.2-1.2	0.32	0.33
Aspartate aminotransferase (IU/l)	0-40	23	20
Alanine aminotransferase (IU/l)	0-30	33	12
Gamma-glutamyl transpeptidase (IU/l)	8-16	6	8

Discussion

Lower respiratory infections (LRIs) continue to threaten the health of children worldwide and are the most common cause of death resulting from infectious disease. The entity of "LRI disease" includes acute lower respiratory tract infections, pneumonia, atypical pneumonia, bronchitis, bronchiolitis, and severe acute respiratory syndrome (SARS) [4]. To date, LRIs remain the most common cause of illness and death in children throughout developing countries, where poor nutrition prevails and access to health care is scarce.

The human coronaviruses HCoV-229E in serogroup 1 and HCoV-OC43 in serogroup 2 have been known for 30 years and are an important cause of upper respiratory tract infection [1]. Children are affected by coronavirus infection 5-7 times more often than adults [4]. HCoV-229E has been involved in nosocomial respiratory viral infections in high-risk children [5]. More recently, HCoV-229E and HCoV-OC43 strains were identified in both immunocompetent and immunocompromised patients with acute respiratory syndromes [6]. It has been the impression that HCoVs only cause URI, but the trend changed after 2003 when SARS-CoV induced LRI during a large global outbreak with high fatality rate [7, 8]. SARS was characterised by an initial febrile phase that was followed by interstitial pneumonia, leading to respiratory distress syndrome.

Our patients were admitted to hospital with acute respiratory symptoms and were diagnosed as having RSV acute bronchiolitis and mycoplasma pneumonia respectively. In both, a diagnosis of co-infection with old human coronaviruses was confirmed. The possibility of a "coronavirus carrier status" is thought to be unlikely among children [9]. There were no differences observed in clinical presentation and disease course in these patients that could be attributed to co-infection with HCoV strains. The possibility that the LRI of the two patients was caused or co-caused by CoV could not be ruled out, although there also existed hard evidence that RSV and *Mycoplasma* were the pathogens. It is not possible to know whether the CoV of the two patients only caused URI and at the same time the RSV and *Mycoplasma* caused LRI, or the CoV served as a co-infection pathogen in the LRI.

In conclusion multiple infectious agents are identified in 27-50% of children hospitalized for LRIs [10, 11]. The role of the presence of old human coronaviruses as co-infectious agents in the cases of our patients cannot be determined. Future progress in the clinical management of lower respiratory infection diseases will entail improved methods of early diagnosis and broader options for treatment [4]. PCR-based methodologies offer increased sensitivity for the detection of most respiratory viruses in young children. The inclusion of PCR into diagnostic testing strategies is needed to broaden our understanding of the natural ecology of respiratory viruses and the significance of multiple infections.

References

1. Holmes KV. Coronaviruses. In: Fields Virology. Knipe DM, Howley PM, Griffin DR, et al. (eds). Lippincott Williams and Wilkins, Philadelphia 2001; 1187-203.
2. Vabret A, Mourez T, Gouarin S, Petitjean J, Freymuth F. An outbreak of coronavirus OC43 respiratory infection in Normandy, France. Clin Infect Dis 2003; 36: 985-9.
3. Papa A, Papadimitriou E, Luna LK, et al. Coronaviruses in children, Greece. Emerg Infect Dis 2007; 13: 947-9.
4. Klig JE. Current challenges in lower respiratory infections in children. Curr Opin Pediatr 2004; 16: 107-12.
5. Gagneur A, Legrand MC, Picard B, et al. Nosocomial infections due to human coronaviruses in the newborn. Arch Pediatr 2002; 9: 61-9.
6. Gerna G, Campanini G, Rovida F, et al. Genetic variability of human coronavirus OC43-, 229E-, and NL63-like strains and their association with lower respiratory tract infections of hospitalized infants and immunocompromised patients. J Med Virol 2006; 78: 938-49.
7. Drosten C, Günther S, Preiser W, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med 2003; 348: 1967-76.
8. Fouchier RA, Kuiken T, Schutten M, et al. Aetiology: Koch's postulates fulfilled for SARS virus. Nature 2003; 423: 240.
9. Van Bever HP, Chng SY, Goh DY. Childhood severe acute respiratory syndrome, coronavirus infections and asthma. Pediatr Allergy Immunol 2004; 15: 206-9.
10. Jennings LC, Anderson TP, Werno AM, Beynon KA, Murdoch DR. Viral etiology of acute respiratory tract infections in children presenting to hospital: role of polymerase chain reaction and demonstration of multiple infections. Pediatr Infect Dis J 2004; 23: 1003-7.
11. Sloots TP, McErlean P, Speicher DJ, Arden KE, Nissen MD, Mackay IM. Evidence of human coronavirus HKU1 and human bocavirus in Australian children. J Clin Virol 2006; 35: 99-102.