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CASE REPORT

Human bocavirus infection in a neonatal intensive care unit

C. Calvo [a,*], M.L. García-García [a], C. Blanco [a], M.J. Santos [a], F. Pozo [b], P. Pérez-Breña [b], I. Casas [b]

[a] *Pediatrics Department, Severo Ochoa Hospital, Madrid, Spain*
[b] *Influenza and Respiratory Viruses Laboratory, Virology Service, National Microbiology Center, ISCIII, Madrid, Spain*

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Summary Human bocavirus (HBoV) plays a non-insignificant role as a pathogen in respiratory tract diseases in the pediatric population, especially in infants younger than 2 years of age. In this paper, we have described two cases of a possible nosocomial infection in a neonatal intensive care unit being HBoV the sole detected respiratory virus in clinical samples.

Introduction

Viruses are a common cause of lower and upper respiratory tract infection in children, and they are responsible for a high morbimortality rate.[1] All of these viral agents can produce nosocomial infections in hospitalised patients.[2–4] Due to the special sensitivity of the patients in the neonatal intensive care unit, this location is a high risk setting. A nosocomial infection in a premature newborn child could become very serious.[4,5]

Human bocavirus (HBoV), was firstly detected in 2005 from samples obtained in Swedish children and infants with lower respiratory tract infection.[6] Soon after, new series were published around the world describing different incidence of infection by HBoV.[7–13] In the majority of these series, HBoV is found as a frequent virus in patients between 6 months and 4 years of age with upper or lower respiratory tract infection.

The ability of the HBoV to produce nosocomial infections in hospitalised children has only been recently described.[8,10,11] We report two patients from a neonatal intensive care unit with nosocomial infection caused by HBoV.

Clinical cases

Case 1

The patient was a pre-term male newborn at 24 weeks of gestational age and normal weight (725 g) who was admitted to the intensive care unit after delivery by caesarean incision due to pathological registry. He received a dose

* Corresponding author. C/Viento, 5, 5° A, 28760 Tres Cantos, Madrid, Spain. Tel.: +34 914 818 460.
E-mail address: ccalvo@mi.madritel.es (C. Calvo).

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of surfactant because of hyaline membrane disease and was put on mechanical ventilation. At the 10th day, he suffered a worsening of his respiratory condition associated with atelectasis, treated with Pulmozyme (dornase alpha). Fever was not present. A sample of nasopharyngeal aspirate was collected and sent, in viral transport medium, to the Influenza and Respiratory Viruses Laboratory of the National Microbiology Center, Health Institute Carlos III, Madrid. HBoV was detected using PCR assay.[13] No other respiratory virus was detected using different multiplex PCR assays.[14,15] Simultaneously, the patient developed a muco-cutaneous candidiasis that was treated with Amphotericin B. Blood, cerebrospinal fluid and urine samples were negative for bacteria and yeast. At the 14th day, mechanical ventilation was withdrawn. The patient then developed a chronic pulmonary disease that required nasal continuous positive airway pressure, bronchodilator treatments, and inhaled corticosteroids. Oxygen therapy was discontinued at the 33rd day. He was released from the intensive care unit at the age of 3 months.

Case 2

The patient was a pre-term female newborn at 24 weeks of gestational age and low weight adjusted for age (705 g) who was admitted to the neonatal intensive care unit after delivery by caesarean incision due to maternal eclampsia. She received two doses of surfactant due to hyaline membrane disease and was put on mechanical ventilation until day 30. She underwent surgery to correct a persistent arterial duct at day 19. The patient developed chronic pulmonary disease, requiring continuous oxygen therapy and several cycles of systemic corticoids. At day 107, her respiratory condition worsened, and it was necessary to start again with mechanical ventilation due to an increase in respiratory difficulty, a requirement for 100% oxygen, and the presence of radiological infiltrates. Disseminated wheezing and *rales* were detected. Fever was not present. Nosocomial sepsis was suspected, and the patient was treated with wide spectrum i.v. antibiotic therapy, although blood, cerebrospinal fluid and urine samples proved to be negative. Inhaled bronchodilator and Pulmozyme (dornase alpha) were administered. A sample of nasopharyngeal aspirate was collected and HBoV was the only respiratory virus detected. The patient's respiratory condition showed a progressive deterioration, and she died at day 130.

Discussion

This paper describes nosocomial infections caused by HBoV in a neonatal intensive care unit setting. So far, only three authors have communicated the existence of nosocomial infection caused by HBoV in children of more than 1 month of age.[8,10,11]

Bastien N et al.[11] assumed nosocomial transmission of HBoV in 12 children, because this virus was detected more than 10 days after admission to the hospital. Weissbrich et al.[10] also assumed nosocomial infection by HBoV, since they presented three patients who developed respiratory symptoms during their stay at the hospital after admission for other reasons. Finally, Kesebir et al.[8] published a set of patients who, similar to ours, were hospitalised since birth after developing respiratory pathology. Ages ranged from 1 to 6 months, and in all these cases there was a clear nosocomial transmission of HBoV.

The clinical manifestations described in patients in which HBoV was detected mainly include recurrent wheezing, asthmatic aggravation, bronchiolitis, and pneumonia.[12] Most papers describe fever, variable hypoxic rates, and radiological infiltrates.[6–9] However, as far as we know, infections by HBoV during the neonatal period have not already been described. In general, during this period of life it is very difficult to identify any infection, especially in the case of new infectious agents, if a specific investigation is not carried out. In our hospital we are performing a prospective study of respiratory infections in hospitalised children for more than 10 years, and this may be helpful in assigning an etiologic role and define a viral infection in our both individual patients. However, these two patients did not show any specific clinical symptoms of infection by HBoV or any analytical data that could set them apart from other pre-term newborns with respiratory complications. The first patient required increased oxygen therapy and mechanical ventilation and had a radiological image compatible with atelectasis. The second patient had symptoms of a worsening basal condition of bronchopulmonary dysplasia that was later diagnosed as a nosocomial infection. The respiratory pathology in this second patient was increasing in severity over time, ultimately causing her death. To determine the extent to which infection by HBoV played a role in the clinical outcome of these two children is not possible, although the absence of other microrganisms supports the possible association of HBoV presence with illness. On the other hand, could be considered the possibility that these infants may have acquired the virus from their mothers, either before or during the delivery process. Since it is not known any data considering the maternal–fetal transmission of the HBoV, this possibility could not be ruled out.

We do not know whether HBoV is able to produce mild or asymptomatic respiratory infections because the available studies have been focused on severe infections that required admission to hospitals. No HBoV was detected in 96 healthy children,[8] leading to the assumption that the first infection by HBoV should be symptomatic. We have also conducted a study in healthy children, aiming to get a better knowledge of the prevalence of HBoV by isolation in nasopharyngeal aspirate. The prevalence in this study, not associated to pathology, is bellow 5% of the studied population.[16] HBoV might cause banal infections in adults, which could be the origin of the nosocomial infection, as has already been demonstrated for other virus such as coronavirus.[3] Unfortunately, we did not get samples from the mothers or other personal in the intensive care unit which, if positive, could explain the origin of the infection. We do not have urine, stool or CSF samples of the babies. Nevertheles, our group, Pozo et al.[13] as well as other authors as Vicente et al.[17] have published patients with positive urine and stool samples and that could be explained by a systemic infection.

From now, HBoV must be included among the potential agents that can associate virus presence with a nosocomial infection in this setting. Diagnostic techniques and

prophylactic and therapeutic measures must be established to avoid potentially severe complications in these patients.

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