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Scientific letters

Could human bocavirus be a causative agent of parotitis in children?

¿Puede ser el bocavirus humano un agente causal de parotiditis en niños?

Dear Editor,

Parotitis is usually associated with mumps viral infections, but since trivalent measles–mumps–rubella vaccine started to be administrated in different countries, the burden of the disease has been steadily reduced. Nowadays the parotitis cases are usually related to other viral infections in countries with high vaccination coverage.[1,2] Although Epstein Barr virus (EBV) has been recognized as the most frequently detected microorganism, other respiratory viruses such as parainfluenza virus (PIV) or adenovirus[1] have been described associated with parotitis.

The human bocavirus (HBoV) has been identified in respiratory infections in children in a large number of studies, mainly in infants less than 2 years of age during late autumn[3] being recurrent wheezing episodes and fever the most frequent symptomatology. To date, only two cases of parotitis have been reported associated with bocavirus infection, one of which being a coinfection with PIV 3.[1,2] These two cases were detected in two prospective studies that surveyed the frequency of several viruses in sporadic parotitis in Korea and U.S.A. The authors observed an incidence of HBoV infection of 0.4–1% in their studied cases.

We report a child with parotitis and an acute respiratory tract infection in whom HBoV was the only virus identified.

A 17-month-old male, with a history of recurrent wheezing presented at the emergency room in November with 48 h of left parotid swelling. He had had fever for a few hours (maximum 39.2 °C), and respiratory distress that had not improved despite receiving bronchodilators and amoxicillin-clavulanate for two days. Physical examination revealed high fever, left parotid inflammation without erythema, expiratory wheezing and hypoxaemia, requiring admission and treatment with bronchodilators and oxygen therapy. The chest X-ray demonstrated an infiltrate in the right middle lobe. Cervical ultrasound revealed an enlarged left parotid gland, with multiple internal lesions of low echogenicity in relation to intraglandular inflammatory changes. Intraglandular adenopathy and bilateral laterocervical chains were also observed. The blood test showed normal haemoglobin and platelets; 13,000 leukocytes (44% neutrophils); C-reactive protein 41 mg/L and amylase 381 U/L. Blood culture was negative, and a multiplex polymerase chain reaction in nasopharyngeal aspirate taken at admission (CLART® Pneumovir array assay that identifies adenovirus, metapneumovirus A,B, parinfluenza 1,2,3,4, rhinovirus, respiratory syncytial virus A,B, bocavirus, influenza A,B,C, enterovirus and coronavirus 229E, OC43 & NL63) was positive for HBoV. Mumps serology detected negative IgM and positive IgG titres. He remained afebrile during admission, with improvement in his respiratory distress and disappearance of parotid swelling, then being discharged within 3 days.

Two weeks after admission the patient was asymptomatic, cervical ultrasound was normal except for some intraparotid adenopathy, and amylase titre was 77 U/L. Control nasopharyngeal aspirate in this moment was negative.

Human bocavirus has been associated with lower respiratory tract infections, mainly wheezing and pneumonia, in young children.[3–5] It has also been described as a causative agent of upper respiratory tract infections, mainly adenoiditis and otitis, demonstrating its affinity with this type of tissues.[6,7] To date, only in two cases has HBoV been associated with mumps but its pathogenic role as a causative agent of parotitis is discussed, since in one case it has been detected in coinfection with PIV 3.[1,2] However, the parotid gland could be a target of infection for this virus, as occurs in adenoids, where some authors have identified HBoV in up to 43% of the specimens obtained from children with adenoidal disease.[7]

Our patient had the typical symptomatology associated with HBoV infections with a wheezing episode, and with infiltrate in the chest X-ray. In addition, he was in the most frequent age-range for this virus infection, developing the disease during late autumn when most HBoV infections occur.[3] The analytical data were also consistent with those described in HBoV infections.[3] Bacterial agents were not detected. He was correctly vaccinated and mumps serology showed the presence of IgG titres. Acute EBV infection was also ruled out. The clinical picture evolved favourably and the nasopharyngeal aspirate control was negative two weeks after the acute episode. Although causality of HBoV is difficult to establish, serology has demonstrated that HBoV has a pathogenic role in respiratory infections.[8–10] Unfortunately in our centre we do not have HBoV serology available, but we think that our case adds to those already described to make it consider that it may have an etiological role.

We consider that HBoV should be taken into consideration as an infrequent but possible causative agent of acute parotitis in young children. Prospective studies should be designed to verify the truly pathogenic role in parotitis cases.

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Cristina Calvo[a,b,c,*], Claudia Millan[a], María Pilar Romero[d], Ana Méndez-Echevarría[a,b]

[a] *Pediatric Infectious Diseases Department, Hospital Universitario La Paz, Madrid, Spain*
[b] *Fundación IdiPaz, Madrid, Translational Research Network in Pediatric Infectious Diseases (RITIP), Madrid, Spain*
[c] *TEDDY Network (European Network of Excellence for Pediatric Clinical Research), Italy*
[d] *Microbiology Department, Hospital Universitario La Paz, Madrid, Spain*

* Corresponding author.
E-mail address: ccalvorey@gmail.com (C. Calvo).

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Use of adenosine deaminase as a marker for selecting pleural fluids for culture and/or molecular techniques for detection of mycobacteria☆

Uso de adenosin deaminasa como indicador para seleccionar líquidos pleurales para cultivo y/o técnicas moleculares para detección de micobacterias

Dear Editor:

Pleural tuberculosis (PT) is a significant cause of tuberculosis (TB) in our region of Castile and León and, along with genitourinary tuberculosis, is the most common cause of extrapulmonary TB. With respect to all positive cultures for *Mycobacterium tuberculosis* (MT), the proportion of positive cultures in pleural fluid (PF) ranged from 5.18% in 2013 to 6.54% in 2016. The number of cases of PT has remained around 14 annual cases confirmed by culture, while over the same time there was a decrease in the number of cases of pulmonary TB. A previous 17-year study conducted in our Bierzo health board area[1] revealed that only 2.5% of PF samples are positive for MT culture. In view of this situation, we decided to look for a system for selecting PF samples to improve the performance of mycobacterial cultures and optimise the use of molecular techniques on those samples. We assessed a total of 200 PF samples collected from 2015 to 2018. The adenosine deaminase (ADA) value was determined in all of the samples, establishing the cut-off point at 30 U/l, above which PT is suspected in our health board area. All samples were seeded in solid culture media (Coletsos and Middlebrook 7H11) and automated liquid media (BacT/ALERT® MP) and incubated for at least 6 weeks. When ADA was found to be above the cut-off point, the automated liquid medium was re-seeded at the end of the incubation period and incubation of all the bottles was prolonged for at least three more weeks. Identification of MT was performed by molecular techniques (GenoType® MTBC and GenoType® MTBDR, Hain) and the PCR on direct sample was performed with GeneXpert® MTB-RIF (Izasa®). When the ADA value is dispensed with, MT growth/PCR+ is only obtained in 3% of the PF samples. When an ADA value of 30 U/l or above is used (51 cases, 25.5% of PF), the rate of growth/detection by PCR increases to 11.76% (6 cases). As shown in Table 1, there was no doubt that the pleural effusion was predominantly lymphocytic in all the samples, with figures ranging from 54% to 100%. MT growth was obtained in solid media in only two cases, and only two to three colonies grew after the first six weeks of incubation. The growth of MT in liquid media occurred in four cases, with a mean of 22 days; growth was negative in two cases. No MT growth was obtained in any of the 149 PF samples with ADA values below 30 U/l. According to a recent review, the method of determining ADA values and establishing cut-off points adapted to regions with a high TB rate has a high discriminatory power; in contrast, in low-incidence regions, it would have a high negative predictive value.[2]

The main disputable factor is the determination of the cut-off point which enables differentiation of TB from other processes, and varies widely according to the following parameters: (1) the prevalence of TB in the geographical area studied; (2) the age of the patients, as in patients over 55, the cut-off point would drop to 26 IU/l, while in the under-55s it would rise to 72 IU/l,[3] and (3) the number of cases studied. In a study of 2413 cases of pleural effusion duly classified according to aetiology and with a mean age of 65, the mean cut-off point was set at 28.26 IU. Values above 100 IU/l were related to lymphoproliferative processes, carcinomas, para-malignant effusions and empyema.[4] In 2015, the average incidence of TB in Castile and León was 9.93 cases per 100,000 population, with an average incidence of PT of 0.77 cases per 100,000 population.[5] The province of León, and especially the county of Bierzo, continue to be the areas with the highest incidence of TB in the region. The selection of PF samples for TB detection could be established initially through the use of ADA, accompanied by other markers, particularly the percentage of lymphocytes and other biochemical parameters. We would need to start by studying a larger number of samples in order to determine the most appropriate cut-off point in our health area. In our study, if we had used 40 IU/l as the cut-off point, we would have missed two cases. Pleural fluids tend to be paucibacillary samples, and greater sensitivity would raise the limit of microbiological and molecular detection. In view of the fact that in most of the PF samples studied (74.5%) the ADA value was below 30 IU/l, that alone would enable us to select the remaining 25.5% (with ADA >30 IU/l) for application of the microbiological and/or molecular techniques, obtaining both a higher diagnostic yield and cost savings. Based on these preliminary results and in the absence of a more exhaustive study, we conclude that the use of molecular techniques for the detection of MT in PF with ADA values below 30 IU/l does not appear to be reasonable in our area.

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