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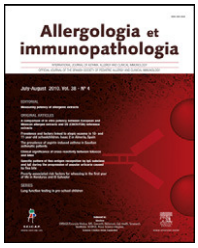

EDITORIAL

Cytokines profile and acute bronchiolitis

Acute viral bronchiolitis is a major cause of morbidity and mortality in infants. It is characterised by acute inflammation, oedema, and necrosis of epithelial cells lining small airways, increased mucus production, and bronchospasm.[1] Several different viruses can cause a similar pattern of symptoms and signs. The most common aetiology is the respiratory syncytial virus (RSV), but other viruses are also identified, such as human metapneumovirus, influenza, adenovirus, rhinovirus, and parainfluenza. Virtually all children will be infected with RSV during the first two years of life, and up to 40% will develop lower respiratory infections. Severe bronchiolitis requiring hospitalisation is estimated to occur in one to three percent of those children.[2]

Over the last decades our understanding of the microbiology and pathophysiology of acute bronchiolitis has increased, but many questions remain with regard to the optimal management approach for infants requiring hospitalisation and we still do not have an effective drug against those viruses. Actual recommendations are based mainly on supportive care. Humanised monoclonal antibody palivizumab has demonstrated to be a safe and effective option for RSV prevention, but its high cost limits its use to high risk infants.[3]

It is known that viral infections can damage the airway epithelium, induce inflammation, and stimulate both innate and adaptive immune response. Host immune response has been the focus of several studies over the last decade. It is probably one of the principal determinants of bronchiolitis severity (together with others such as airway size, passively acquired maternal IgG antibody and viral load) and could be related to persistent or recurrent wheezing over the following years.[4]

In this issue of Allergologia et immunopathologia, Flores et al. present an interesting study of cytokine expression in infants during acute bronchiolitis.[5] Expressions of interleukin (IL)-4, IL-12, IL-13 and interferon (INF)-γ were determined from nasal swabs of 143 infants with their first episode of acute bronchiolitis in order to study Th1-Th2 activity. Antigen viral identification was performed by immunofluorescence to RSV, influenza, parainfluenza, and adenovirus. Cytokine expression was analysed according to several personal characteristics and also according to virus identification and severity of the bronchiolitis. In summary, the authors found Th1 bias in older children, in those who had been breastfed, and in those attending day-care centres, whereas Th2 bias was found in children exposed to cigarette smoke. RSV infection determined lower expression of IL-4 when compared to negative samples. No significant association was found between the severity score and virus identification or cytokine expression.

Studies of cytokine expression during acute bronchiolitis may contribute to our understanding of this triggering disease. Unfortunately we are still at the beginning of this road and at the moment there are many more questions than answers. It has still not been established, for example, if a specific pattern of Th1-Th2 imbalance is really present in these infants. Results from previous studies diverge largely, showing Th1 polarisation in some[6,7] and Th2 in others.[8,9] The division of cytokine response in two dichotomous categories seems to be a too simplistic approach to explain the immune response, since other cytokine profiles have already been identified and it is not rare to find concomitant diseases with opposite cytokine profiles. Additionally, some studies found that both Th1 and Th2 cytokines are stimulated during acute bronchiolitis.[10] No clear bias was found in the four cytokines studied by Flores et al.

The main purpose of this study was to compare the immune response among different viral agents. The small number of viral identification, however, limited this analysis. Influenza and parainfluenza virus were identified in a very small group, and some other viruses such as rhinovirus, human metapneumovirus and human bocavirus were not investigated. RSV was the most frequently identified virus and induced a significant lower expression of IL-4, suggesting a Th1 bias. It is still hard to define if statistical differences (like this one) have clinical importance. In theory, a Th2 bias could be associated with a more severe disease. IFN-γ, a Th-1 cytokine with well-characterised antiviral activity, was inversely associated with clinical severity of acute bronchiolitis in other studies,[11] but not in the study of Flores et al.

Another triggering question is the role of cytokine profile during acute bronchiolitis in the development of asthma and allergy. Acute bronchiolitis, particularly RSV bronchiolitis, is

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clearly associated with recurrent wheezing in preschool and school age, but it is still in debate whether this infection acts as a real cause in subsequent asthma or if it is only a marker of predisposition.[3] In the first hypothesis, the virus could induce a persistent Th2 predominant response profile, with elevated Th2 cytokines, like IL-4 and IL-13. In a prospective cohort of infants hospitalised with severe RSV bronchiolitis, Castro et al. analysed peripheral blood T cells expression for IL-2, IL-4, IL-13 and IFN-γ immediately after RSV and at two, four and six years of age.[12] They found that Th1 cytokines tend to decrease over time after the infection, while Th2 cytokines tend to increase. However, these patterns were unrelated to asthma and allergy outcomes by six years of age. In this study, the degree of Th1 and Th2 cytokine responses during RSV infection was not associated with the subsequent development of asthma, eczema, or allergic sensitisation.[12] More studies are needed to confirm these findings and we are awaiting with great interest the results from the follow-up of these children studied by Flores et al.

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