Induction of Cytotoxic T-Cell Response Against Hepatitis C Virus Structural Antigens Using a Defective Recombinant Adenovirus

O. Bruña-Romero¹, J. J. Lasarte¹, G. Wilkinson², K. Grace³, B. Clarke³, F. Borrás-Cuesta¹, and J. Prieto¹

From the ¹Department of Medicine and Liver Unit, University Clinic and Medical School, University of Navarra, Pamplona, Spain; ²the Department of Medicine, University of Wales College of Medicine, Cardiff, UK; and ³the Department of Molecular Sciences, Wellcome Foundation LTD, Beckenham, Kent, UK

Abstract of:
Hepatology 1997; vol. 25, nº 2

A replication-defective recombinant adenovirus (RAd), RAdCMV-CE1, containing core and E1 genes of hepatitis C virus (HCV) was constructed. RAdCMV-CE1 was able to express core and E1 proteins both in mice and human cells. Immunization of BALB/c mice with RAdCMV-CE1 induced a specific cytotoxic T-cell response against the two HCV proteins. This response was characterized using a panel of 60 synthetic 14-or 15-mer overlapping peptides (10 amino-acid overlap) spanning the entire sequence of these proteins. Five main epitopes were found in the core protein, four of which had been previously described either in mice or humans. One single novel epitope was found in E1. Fine mapping of this E1 determinant, showed that octamer GHRMAWDM is the minimal epitope recognized by cytotoxic T lymphocytes (CTL). The cytotoxic T-cell response was H-2ª restricted, lasted for at least 100 days, and was mediated by T cells with the classic CD4- CD8+ phenotype. This work demonstrates that replication-defective recombinant adenoviruses can efficiently express HCV proteins and are able to induce an in vivo cytotoxic T-cell response against a diversity of epitopes from HCV antigens. These vectors should be taken into consideration in the design of vaccines and also as a means to stimulate specific T-cell responses in chronic HCV carriers. (Hepatology 1997; 25: 470-477.)

Serum eosinophil peroxidase (EPO) levels in asthmatic patients

M. L. Sanz, A. Parra, I. Prieto, I. Diéguez, A. K. Oehling

Department of Allergology and Clinical Immunology, University Clinic, Faculty of Medicine, University of Navarra, Pamplona, Spain

Abstract of:
Allergy 1997; 52: 417-422

Eosinophil granular proteins are a useful eosinophilic activation marker in asthmatic patients. In this study, the eosinophil peroxidase (EPO) levels were assessed in different stages of bronchial asthma, in 123 patients suffering from asthma, classified as mild (n=49), moderate (n=49), and severe (n=25), according to the International Consensus Report on Diagnosis and Treatment of Asthma, as well as in 27 healthy controls, with the aim of evaluating the importance of this protein as a severity marker in bronchial asthma, and its possible correlation with parameters such as anamnesis, respiratory function tests, and peripheral blood eosinophil count, and also with some allergologic diagnostic tests, both in vivo and in vitro. The geometric
mean serum level of EPO was 9.3±11.3 ng/ml (median±SD) in controls, and 28±37.8 ng/ml in the asthmatic patients. Depending on the asthma severity, the EPO levels were 25±30.5; 29±37.1, and 41±47.3 ng/ml in mild, moderate, and severe asthmatics, respectively, being the significant differences between the group of patients with mild and severe asthma (p<0.001). The number of eosinophils (eos) in peripheral blood was 157±20 eos/mm³ in the controls, 334±35 eos/mm³ in mild asthmatics, 510±87 eos/mm³ in moderate asthmatics, and 658±72 eos/mm³ in severe asthmatics, with significant differences between all the groups (from p<0.05 to p<0.001). Both the serum levels of EPO and the number of eosinophils were greater in patients with active asthma than in patients with inactive asthma (p<0.001). Significant negative correlations (p<0.001) were found between serum levels of EPO and FEV₁ (r = 0.30), MEF₂₅₋₇₅ (r = −0.33), and MEF₅₀ (r = −0.34), and a good positive correlation (r = 0.80, p<0.001) was found between EPO levels and the number of eosinophils in peripheral blood. We also found a significant positive correlation between eosinophil number and clinical score (r = 0.54, p<0.001) and between EPO levels and the mentioned score (r = 0.46, p<0.001).

Key words: Bronchial asthma; Eosinophil peroxidase; Eosinophils; Inflammation Marker.

Bacterial immunotherapy in bronchial asthma

A. Oehling

Department of Allergology and Clinical Immunology, University Clinic, Faculty of Medicine, University of Navarra, Pamplona, Spain

Abstract of:


Nowadays, bacterial etiology is probably the least considered and most controversial in the etiopathogenesis of bronchial asthma. It was in the first decades of this century when several authors insisted on the close relation between infection and asthmatic response. This is why, since antibiotics have appeared, many renowned authors insist on the basic treatment of the infection with antibiotics. Also, the need of immunotherapy with bacterial antigens is being emphasized, considering the importance of this factor in bronchial asthma. Nevertheless, there are some detractors who, in our opinion, do not base their criteria on experience or precise data which support the rejection of the bacterial infectious factor as a causal triggering factor. It has been in the last decade when several authors, none among them, confirm the importance of the bacterial antigen, and especially its potentiating role on the inhalant allergens. On the other hand, in the last decade the symptomatic treatment of asthma by means of bronchodilators and corticosteroids is being fomented. That is, the maintenance of the asthmatic patient is being fomented instead of his consequent treatment, fighting the infection. According to our long experience and the positive number of cases obtained, again we insist on the need to treat bronchial asthma with bacterial immunotherapy. Therefore, it is necessary to study this aspect more in depth in order to reach a real knowledge of all of the above.

Key words: Bacterial immunotherapy; Bacterial infectious asthma; Bacterial antigen potentiation; Dendritic cells and bacterial infection; ECP and bacterial infection.