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Therapeutic Action Research of Bacille Calmette Guerin (BCG) on a Systemic Lupus Erythematosus Mouse Model.

Corresponding author : Chang ran ZHANG
Huang Pu Hospital of the First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, 510700, China
E-mail: zhcr2303@sina.com

Abstract:

We have been determined that for patients with systemic lupus erythematosus (SLE), after becoming infected with tuberculosis, the damages in their hematologic and complement systems were alleviated to a certain extent, this was an interesting phenomenon. So we hypothesized that tuberculosis infection could be useful for treating the SLE activity. In order to verify the above research conclusions, the animal experiments were conducted in combination with an SLE model mouse with BCG vaccinations. The research results showed that, for the mice receiving BCG vaccinations, the serum protein complement C4 concentration was significantly higher than that of the normal saline control group. Also, the kidney damages of the experimental mice were alleviated, and their lifetimes were significantly extended. The research results indicated that the BCG vaccine may have therapeutic effects on systemic lupus erythematosus (SLE).

However, an interesting phenomenon has been observed in recent clinical studies, i.e. after being infected with mycobacterium tuberculosis, the patients with systemic lupus erythematosus (SLE) demonstrated that the disease activities of their systemic lupus erythematosus (SLE) were under control. These patients mainly displayed decreases in white blood cells, revering of platelets, complement C3 and C4, and the mitigation of skin damages. It has usually been considered that for SLE patients infected with tuberculosis, the illness will be accentuated. The question remains as to why the lupus activities become reduced instead. Subsequently, this research study carried out a retrospective analysis of the clinical data of more than 2,000 cases of SLE patients in our hospital over the span of a decade. It was determined that the hematologic system damages (including white blood cells and platelets) of the SLE amalgamative tuberculosis patients were in fact alleviated over the relatively pure SLE patients. Furthermore, the levels of complement C3 and C4 were higher than the control group. However, the IgG, IgM, and IgA of both groups showed no significant differences ($P>0.05$). The inflammatory biomarkers of the SLE patients with amalgamative tuberculosis were observed to be aggravated, such as the acceleration of erythrocyte sedimentation, and the elevation of C-reactive protein. According to the research results, after the SLE patients were infected with tuberculosis, the illness was aggravated. However, the inflammatory response was aggravated, while the lupus activities were alleviated. Therefore, the data have been summarized, and many other researchers in this field have expressed concerns and interests in the results of this study.

The MRL/LPR mice were the 12th generation among the different strains of LG/J, AKR/J, C3H/D, and C57BL/6 mice, through a series of complex hybridization. Because the Fas recessive mutations were associated with spontaneous programmed cell death, lymphocyte proliferation genes occurred, which led to T cell proliferation. This was like the clinical manifestations of human lupus erythematosus (SLE), including systemic lymph node enlargement, DNA antibodies, sm antibodies, RNP antibodies, high degrees of ANA, immune complex glomerulonephritis, vasculitis, and so on. The MRL/LPR mice are one of the commonly used SLE animal models. The MRL/LPR mice (SPF level) had a weight of 18.4 to 23.8 g, were female, and were provided for this study by the Shanghai Slack Laboratory Animal Co., Ltd. Animal Ethical approval for the study was obtained from the Sun Yat-Sen University Ethics Committee.

According to similar weights, the mice were matched in order to randomly be divided into normal saline and BCG treatment groups, with five mice per each group. They were caged for feeding, and then the mouse auricle was punched in order to number. Beginning in the second week of the experiment, each of the mice of the BCG treatment group was injected with 0.1 ml BCG subcutaneously on its back, and each of the mice of the normal saline group was injected with 0.1 ml of saline solution subcutaneously on its back. The injections were carried out again a week later, and then once a week, for a total of four injections.

A supine position was adopted for the experimental animals, which was sprawled and fixed, and then the abdominal walls were cut along the belly line from the xiphoid cartilages to the anus, followed by the cutting of the abdominal wall along the last left and right frames to the spine. All of the abdominal organs were exposed in order to check the quantity and shape of peritoneal fluid, whether the peritoneum was smooth, and the viscera position was normal, for the purpose of cleaning up the abdominal cavity organs (spleen, pancreas, stomach, and so on). Then, tweezers were used to strip the kidney fat, and to extract the kidneys in to check the kidney specimens. The specimens were fixed with tissue fluid for 24 hours, and the paraffin embedded slices where HE stained for optical microscopy.

Keywords: Systemic lupus erythematosus; Bacille Calmette Guerin;Vaccination; Complement; Therapy; Immunology

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