LETHAL BCG INFECTION IN THYMECTOMIZED MICE

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Experiments on CBA mice showed that adult animals injected intravenously with BCG mycobacteria in a dose of 2 mg 12 months after thymectomy died within 2.5 months from disseminated BCG infection against the background of depression of hypersensitivity of delayed type. Mice undergoing a mock operation developed the ordinary BCG vaccination process.

KEY WORDS: thymectomy; BCG vaccine; infection.

After thymectomy in adult animals ability to give an immune response, mainly cellular, is disturbed. However, this phenomenon is not manifested at once, but only after a fairly long period of time, for the T cells in the peripheral lymphoid organs continue to perform their functions [6, 7]. It is only after exhaustion of this pool that the animal comes to resemble the neonatally thymectomized animal [1].

The writers' previous investigations [1] showed that ability to develop hypersensitivity of delayed type (HDT) was disturbed and resistance to infection with tuberculosis was lowered in adult CBA mice 8-12 months after thymectomy.

In this investigation the effect of thymectomy in adult animals on the course of the vaccination process after immunization with BCG was studied.

EXPERIMENTAL METHOD

CBA mice underwent thymectomy at the age of 2 months by the method described earlier [3]. Twelve months after the operation the mice (and, at the same time, control animals undergoing a mock operation) were given an intravenous injection of 2 mg BCG vaccine. One month after infection 10 mice of each group were tuberculin tested (0.05 ml of Koch's old tuberculin was injected into the left hind foot pad and the reaction was read after 24 h, when thickening of the foot pad was assessed). The reaction was considered to be positive if the thickening was at least 0.15 mm. As a control, physiological saline was injected at the same time into the right hind foot pad (the method is described in more detail by Crowle [5]). Titers of circulating antibodies were determined by Boyden's passive hemagglutination test (PHT), with at least five mice in each group. The histological changes in immunocompetent organs and in the lungs and the survival rate of the mice in each group also were studied.

EXPERIMENTAL RESULTS

As was shown previously [1], marked depopulation of the thymus-dependent zones of the spleen and lymph nodes and the replenishment of these zones with macrophagal cells were observed in the mice 8-12 months after thymectomy. One month after injection of BCG mycobacteria into the thymectomized mice (by contrast with the intact vaccinated animals), signs of activation of lymphocytes were absent in the thymus-dependent zones. Meanwhile, many more specific epithelioid-cell granulomas were found in the spleen, lymph nodes, and lungs of these animals than of vaccinated mice undergoing the mock operation.

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Analysis of the tuberculin tests showed that the HDT revealed by them was depressed in the thymectomized mice compared with those undergoing the mock operation. The reaction was positive in 9 of the 10 mice undergoing the mock operation (mean rating of the tests 0.255 ± 0.053) but in only 2 of the 10 thymectomized mice (mean rating of the tests 0.095 ± 0.019; $P < 0.01$). The PHT revealed antibodies in the thymectomized mice in rather lower titers than in those undergoing the mock operation but the difference between them was not statistically significant ($P > 0.05$).

In the course of the 2.5 months after injection of BCG mycobacteria 9 of the 10 thymectomized mice died (mainly within the interval 1.5-2.5 months), whereas only one mouse undergoing the mock operation died before 2.5 months. Marked dissemination of specific granulation tissue was found in the lymph nodes, spleen, and lungs of the thymectomized mice that died.

Thirteen mice undergoing the mock operation 12 months previously were infected 2.5 months after BCG vaccination with a virulent culture of Mycobacterium tuberculosis strain H37RV in a dose of 0.1 mg intravenously (simultaneously with 15 intact mice of the same age). Of the 15 intact mice 14 died during the 27 days after infection. By that time only two of the mice vaccinated with BCG had died. Consequently, the changes revealed by these experiments were not connected with the inability of the old mice to develop postvaccination immunity against tuberculosis.

Intravenous injection of BCG vaccine in a dose of 2 mg, which causes the development of a vaccination process in intact animals and stimulates immunity against tuberculosis [2], in adult mice thymectomized 12 months before vaccination thus leads to the development of a disseminated process and death. It will be noted that the caseation component characteristic of tuberculosis caused by virulent myobacteria did not develop in this case. It was also found that in these animals the HDT revealed by tuberculin tests is also depressed. In other investigations on adult thymectomized, irradiated mice, whose bone marrow was restored it has been shown that dissemination of mycobacteria is intensified in such animals and lethal BCG infection develops [4].

A similar course of infection is also observed in BCG-vaccinated children with immunodeficient states, mainly with aplasia of the thymus. The investigations described above thus confirm that the thymus plays an essential role in resistance to infections in adults also, and that the development of serious complications after vaccination with live vaccines (especially BCG) may, in some cases, be associated with defective function of the thymus.

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