ABSTRACT

IMMUNOPATHOLOGICAL SIMILARITIES OF LEPROSY TO TUBERCULOSIS

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1. Classification of leprosy

It has been generally accepted to devide leprosy into two polar types, lepromatous and tuberculoid. In lepromatous cases histological examination of lesions reveals accumulation and proliferation of lepra cells which are foam-cell type histiocytes bearing many bacilli in the protoplasma, and Mitsuda skin reaction is negative. In contrast, epithelioid cell granulomas are characteristic of histological findings in patients with tuberculoid type disease. No pathogens are detectable in the lesions and Mitsuda reaction is positive. Therefore, it is a possibility to propose that the symbiosis of the bacilli and host cells in the lepromatous type disease may be due to defective immune status like immune tolerance and the proliferation of sterile epithelioid cells may be under control of immune status mediated by cellular immunity.

2. Types of disease in experimental tuberculosis

When a large and small number of avian type tubercle bacilli are injected into the rabbit intravenously, Yersin and Villemin type tuberculosis is induced respectively. Tuberculin skin reactivity is negative in the former and positive in the latter. Bacillemia with vigorous proliferation of the organisms in the cells of the spleen and the other RES organs is of characteristic in Yersin type disease. In contrast, no or only limited number of bacilli can be detectable in Villemin type disease whose lesions are tubercles consisting of epithelioid cells in nature. These findings support that Yersin and Villemin type tuberculosis are comparable in pathogenesis to lepromatous and tuberculoid type leprosy respectively.

When the tubercle bacilli are injected into the rabbit subcutaneously, they are ingested by leucocytes infiltrating the injected site in the first day of application and are transfered to macrophages in the following day. The bacilli begin to multiply in the cells which are filled up with the bacilli on the 4th to 6th day of infection. Tuberculin reaction is negative in these days during which the growth of bacilli is evident. One week after the infection, the injected focus becomes necrotic in the center which is surrounded by epithelioid cell granulomas where the growing bacteria cannot be seen. The suppression of bacterial growth in the cells is coincidental

in time with the aquisition of tuberculin sensitivity in the animal. This means that the lesion induced in the subcutaneous tissue is lepromatous in the early stage of infection and tuberculoid in the late stage. In addition, repeated injection of old tuberculin or culture filtrates of tubercle bacilli into tuberculo-sensitized rabbits make the skin reaction turn negative and a subcutaneous infection of the bacilli results in the lepromatous lesion in the desensitized animals.

3. Immunopathology of sarcoidosis

Pathogenesis of sarcoidosis is unknown as yet, but the histological appearance of this disease is characteristic of epithelioid cell granulomas without necrosis. The lesions similar in appearance to sarcoidosis can be induced by application of a chemical fraction of tubercle bacilli, wax D, into tuberculosensitized animals. The sarcoid lesion induced by wax D is very delayed in occurrence and this is comparable to the delayed appearance of Kveim reaction in sarcoidosis as well as Mitsuda reaction in Leprosy. The Kveim antigen as well as Mitsuda antigen is a emulsion of lesion and its active component may be lipoid substances originating from membraneous constituents of invaded cells or of invading organisms if present. Beside the delayed reaction, an intracutaneous injection of wax D into sensitized animals results in tuberculin type delayed reaction. This early reaction is comparable to William-Nickerson's reaction in sarcoidosis and also to Fernandez's reaction in leprosy. In addition, it has been reported that Kveim antigen on occasion produces positive reaction in control patients. This is the same phenomenon seen in the test injection of Mitsuda antigen into noninfectious controls and in wax D injection into tuberculin-negative controls. This phenomenon may be depend on the sensitizing ability of these antigens for the late reaction inducing epithelioid cell granulomas.

STUDIES ON THE TRANSFER FACTOR OF TUBERCULIN HYPERSENSTITIVITY IN GUINEA PIGS

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It has been demonstrated that passive transfer of tubreculin hypersensitivity is possible by using a certain fraction of spleen extract obtained from guinea pigs vaccinated and challenged with heat-killed BCG. It is suggested that the "Transfer Factor" is high molecular substance which does not pass through cellophane membrane, and that "Inhibitor" is low molecular substance. The behavior on Sephadex columns suggests that the molecular weight of the Transfer Factor is 15,000～67,000.

This factor seems to be a protein-like substance, because the activity disappears after trypsin treatment but resists RNAse treatment. The histological finding of biopsy material obtained from recipient animals. This is an evidence for successful transfer of tuberculin hypersensitivity. The Transfer Factor is liberated from spleen cells to blood stream by ^{60}Co irradiation (800 γ) on the sensitized and challenged guinea pigs. It is concluded that the Transfer Factor of tuberculin hypersensitivity in guinea pigs is very similar to the Transfer Factor found in alveolar macrophages of rabbits which Okada reported already.