Sarcoidosis: Changing Clinical Manifestation in Japan

An increase in the number of patients with sarcoidosis in Japan has been recognized since the 1960's. Sarcoidosis is a systemic disorder, the lesion of which is characterized as an epithelioid cell granuloma formation stimulated by unknown agents. In Japan, the majority of the patients show thoracic involvement which can easily be detected by annual check-up even when they are asymptomatic. The increase in the numbers became prominent during the 1970's and 1980's. However, as half of the patients were asymptomatic, and 75% of cases recovered, sarcoidosis was not clinically recognized as a serious disease during that period. However, in the 1990's, a substantial number of these patients developed serious respiratory failure due to pulmonary fibrosis. The reason is that in 5% of the cases who were detected during the 1960's and 1970's the disease progressed within 10–15 years after the onset/detection (1). They could be justly evaluated as recipients for lung transplantation.

Current issues to be solved are as follows: 1) What are the causative agent(s), 2) What pathophysiological processes cause epithelioid cell formation. From the histopathological similarity of the lesions between sarcoidosis and tuberculosis, sarcoidosis has been noted to be a disease mediated by an immune response (2). However, since the causative agent was unknown, the mechanism of the formation of sarcoidosis lesions has been unclarified. Clinically it is a most important factor to determine what mechanisms or factors are required for the fibrotic processes after many years of the persistence of granuloma. And 3) Is there disease susceptibility? And how to determine disease susceptibility and how to detect prognostic factors? After solving these issues, we can treat the patients in a more rational way.

The development of bronchoalveolar lavage (BAL) in 1974 by Reynolds et al enabled us to analyze the cellular or fluid components which reflect lesions in the lung. As a result, we obtained a great deal of information in relation to the pathogenetic processes in sarcoidosis (3). We understand that macrophage T cell activation by unknown agents precedes epithelioid cell granuloma formation and CD4 positive cells are dominant at the lesion site and release various mediators and cytokines to drive the processes. Th1 equivalent T cells which release IL-2 and γ-interferon are important for granuloma formation compared with Th2 equivalent T cells which release IL-4 and IL-6 for B cell activation.

On the other hand, many studies have been done by using immunohistochimical methods since the report of van Maarseveen in 1984 in which a distribution of T cells on tissue specimens was analyzed for comparison to the results of studies using BAL fluid cells. Kita et al in this issue intensively examined a topographical evaluation using this method (4). They found that CD4 memory cells are centered in the epithelioid cell granulomas and epithelioid cells are arranged in a layer-like distribution. The later pattern is different from that of the tuberculosis granuloma. Does the difference in the cellular distribution within granuloma relate to the chronicity of the granuloma? When such immunohistological studies are done using various patients, such as cured cases and chronic cases with fibrosis, more useful results can be obtained in finding prognostic markers.

Prospective investigations should be done in well-designed way, and if a tissue bank could supply adequate tissue specimens to the researcher, we expect to obtain clues about how to treat and prevent the fibrotic processes after post granulomatous inflammation.

Takateru Izumi, MD
Department of Pulmonary Medicine,
Chest Disease Research Institute,
Kyoto University,
Kyoto 606-01

References