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A nationwide epidemiological survey of chronic hypersensitivity pneumonitis in Japan

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ABSTRACT

Background: In 1999, a Japanese epidemiological survey of chronic hypersensitivity pneumonitis (HP) showed that summer-type HP was the most prevalent variant of the disease. The number of reported cases of chronic HP has recently been increasing, and the clinical features of the disease seem to have changed. We conducted another nationwide epidemiological survey of chronic HP in Japan to determine better estimates of the frequency and clinical features of the disease.

Methods: A questionnaire was sent to qualified hospitals throughout Japan, and data on cases of chronic HP diagnosed between 2000 and 2009 were collected.

Results: In total, 222 cases of chronic HP from 22 hospitals were studied. Disease subtypes included bird-related HP ($n=134$), summer-type HP ($n=33$), home-related HP ($n=25$), farmer's lung ($n=4$), isocyanate-induced HP ($n=3$), and other types ($n=23$). The median proportion of lymphocytes in bronchoalveolar lavage fluid was high (24.5%). The primary findings of computed tomography of the chest were ground-glass attenuation and interlobular septal thickening. Centrilobular fibrosis was the major pathological finding on examination of surgical lung biopsy specimens from 93 patients. The median survival time was 83 months.

Conclusions: The proportion of bird-related HP was higher than that in the previous epidemiological survey, and the proportions of isocyanate-induced HP and farmer's lung were lower. A crucial step in diagnosing chronic HP is to thoroughly explore the possibility of antigen exposure.

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1. Introduction

Hypersensitivity pneumonitis (HP) is an immunologically mediated lung disease induced by inhalation of antigens contained in a variety of organic dusts. HP is usually classified into acute, subacute, and chronic forms, although the subacute form might be a variant of acute HP [1]. Chronic HP is thought to be influenced by persistent or recurrent exposure to an antigen. Potential sources of inciting antigen vary among geographic regions and are influenced by multiple climatic, cultural, socioeconomic, and occupational factors. The clinical manifestations are heterogeneous and are likely to be determined by the intensity and frequency of exposure to etiologic antigens, as well as by genetic susceptibility [2]. The clinical features of chronic HP, namely, the physical findings, radiological and pathological abnormalities, and poor prognosis, are similar to those of idiopathic pulmonary fibrosis (IPF) [3].

A nationwide epidemiological survey of chronic HP in Japan was reported in 1999 [4]. The report covered 36 cases of chronic HP, including summer-type HP ($n=10$), bird fancier's lung (BFL, $n=7$), home-related HP ($n=5$), isocyanate-induced HP ($n=5$), farmer's lung ($n=4$), and other variants of the disease ($n=5$). Among the forms of acute HP in Japan, summer type was reported to be the most prevalent (81.9% of 331 cases) and BFL accounted for only 5.7% of cases [5]. Pulmonary physicians, radiologists, and pathologists now take steps to differentiate chronic HP from IPF. An important step in discriminating chronic HP from IPF/unusual interstitial pneumonia is to thoroughly explore the possibility of antigen exposure, because avoidance of antigen exposure may improve a patient's condition or halt disease progression. Since the last epidemiological survey was conducted, the number of reported cases of chronic HP has been increasing and the clinical characteristics of the disease seem to have changed.

Our group conducted another nationwide epidemiological survey of chronic HP in Japan to determine better estimates of the frequency and clinical characteristics of the disease over the past decade.

2. Materials and methods

2.1. *Patient selection*

The Research Committee on Diffuse Lung Diseases, a study group organized and sanctioned by the Japanese Ministry of Health, Labour and Welfare, conducted a survey on the status of chronic HP from 2000 to 2009. The committee sent a questionnaire to 25 qualified hospitals throughout Japan; data on 253 cases were collected from 22 hospitals, and data on 222 patients who satisfied the diagnostic criteria for chronic HP [4,6] were collected from the questionnaires. The diagnostic criteria for chronic HP included clinical improvement after withdrawal from the suspected environment and/or reproduction of symptoms by an environmental provocation or laboratory-controlled inhalation of a causative antigen and/or antibodies or lymphocyte proliferation to the presumptive antigen, evidence of pulmonary fibrosis on a pathological examination or on computed tomography (CT) scans, and respiratory symptoms related to HP for 6 months or longer [4].

2.2. *Questionnaire*

The questionnaire survey covered the following topics: causative antigens, symptoms, physical findings, laboratory findings, pulmonary function tests, bronchoalveolar lavage (BAL), radiography and CT findings, pathological findings of surgical lung biopsy specimens, immunological findings on specific antibodies, the lymphocyte proliferation test [7], the provocation test [8], treatment, and prognosis. Data on each patient were described by members of the Research Committee or by members of the Japan Respiratory Society serving as staff at the hospitals that returned the questionnaires. The study conformed to the Declaration of Helsinki and was approved by the internal review board of every institution that responded. Approval was obtained from the institutional review board on April 12, 2012, and the approval number was 1040.

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