LETTER TO THE EDITOR

Clinical remission in elderly patients with sarcoidosis

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To the editor,

We previously read with interest the article by Doğan et al (September 2023) (1) on elderly-onset pulmonary sarcoidosis. In their study, clinical remission (CR) rates were found to be significantly lower in elderly-onset patients (1). There is little information available about CR in elderly-onset patients, particularly regarding the clinical characteristics of patients who achieved CR and the time when CR was achieved. Recently, we treated an elderly patient who had maintained CR for more than 3 years. We consider CR to be a state in which symptoms and findings of sarcoidosis disappear without treatment. Regarding CR, it is important to note that there is no consensus on specifics regarding duration of follow-up and no criteria for investigation at follow-up. We would like to share our experience with our patient and discuss this point. A 61-year-old asymptomatic woman was referred to a hospital due to bilateral hilar lymphadenopathy (BHL) on chest radiography in a mass screening (Figure 1-A). The patient was a non-smoker and had no history of malignant disease. Chest computed tomography (CT) scan confirmed the presence of BHL (Figure 1-B), but the patient did not wish to undergo further investigation, so the patient was followed up thereafter. At age 66, BHL was again detected in a mass screening, and the patient was referred to our hospital. Physical examination revealed no skin lesion or superficial lymphadenopathy, and ophthalmologic examination revealed no uveitis. Serum lysozyme was 9.3 μg/ml, adenosine deaminase 30.1 U/l, serum calcium 9.5 mEq/l and serum albumin 4.5 g/dL. Electrocardiogram showed a heart rate of 72 beats per minute, sinus rhythm, no abnormalities in the PR interval, QRS interval, or QTc interval, and no ST-T changes. Echocardiogram and Holter electrocardiography had no abnormalities. Chest CT scan revealed enlarged bilateral hilar and mediastinal lymph nodes, but no abnormal opacities were found in the lung fields. No macroscopic abnormalities were found in bronchoscopy. Bronchoalveolar lavage fluid analysis showed a cell count of 2.20×10^5/mL, with a cell differentiation of 52.0% macrophages, 47.0% lymphocytes, and a CD4/CD8 ratio of 6.29. TBLB revealed noncaseating granulomas. These findings, combined with the BHL on chest imaging, led

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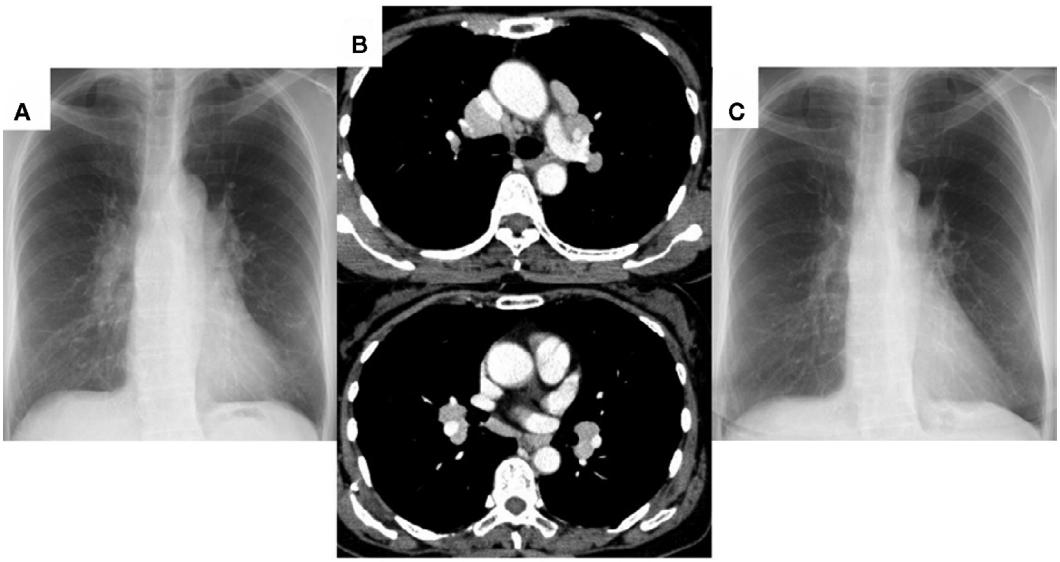

Figure 1. A chest radiograph taken at the age of 61 in a mass screening examination revealed bilateral hilar lymphadenopathy (BHL) (A), and computed tomography (CT) scan confirmed the presence of BHL (B). BHL remained unchanged, but eight years later at her age of 74, chest radiograph showed disappearance of BHL (C).

to a diagnosis of sarcoidosis. Although the BHL was significant, the patient was asymptomatic and had no cardiac, ocular, or pulmonary lesions, so corticosteroids were not administered. Follow-up was performed on chest imaging, electrocardiogram, ophthalmologic examination, and the presence or absence of subjective symptoms. Seven years after diagnosis, BHL remained unchanged, but eight years later at her age of 74, chest radiograph showed disappearance of BHL (Figure 1-C). A chest radiograph taken 11 years after the diagnosis at the age of 77 did not show BHL. The patient is in good condition with no symptoms or findings of sarcoidosis. In the article by Doğan et al, they showed CR rate in a fairly large population (38 elderly patients compared to 125 non-elderly)(1). However, in the method section of the article, they defined that clinical outcomes were classified as CR (disappearance of symptoms and radiological findings) or progressive-chronic disease (symptomatic or persistent disease of more than 5 years). We would like to point out that there was a lack of specifics about duration of follow-up and no criteria for investigation at follow-up in the article. We do consider that clear definition of these time periods in defining CR might lead to better research in the future. Therefore, it might be necessary to discuss the standard criteria for the term 'CR' and the need for a follow-up period before determining even in elderly-onset sarcoidosis patients achieved CR. When considering the definition of CR, two key articles must be cited and discussed. One of the most impactful articles was the A Case Control Etiologic Study of Sarcoidosis (ACCESS) Study (2). In this report published in 2003, data from heterogeneous United States sarcoidosis population indicated that sarcoidosis tended to improve or remain stable over two years in the majority of patients (2). Another important article was that by Baughman et al on the definition of clinical outcome status (COS) in sarcoidosis based on the results of the World Association of Sarcoidosis and Other Granulomatous Diseases (WASOG) Task Force (3). In the article, the authors chose to examine patients five years after diagnosis to determine COS, and several features of the disease were incorporated into the final categories of the disease (3). In addition to these key articles, a relatively recent review by Melani et al recommended evaluation at least

every 3-6 months for the first 2 years, then annually for 3-5 years, after which no more follow-up was necessary unless recurrence or new symptoms occurred (4). Looking specifically at cardiac sarcoidosis, it was reported that approximately half of patients developed cardiac lesions several years after the initial diagnosis (5). Considering the suggestions in these articles, there are currently no strict definitions or consensus on the duration of follow-up and no criteria for investigation at follow-up, but it seems that a duration of several years or more is generally appropriate for each. Our patient was diagnosed with sarcoidosis at age 66, achieved CR at age 74, and remained recurrence-free for the next 3 years. This patient was an elderly-onset sarcoidosis patient as proposed by Doğan et al, and had not experienced recurrence for several years. Therefore, she was considered to have achieved CR. In addition to our patient, there was another interesting patient with elderly-onset sarcoidosis who achieved CR. This female patient was diagnosed with sarcoidosis at age 69 and achieved CR at age 70, but had pleural recurrence 14 years later (6). Although very rare, some elderly-onset sarcoidosis patients, like our patient, could achieve CR, in which the sarcoidosis lesions disappeared without treatment. Collecting and analyzing clinical information about elderly-onset sarcoidosis patients who achieved CR might be important for both these patients and the physicians who treat them.

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