

Acta Medica Okayama

Volume 40, Issue 6

1986

Article 1

DECEMBER 1986

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Abstract

The presence of antibodies against adult T cell leukemia antigen (ATLA) was studied in 59 patients with chronic respiratory diseases. Of 13 patients with diffuse panbronchiolitis, 3, who developed adult T cell leukemia, had the anti-ATLA antibody and 8 had the related, anti-ATLA-like antibody. Of 13 cases of idiopathic interstitial pneumonia, 8 had the anti-ATLA-like antibody. Except for only one case, these antibodies were not detected in 33 patients with bronchial asthma or sarcoidosis and 20 healthy adults examined. These results suggested that the test of these antibodies would be useful for the diagnosis of diffuse panbronchiolitis and idiopathic interstitial pneumonia which frequently develop lung cancers.

KEYWORDS: anti-ATLA antibody, ATLA-related antibodies, diffuse panbronchiolitis, idiopathic interstitial pneumonia, adult T cell leukemia

*PMID: 3493619 [PubMed - indexed for MEDLINE]

Presence of Antibodies against Adult T Cell Leukemia Antigen in the Patients with Chronic Respiratory Diseases

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The presence of antibodies against adult T cell leukemia antigen (ATLA) was studied in 59 patients with chronic respiratory diseases. Of 13 patients with diffuse panbronchiolitis, 3, who developed adult T cell leukemia, had the anti-ATLA antibody and 8 had the related, anti-ATLA-like antibody. Of 13 cases of idiopathic interstitial pneumonia, 8 had the anti-ATLA-like antibody. Except for only one case, these antibodies were not detected in 33 patients with bronchial asthma or sarcoidosis and 20 healthy adults examined. These results suggested that the test of these antibodies would be useful for the diagnosis of diffuse panbronchiolitis and idiopathic interstitial pneumonia which frequently develop lung cancers.

Key words : anti-ATLA antibody, ATLA-related antibodies, diffuse panbronchiolitis, idiopathic interstitial pneumonia, adult T cell leukemia

It is well known that lung cancers frequently develop in the patients with idiopathic interstitial pneumonia (IIP) (1, 2). One of the remarkable symptoms of adult T cell leukemia (ATL), especially of smoldering ATL, is a respiratory disorder (3,4). Pulmonary infections caused by immunodeficiency, leukemic infiltrations in the lung and chronic bronchopulmonary disorders are frequently found in the course of leukemia. These facts prompted us to examine the presence of antibodies against adult T cell leukemia antigen (ATLA) in the patients with chronic respiratory diseases.

Materials and Methods

Fifty-nine patients with respiratory diseases were studied; 12 with bronchial asthma, 21 with sarcoidosis, 13 with IIP and 13 with diffuse panbronchiolitis (DPB). Sera were collected from these patients and 20 healthy adults and tested for

the presence of anti-ATLA or its related antibodies by the immunofluorescent assay, as described by Hinuma *et al.* (5), using ATLA-positive cells, MT-1 and MT-2, established by Miyoshi *et al.* (6, 7). In brief, an acetone-fixed smear of MT-1 or MT-2 cells was sequentially treated with 1 : 10 dilution of human serum and a fluorescein isothiocyanate-conjugated IgG, F(ab)² fragment of rabbit anti-human IgG antiserum, for 30 min at room temperature. In each experiment, sera with and without anti-ATLA antibody were used as the positive and negative controls. The fluorescence-staining pattern was observed by a fluorescence microscope equipped with a vertical illuminator.

Results

Staining patterns. Two types of cytoplasmic fluorescence were observed; gran-

Abbreviations: ATL, adult T cell leukemia; ATLA, adult T cell leukemia antigen; DPB, diffuse panbronchiolitis; IIP, idiopathic interstitial pneumonia.

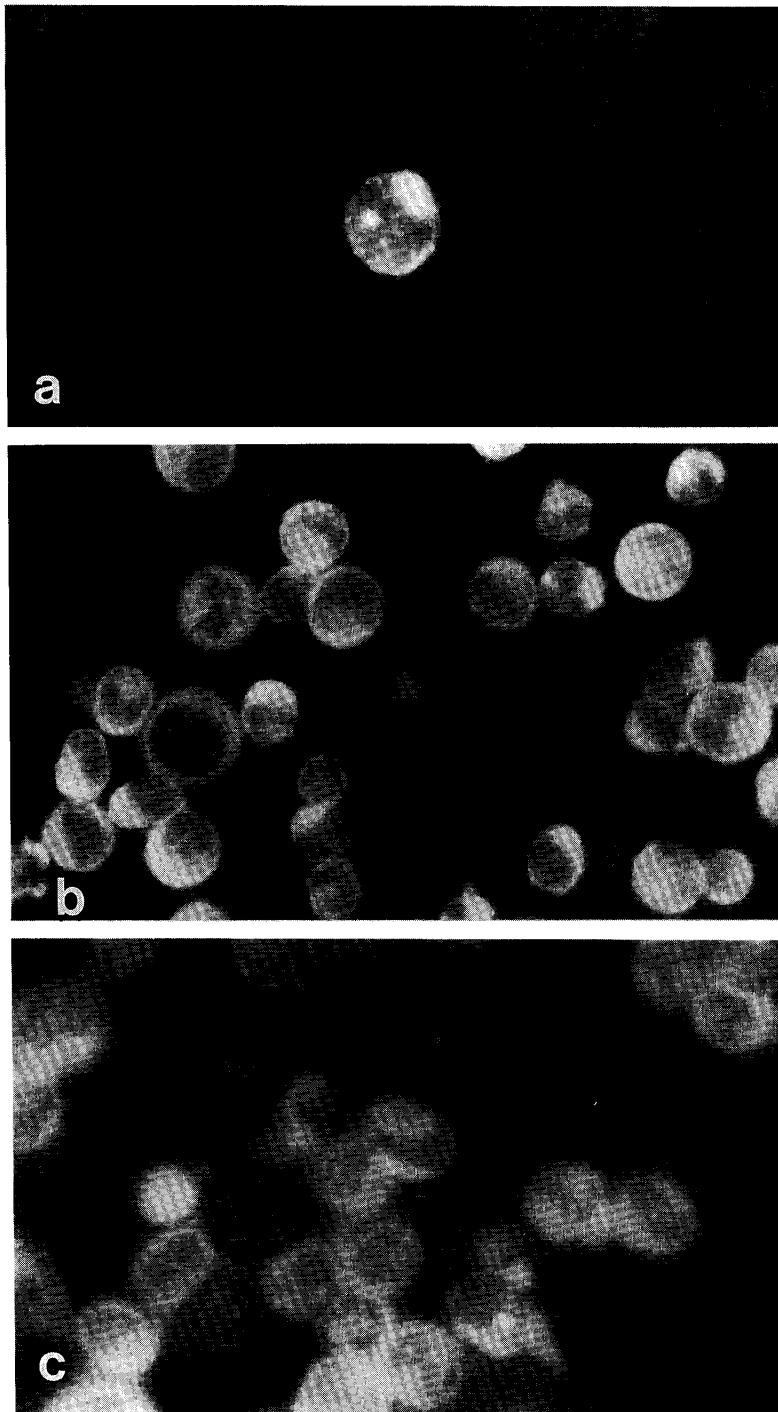


Fig. 1 Fluorescence staining patterns of MT-1 and MT-2 cells with anti-ATLA or related antibodies. a: Granular fluorescence in MT-1 cells stained with anti-ATLA antibody. b: Diffuse fluorescence in MT-1 cells stained with anti-ATLA-like antibody A. c: Diffuse fluorescence in MT-2 cells stained with anti-ATLA-like antibody A.

ular or dotted and diffuse (Fig. 1). In regard to the staining patterns in MT-1 and MT-2 cells, three different patterns were observed. The sera from ATL patients showed the staining pattern typical of the anti-ATLA antibody; the granular pattern in 1-5% of MT-1 cells and the diffuse pattern in 60-80% of MT-2 cells. Some sera showed the diffuse staining pattern in both MT-1 and MT-2 cells, and, in these cases, the antibody was distinguished from the typical anti-ATLA antibody and tentatively designated as the anti-ATLA-like antibody A. Some showed the diffuse staining pattern in MT-2 cells and no staining in MT-1 cells, and the antibody was designated as the anti-ATLA-like antibody B.

Frequency of anti-ATLA and anti-ATLA-like antibodies in patients with chronic respiratory diseases. Of 13 DPB patients, as shown in Table 1, 3 were positive for anti-ATLA antibody, of whom 2 were from an ATL-endemic area. These 3 positive cases were diagnosed as ATL in their clinical course of DPB because of the appearance of leukemic cells in the peripheral blood and the bone marrow. Thirteen cases of IIP, 12 cases of bronchial asthma, 21 cases of sarcoidosis and 20 healthy adults were all negative for anti-ATLA antibody.

Anti-ATLA-like antibody A was detected

in 6 of 13 DPB patients and in 5 of 13 IIP patients. Anti-ATLA antibody B was found in 2 of 13 DPB patients, in 3 of 13 IIP patients and in a patient of sarcoidosis from an ATL-endemic area. In these patients with anti-ATLA-like antibodies, a low percentage of ATL-like cells were sometimes observed in their peripheral blood. These cases with anti-ATLA-like antibodies were all from ATL-non-endemic areas, except for one sarcoidosis patient described above.

In total, 11 of 13 DPB patients, 8 of 13 IIP patients and one of 21 sarcoidosis patients had anti-ATLA or anti-ATLA-like antibodies, showing a diffuse staining pattern in MT-2 cells as a common finding.

Discussion

Anti-ATLA and related antibodies were detected in many cases of DPB and IIP examined in the present study. Three patients with respiratory symptoms of DPB had anti-ATLA antibody and developed ATL with ATL cells in the peripheral blood and the bone marrow. Two of these 3 patients were from an ATL-endemic area. On the contrary, all DPB patients with anti-ATLA-like antibodies were from ATL-non-endemic areas. These results suggest that there may be some im-

Table 1 Anti-ATLA and anti-ATLA-like antibodies in the patients with chronic respiratory diseases

Diagnosis	No. of cases examined	No. of cases with		
		Anti-ATLA antibody ^a	Anti-ATLA-like antibody	
			A ^b	B ^c
Diffuse panbronchiolitis (DPB)	13	3 ^d	6	2
Idiopathic interstitial pneumonia (IIP)	13	0	5	3
Bronchial asthma	12	0	0	0
Sarcoidosis	21	0	0	1
Healthy adult	20	0	0	0

a: Stains 60-80% of MT-2 cells diffusely and 1-5% of MT-1 cells granularly.

b: Stains 60-80% of both MT-2 and MT-1 cells diffusely.

c: Stains 60-80% of MT-2 cells diffusely and does not stain MT-1 cells.

d: All 3 cases were diagnosed as ATL, with ATL cells (28-65%) in peripheral blood.

munodeficiency in DPB patients, which resulted in the infection with HTLV-I (ATLV) or related viruses. On the other hand, it is also considered that the infection with HTLV-I or related viruses induces the state of immunodeficiency, which is responsible for the development of DPB. Another possibility is that ATL and DPB are originally of the same etiology. The clarification of these possibilities must await further studies.

It is reported that lung cancers frequently develop in the course of IIP (1,2). Therefore, the presence of anti-ATLA-like antibodies in many cases of IIP might indicate the possibility that these lung cancers develop from the interstitial pneumonia induced by HTLV-I-related viruses, just like the hepatomas developing in the hepatitis virus-induced liver cirrhosis (8).

As MT-2 cells contain many HTLV-I viruses, over 60% of cells show a diffuse staining pattern when stained with the anti-ATLA antibody, and these cells are recently used for the screening of the presence of the anti-ATLA antibody. On the other hand, the sera of exactly diagnosed ATL patients showed the granular staining pattern in 1-5% of MT-1 cells. In the present study, anti-ATLA-like antibodies showed the diffuse staining pattern in MT-2 cells, and diffuse or no staining in MT-1 cells. Therefore, the diffuse staining pattern in MT-2 cells, as well as the diffuse staining pattern in MT-1 cells, should be further analyzed in relation to HTLV-I and other viruses or antigens in future.

As described above, there still remain many problems to be studied. However, the high incidence of anti-ATLA-like antibodies in the patients with DPB and IIP suggests that the test of these antibodies is useful to

discriminate these two diseases, which might develop cancers, from other chronic pulmonary diseases.

References

1. Turner-Warwick M and Burrows B: Cryptogenic fibrosing alveolitis: Clinical features and their influence on survival. *Thorax* (1980) **35**, 171-180.
2. Kondo A, Iwai K, Umeda H, Fukuchi Y, Honma Y and Yoshimura M: Prognosis of idiopathic interstitial pneumonia; in Annual Report on the Study of Interstitial Lung Disease by Harasawa Michiyoshi. Grant-in-Aid from the Ministry of Health and Welfare in Japan (1985) pp 49-58.
3. Uchiyama T, Yodoi J, Sagawa K, Takatsuki K and Uchino H: Adult T-cell leukemia: Clinical and hematologic features of 16 cases. *Blood* (1977) **50**, 481-492.
4. Yoshioka R, Yamaguchi K, Yoshinaga T and Takatsuki K: Pulmonary complications in patients with adult T-cell leukemia. *Cancer* (1985) **55**, 2491-2494.
5. Hinuma Y, Nagata K, Hanaoka M, Nakai M, Matsumoto T, Kinoshita K, Shirakawa S and Miyoshi I: Adult T-cell leukemia: Antigen in an ATL cell line and detection of antibodies to the antigen in human sera. *Proc Natl Acad Sci USA* (1981) **78**, 6476-6480.
6. Miyoshi I, Kubonishi I, Sumida M, Hiraki S, Tsubota T, Kimura I, Miyamoto K and Sato J: A novel T-cell line derived from adult T-cell leukemia. *Gann* (1980) **71**, 155-156.
7. Miyoshi I, Kubonishi I, Yoshimoto S and Shiraishi Y: A T-cell line derived from normal human cord leukocytes by co-culturing with human leukemia T cells. *Gann* (1981) **72**, 978-981.
8. Hattori S: Hepatoma and Hepatitis Virus. *Gan to Kagakuryoho Sha, Tokyo* (1984) pp 269-271.

Received: September 10, 1986

Accepted: October 1, 1986

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