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ORIGINAL ARTICLE

CD5+ B Cells Ratio In Lepromatous Leprosy

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ABSTRACT

Objective Leprosy is a unique infectious disease, which is chronic and related to cellular immunity. It was known that who have a defect on cellular immunity, they are susceptible to M. leprae infection. CD19+CD5+ B cells are currently defined as B1 cells and they produce polyreactive antibodies. The aim of this study was to investigate the presence and the possible effect of natural antibody producing CD19+CD5+ B cells in leprosy disease patients.

Materials and Methods We investigated B lymphocyte subset and total B and B1 cells by flow cytometry in 40 patients with lepromatous leprosy and 40 healthy controls.

Results Compared to the healthy controls, both CD19+CD5- conventional B cells and CD19+CD5+ B1 cells subsets were found to be higher in leprosy patients group.

Conclusion The observed significant increases in CD19+CD5- and CD19+CD5+ B1 cells subsets in patients with lepromatous leprosy suggests that B1 lymphocytes known predisposed to autoimmunity may have a role on disorganized protective immune response in Lepromatous leprosy.

Key words lepromatous leprosy, CD19+CD5+ B cells, Mycobacterium leprae

Introduction

Leprosy is a chronic infectious disease caused by Mycobacterium leprae, an acid-fast bacillus with high infectivity, low pathogenicity and high virulence. Leprosy is one of the major infectious disease of concern defined by the World Health Organization. In 2003, a total of 451,325 cases were detected worldwide[1].

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This disease has a broad spectrum of clinical manifestations, with tuberculoid leprosy (TL) at one end of the spectrum and lepromatous leprosy (LL) at the other. LL is characterized by the virtual absence of T-cell responses to M. leprae and advanced clinical disease [2],[3],[4],[5],[6],[7],[8]. It is frequently associated with the presence of autoantibodies which might be related to B1 lymphocyte percentages, such as rheumatoid factor (RF), anticardiolipin antibodies (aCL), anti-neutrophil cytoplasmic autoantibodies (ANCA) and antinuclear antibodies (ANA) [9],[10],[11],[12].

CD5+ B cells (B1 lymphocytes) constitute 15-25% of B cell population in secondary lymphoid tissues in

adults. Especially peritoneal cavity contains B1 lymphocytes populations whose antigen receptors are immunoglobulin molecules and have limited diversity. Many of these cells are specific for polysaccharide and lipid antigens on bacterial wall. B1 lymphocytes produce IgM antibodies which called natural antibodies. Although they are found in fetus intensely, a decrease in cell counts is obtained by increasing age. CD5+ B cells differ from T dependent antigens by producing low-affinity polyreactive natural antibodies in response to polyclonal activators [13],[14],[15],[16]. In autoimmune diseases such as rheumatoid arthritis, Sjogren's syndrome and systemic lupus erythematosus, the relationship between the increase of autoantibodies and CD5+ B cells is established [13],[14].

Patients And Methods

Organization

Ethical consent was supplied by the Local Ethics Committee at Firat University Medical Faculty. Informed consent was obtained from all study participants. A total of 40 patients (29 males, 11 females) of Lepromatous leprosy with mean age of 60.00 ± 14.43 and mean years of diagnosis 30.66 ± 17.42 were included. Forty healthy individuals (25 males, 15 females) who have no leprosy contact with mean age of 55.00 ± 8.89 were included as controls. All the patients included in this study were free of other infectious diseases. Those post diagnosis received multidrug therapy (MDT) according to the recommendations of the World Health Organization. Patients undergoing an erythema nodosum leprosum episode and those taking thalidomide or corticoids were excluded.

Flow cytometric analysis of peripheral blood: Venous bloods (2 milliliters) from the participants were taken into the tubes with EDTA in order to examine T cell receptors by flow cytometry. All blood samples were researched within 2 hours. Peripheral blood samples were analyzed at Coulter EPICS XL-MCL (Beckman Coulter U.S.A). Immunotech (Marseille, France) monoclonal antibodies were used. Cell surface expression of lymphocyte antigens were examined by mAb staining of peripheral blood samples with two color flow cytometry. CD45/ CD14, isotype control, CD3, CD19/CD5, CD20 mAb tubes were prepared and analyzed according to the instructions of manufacturer. Results were counted at the same equipment using Expo-32 analysis software. The quality criteria involved the frequency above 95% of total lymphocytes in the analysis gate and homogenous CD45+ lymphocyte population (minimum of 2000 events in the gate; CD45>95%). Statistical analysis was done by using SPSS 11.0 and related sample T test. For the statistical significance threshold, $p<0.05$ value was used.

Results

The mean age of patients with lepromatous leprosy were 60 ± 14 years (range 25–80), of healthy control group was 59 ± 9 years (range 34 – 79). The mean duration of disease was 29 ± 17 years in patient with Lepromatous leprosy [Table/Fig 1].

Table/Fig 1

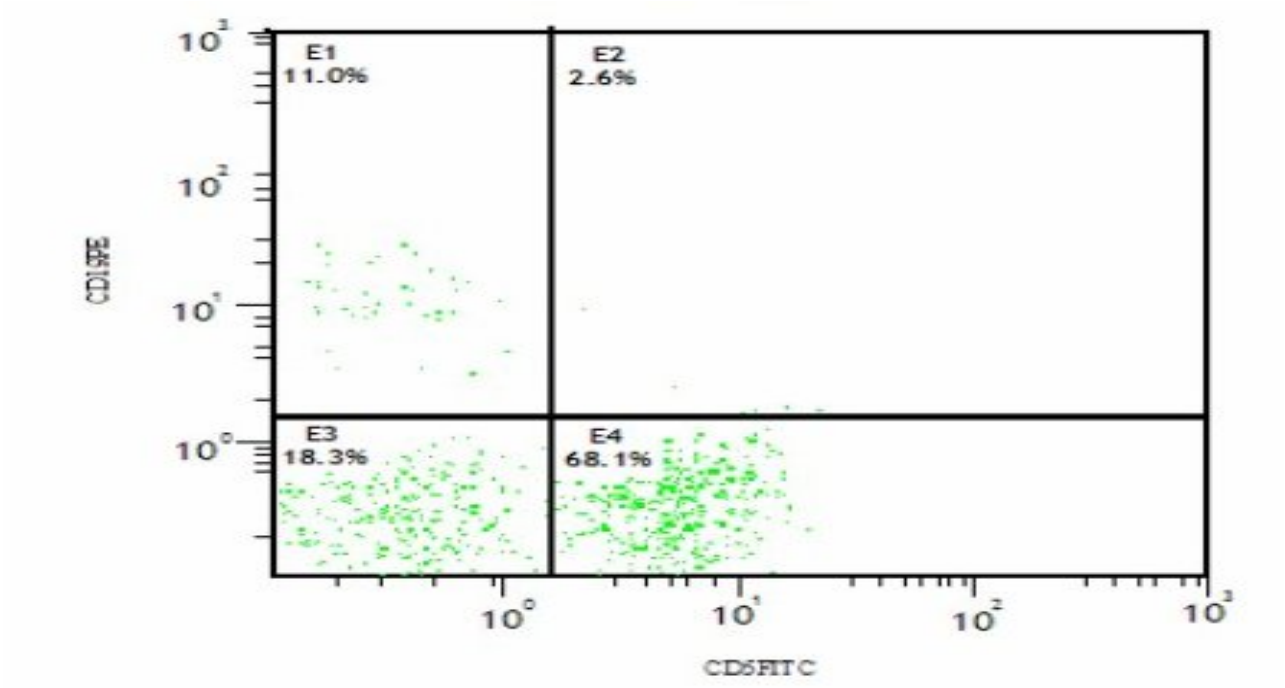
	Lepramatous leprosy patient	Healthy individuals	P value
n	40	40	
Gender (M/F)	28/12	26/14	
Age (years)	60± 14	59 ± 9	
Duration of the disease	29 ± 17		
CD19+CD5- B cell %	15.08 ± 4.83	12.14 ± 2.10	p<0.05
CD19+CD5+ B1 cells %	4.92 ± 3.57	1.10 ± 0.59	p<0.001

*This results presented as (mean ± SD)

Demographic characteristics and laboratory values of patients with Lepromatous leprosy and control subjects

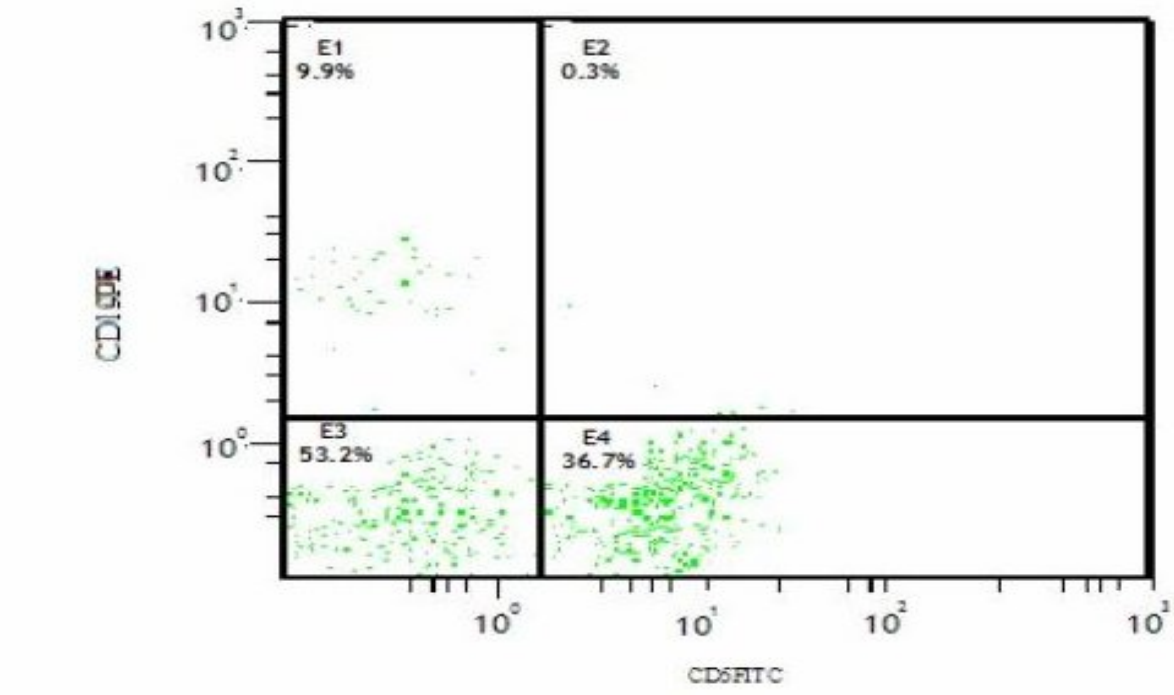
CD19+CD5+ B1 lymphocytes were significantly higher in patients with Lepromatous leprosy compared to healthy controls ($p = 0.001$). CD19+CD5- B lymphocytes were significantly higher in patients with Lepromatous leprosy compared to healthy controls ($p<0.05$) [Table/Fig 1], [Table/Fig 2], [Table/Fig 3].

Table/Fig 2



CD5+ B lymphocytes in leprosy patients

Table/Fig 3



CD5+ B lymphocytes in healthy controls

There was a significant correlation between CD19+ B lymphocytes (total B lymphocyte) and CD19+CD5+ B1 lymphocytes (r = 0,54) however no significant correlation were found between CD19 and CD19+CD5+ B1 lymphocytes percentage and disease duration.

Discussion

Leprosy is a chronic infectious disease caused by Mycobacterium leprae. Its broad spectrum of manifestations depends on distinct M. leprae-responsive T-cell subsets. Type 1 T helper (Th1) cells are associated with tuberculoid leprosy (TT), which is characterized by a protective response against the bacillus with effective control of the dissemination of the disease. In contrast, T helper 2 (Th2) cells are primarily associated with lepromatous leprosy (LL), which is characterized by intense polyclonal activation of B lymphocytes and absence of an M. Leprae specific T-cell response, resulting in multibacillary and disseminated disease, as well as development of hypergammaglobulinaemia and autoantibodies. Between these extremes are immunologically unstable patients with intermediate signs and symptoms corresponding to the borderline tuberculoid (BT), mid-borderline (BB) and borderline lepromatous (BL) forms [2],[3],[4],[5],[6],[7],[8].

Although the CD5+ B1 cells account for a small percentage of B cells in healthy adult individuals, their study gathers importance in view of their involvement in autoimmune states, in early lymphoid recovery after bone marrow (BM) transplantation and in malignancies such as the B-CLL and mantle cell lymphoma [3]. Additional studies have also shown that normal CD5+ B cells may be expanded in autoimmune diseases, such as rheumatoid arthritis (RA) or primary Sjogren's syndrome (SS) [13],[14]. Both splenic CD5+ and CD5- B lymphocytes produce platelet GP-specific auto antibodies in chronic idiopathic thrombocytopenic purpura (ITP) and may play a role in the autoimmune pathogenesis of ITP[5]. Lepromatous leprosy patients have a defect on Th1 type cellular response. It is known that leprosy patients have high autoimmune disease risk than healthy population. Compared to the healthy controls, both CD5- conventional B cells and CD5+ B1 cells subsets were found to be higher in leprosy patients. Observed significant increases in CD19+CD5- and CD19+CD5+ B1 cell subsets in patients of Lepromatous leprosy suggests that B1 lymphocytes with known predisposition to autoimmunity may have a role in disorganized protective immune response in Lepromatous leprosy. About 33% of the B cells in the peripheral blood of the Lepromatous leprosy patients expressed markers for autoreactive features while less than 12% of the circulating B cells in the healthy group exhibited such markers. The Lepromatous leprosy patients contained a substantial number of B cells out of which about 30% demonstrated autoreactive features.

Conclusion

It is suggested that circulating B cells in Lepromatous leprosy patients have a higher propensity to autoreactive properties than B cells of healthy populations.

Conflict of Interest: None declared

References

[1] World Health Organization. Global Strategy for Further Reducing the Leprosy Burden and Sustaining Leprosy Control Activities (Plan period: 2006-2010). Bulletin of the World Health Organization, 2005;1-19.

[2] Ridley D, Jopling W. Classication of leprosy according to immunity. A five-group system. Int J Lepr Other Mycobact Dis 1966; 34:255-73.

[3] Modlin RL. Th1-Th2 paradigm: insights from leprosy. J Invest Dermatol 1994; 102: 828-32.

[4] Sieling PA, Modlin RL. Regulation of cytokine patterns in leprosy. Ann N Y Acad Sci 1994; 730: 42-52.

[5] Choudhuri K. The immunology of leprosy: unraveling an enigma. Int J Lepr Other Mycobact Dis 1995; 63: 430-47.

[6] Misra N, Murtaza A, Walker B et al. Cytokine profile of circulating T cells of leprosy patients reflects both indiscriminate and polarized T-helper subsets: T-helper phenotype is stable and uninfluuenced by related antigens of Mycobacterium leprae. Immunology 1995; 86: 97-103.

[7] Verhagen CE, van der Pouw Kraan TC, Buffing AA, Chand MA, Faber WR, Aarden LA, Das PK.

Type 1- and type 2-like lesional skin-derived Mycobacterium leprae-responsive T cell clones are characterized by coexpression of IFN-gamma/TNF-alpha and IL-4/IL-5/IL-13, respectively. J Immunol 1998; 160: 2380-7.

[8] Panunto-Castelo A, Almeida IC, Rosa JC, Greene LJ, Roque-Barreira M. The Rubino test for leprosy is a beta2-glycoprotein 1-dependent antiphospholipid reaction. Immunology 2000; 101: 147-53.

[9] Chavez-Legazpi M, Gomez-Vazquez A, Garcıa-De La Torre I. Study of rheumatic manifestations and serologic abnormalities in patients with lepromatous leprosy J Rheumatol 1985;12:737–41.

[10] Kirsztajn GM, Nishida SK, Silva MS, Lombardi C, Ajzen H, Pereira AB. Specific and nonspecific aspects of humoral immune response in leprosy. Braz J Med Biol Res 1994; 27: 43-54.

[11] Martinuzzo ME, de Larranaga GF, Forastiero RR, Pelegri Y, Farina MH, Alonso BS, Kordich LC, Carreras LO. Markers of platelet, endothelial cell and blood coagulation activation in leprosy patients with antiphospholipid antibodies. Clin Exp Rheumatol 2002; 20: 477-83.

[12] Medina F, Camargo A, Moreno J, Zonana-Nacach A, Aceves-Avilla J, Fraga A. Anti-Neutrophil Cytoplasmic Autoantibodies in Leprosy. British Journal of Rheumatology 1998; 37: 270–273.

[13] Smith HR, Olson RR. CD5+ B lymphocytes in systemic lupus erythematosus and rheumatoid arthritis. J Rheumatol 1990; 17: 833-5.

[14] Zeher M, Suranyi P, Nagy G et al. B cells expressing CD5 in minor labial salivary glands of patients with primary Sjogren's syndrome. Arthritis Rheum 1990; 33: 453.

[15] Dono M, Cerruti G, Zupo S. The CD5+ B-cell. Int J Biochem Cell Bio. 2004; 36: 2105-11.

[16] Abbas A, Lichtman AH, Pober JS Cellular and Molecular Immununology 4th Ed 2000 Saunders company New York.