The Turkish Journal of Pediatrics 32:79-83, 1990

NEUTROPHIL AND LYMPHOCYTE LOCOMOTION IN PATIENTS WITH SELECTIVE IgA DEFICIENCY*

*Yavuz Coşkun MD**, Özden Sanal MD***, Fügen Ersoy MD****

Summary: Coşkun Y, Sanal Ö, Ersoy F. (Immunology Unit, Hacettepe University Institute of Child Health, Ankara, Turkey). Neutrophil and lymphocyte locomotion in patients with selective IgA deficiency. Turk J Pediatr 32: 79-83, 1990.

Neutrophil chemotaxis was studied in 14 patients, twelve with selective and two with partial IgA deficiency. Twelve of the 14 patients were also evaluated for lymphocyte locomotion. Zymosan activated serum was used to stimulate cell migration, and Boyden chambers were used for both neutrophil and lymphocyte chemotaxis assays. Evaluation of the results of neutrophil and lymphocyte locomotion showed that chemotaxis to ZAS, random migration and chemotactic index values were not significantly different when comparing the patients with the controls. *Key words: selective IgA deficiency, lymphocyte locomotion, neutrophil locomotion.*

Neutrophil chemotaxis has been investigated in various diseases including immunodeficiencies and has been found to be impaired in some of these diseases[1-2]. Defective neutrophil locomotion has been described particularly in the Hyper–IgE, Chédiak–Higashi and lazy leukocyte syndromes[3-6]. Few studies are available regarding chemotaxis in other immunodeficiencies.

Although various aspects of neutrophil locomotion are known, studies on lymphocyte locomotion have only been carried out in recent years[7-11]. Reports have shown that defective lymphocyte locomotion may be present in some cases with primary immunodeficiencies[7,12-13]. In this study, we investigated neutrophil and lymphocyte chemotaxis in patients with selective IgA deficiency. As far as we know, studies on lymphocyte locomotion in selective IgA deficiency have not been reported in the literature.

Material and Methods

Neutrophil chemotaxis was studied in 14 patients, twelve with selective and two with partial IgA deficiency. Twelve of the 14 patients were also evaluated for

* From the Immunology Unit, Hacettepe University Institute of Child Health, Ankara.

** Associate Professor of Pediatrics, Gaziantep University Faculty of Medicine, Gaziantep.

*** Professor of Pediatrics and Pediatric Immunologist, Hacettepe University Faculty of Medicine.

**** Professor of Pediatrics and Pediatric Immunologist, Hacettepe University Institute of Child Health.

lymphocyte locomotion. One of the patients with selective IgA deficiency had no symptoms, three patients suffered from hematologic disorders, and six patients, four with selective and two with partial IgA deficiency were diagnosed as having allergic diseases. The other four patients had chronic, recurrent infections. At the time of the study, the patients had no evidence of infection and neither had they been recipients of any medication. In addition, neutrophil chemotaxis was studied in 13 healthy controls and lymphocyte chemotaxis in 11 healthy controls whose ages ranged between 15-23 years.

Neutrophil locomotion was evaluated using the Boyden[14] filter method (three μ m pore size millipore filtres) with Zymosan activated serum (ZAS). Cell migration was measured using the leading front method[15].

Lymphocyte locomotion was evaluated by the method described by Gupta et al[16]. Briefly, after the isolation of mononuclear cells, monocytes were eliminated by carbonyl iron treatment. The number of contaminated monocytes, which was determined morphologically with peroxidase staining[17], was less than four percent. Chemotaxis was studied by using ZAS as a chemotactic factor and five μ m pore size millipore filters, and cell migration was measured by the leading front method[15].

Cell locomotion to ZAS stimulation / random migration (RM) ratios were expressed as a chemotactic index (CI) in both assays.

The Mann–Whitney *U* test was used for statistical analyses.

Results

Neutrophil chemotaxis to ZAS, random migration, and chemotactic index values in the patients were as follows: 66.7 ± 20.9 μm (42.7–111.0μm), 21.9 ± 4.7 μm (15.7–28 μm) and 3.0 ± 0.7 μm (2.2–4.5 μm), respectively. When compared with the control values, no significant difference was found (Fig. 1). Neutrophil chemotaxis, RM and CI values in controls were 60.9 ± 21.0 μm (117.1 ± 40.0 μm), 20.1 ± 4.6 μm (13.2 random 27.4 μm) and 3.0 ± 0.7 μm (2.3–4.8 μm), respectively. The mean values of lymphocyte chemotaxis to ZAS, random migration and chemotactic index in the patients were as follows: 43.9 ± 10.1 μm (29.4–60.0 μm), 16.1 ± 5.6 μm (9.7–28.0 μm) and 2.9 ± 0.7 μm (1.5–4.1 μm), respectively. Lymphocyte chemotaxis, RM and CI mean values of controls were as follows: 40.3 ± 10.2 μm (27.6–59.2 μm), 14.5 ± 3.0 μm (10.0–17.7 μm) and 2.8 ± 0.76 μm (1 6–3.4 μm), respectively. The chemotactic index was low (just below two standard deviations of the mean value) in only one patient, who had lower chemotaxis and higher random migration. In other patients, the values were not significantly different from the controls (Fig. 2).

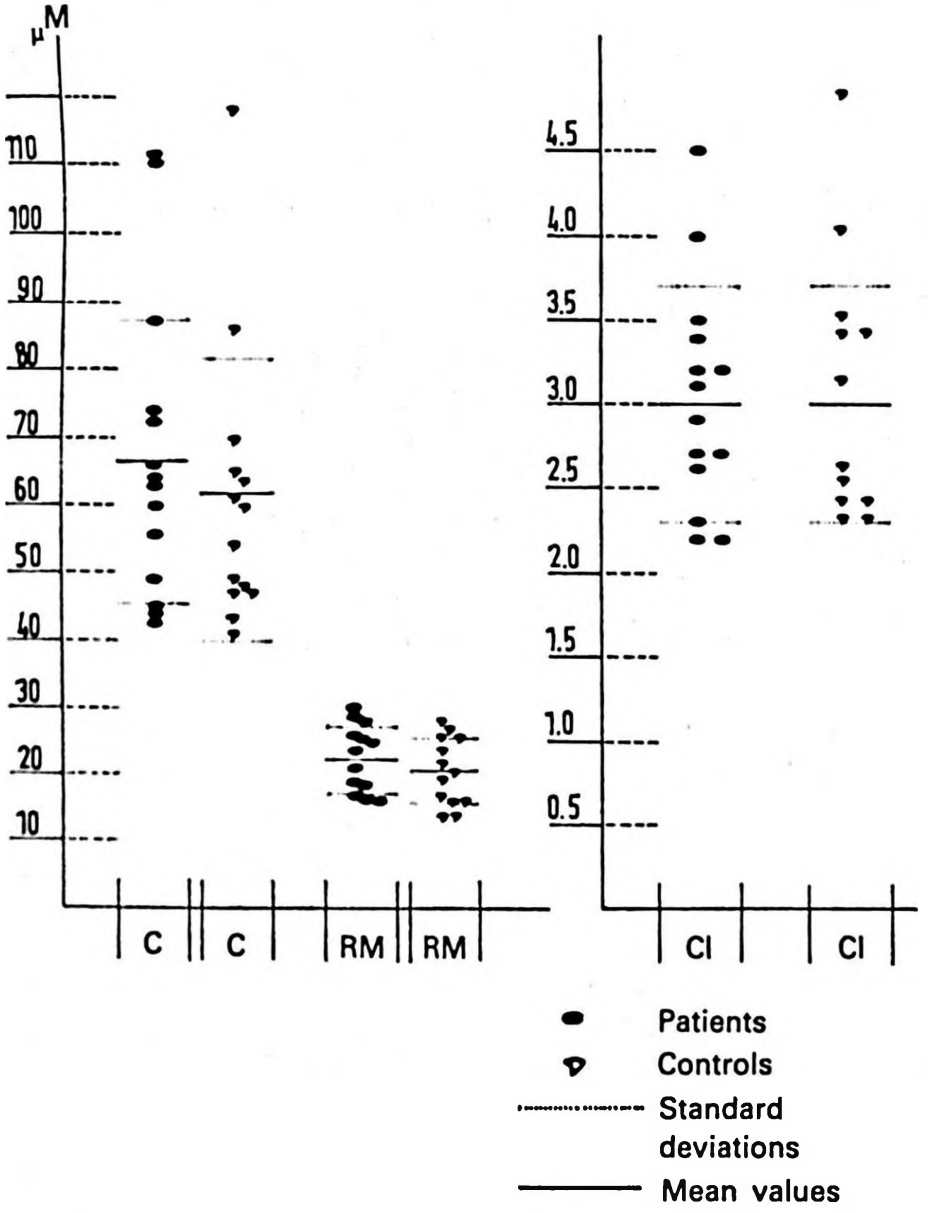

Fig. 1: Neutrophil chemotaxis (C), random migration (RM), and chemotactic index (CI) values in patients and controls.

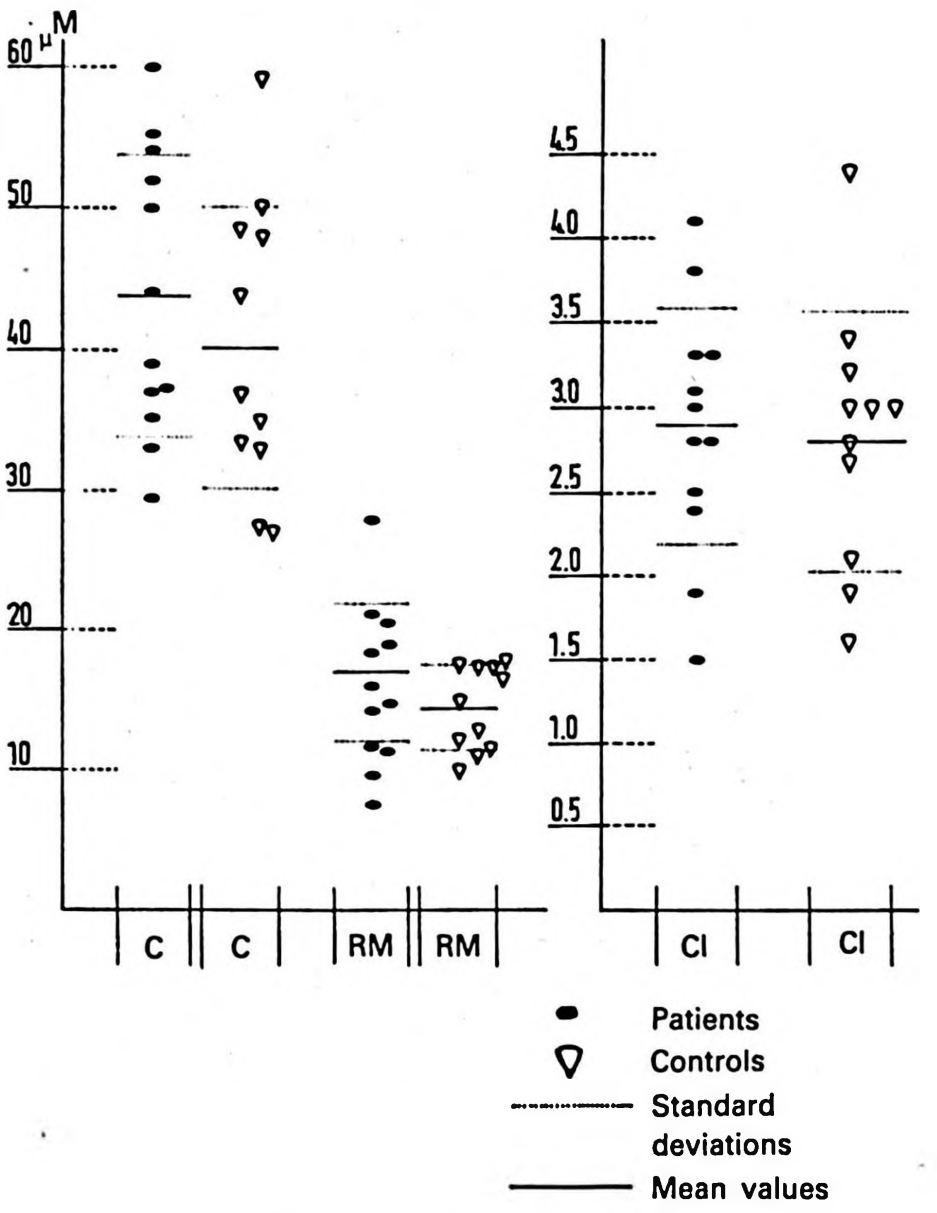

Fig. 2: Lymphocyte chemotaxis (C), random migration (RM), and chemotactic index (C) values in patients and controls.

Discussion

Chemotaxis, which is defined as the vectoral movement of cells governed by certain chemical substances, has an important role in the defense of microbial invasion. In addition to defects in other immune functions, the presence of a defective chemotactic response increases susceptibility to infection. It is known that in patients with the hyper–IgE, Chédiak–Higashi and lazy leukocyte syndromes, neutrophil locomotion is impaired[3-6]. It also has been demonstrated that there may be impaired neutrophil chemotaxis in patients with X–linked hypogammaglobulinemia, severe combined immunodeficiency, common–variable immunodeficiency, selective IgA deficiency and AIDS[18-22]. D'Amelio et al[18] found that nine out of ten patients with IgA deficiency had impaired leukocyte chemotaxis. But in our study no significant difference was observed in the chemotactic response, random migration or the chemotactic index when our patients were compared with the controls. It has been demonstrated that the chemotactic response reaches adult values after three years of age[23]. Therefore, the age difference between the patient and control groups had no effect on our results. D'Amelio et al[18] used the agarose method and ZAS as the chemotactic factor to evaluate chemotaxis. We also used ZAS to stimulate cell migration, but chemotaxis was evaluated using Boyden's[14] method. Even though we both used different techniques, it is unlikely that this caused a difference in our results. Impaired neutrophil motility may be caused either by a cellular defect or the presence of chemotactic inhibitors in serum. In this study, we could not find any cellular defect in our patients. However, additional studies are needed for the evaluation of chemotactic defects due to serum factors.

The results of lymphocyte chemotaxis in our patients also showed that there was no abnormality of lymphocyte locomotion in selective IgA deficiency. Van Epps et al[12] found impaired lymphocyte locomotion in some patients with primary immunodeficiencies by using C5a and casein as the chemotactic factors. In their study, lymphocyte chemotaxis was found to be defective in patients with common variable immunodeficiency, the hyper–IgE syndrome, and immunodeficiency with normal immunoglobulin concentrations, whereas it was found to be normal in patients with X–linked agammaglobulinemia and the hyper–IgM syndrome. Our findings do not exclude the fact that there might be, a part from this, a defect in T or B cell locomotion. Detailed studies regarding T and B cell locomotion are needed to clarify this subject.

REFERENCES

1. Clark RA. Disorders of granulocyte chemotaxis. In Gallin JI, Quie PG (eds). *Leukocyte Chemotaxis: Methods, Physiology, and Clinical Implications.* New York: Raven, 1978, p 329.

2. White CJ, Gallin JI. Phagocyte defects. *Clin Immunol Immunopathol.* 40:50, 1986.

3. Blum R, Geller G, Fish LA. Recurrent severe staphylococcal infections, eczematoid rash, extreme elevations of IgE, eosinophilia, and divergent chemotactic responses in two generations. *J Pediatr* 90:607, 1977.
4. Hill HR, Quie PG. Raised serum IgE levels and defective neutrophil chemotaxis in three children with eczema and recurrent bacterial infections. *Lancet* 1:183, 1974.
5. Boxer LA, Watanabe AM, Rister M, et al. Correction of leukocyte function in Chédiak-Higashi syndrome by ascorbate. *N Engl J Med* 295:1041, 1976.
6. Miller ME, Oski FA, Harris MB. Lazy-leukocyte syndrome. A new disorder of neutrophil function. *Lancet* 1:665, 1971.
7. Gupta S, Kirkpatrick CH, Good RA. Subpopulations of human T lymphocytes. XI. T cells with receptors for IgM or IgG and locomotion of T and non-T cells in peripheral blood from patients with chronic mucocutaneous candidiasis. *Clin Immunol Immunopathol* 14:86, 1979.
8. Wilkinson PC, Haston WS, Shields JM. Some determinants of the locomotory behaviour of phagocytes and lymphocytes in vitro. *Clin Exp Immunol* 50:461, 1982.
9. El-Naggar A, Van Epps DE, Williams RC Jr. Effect of culturing on the human lymphocyte locomotion response to casein, C_{5a}, and fMet-Leu-Phe. *Cell Immunol* 60:43, 1981.
10. Shimokawa Y, Harita S, Higuchi Y, Hayashi H. Lymphocyte chemotaxis in inflammation. III. Demonstration of lymphocyte chemotactic activity in extract from PPD-induced delayed hypersensitivity skin reaction site in the guinea-pig. *Br J Exp Pathol* 63:355, 1982.
11. Harita S, Shimokawa Y, Mibu Y, et al. Lymphocyte chemotaxis in inflammation. IX. Further characterization of lymphocyte chemotactic lymphokines produced by purified protein derivative-stimulation in vitro and in vivo. *Immunology* 51:295, 1984.
12. Van Epps DE, El-Naggar A, Ochs HD. Abnormalities of lymphocyte locomotion in immunodeficiency disease. *Clin Exp Immunol* 53:678, 1983.
13. Yeğin O, Sanal Ö, Yeralan D, et al. Defective lymphocyte locomotion in Chédiak-Higashi syndrome. *Am J Dis Child* 137:771, 1983.
14. Boyden S. The chemotactic effect of mixtures of antibody and antigen on polymorphonuclear leukocytes. *J Exp Med* 115:453, 1962.
15. Zigmond SH, Hirsch JG. Leukocyte locomotion and chemotaxis. New methods for evaluation, and demonstration of a cell-derived chemotactic factor. *J Exp Med* 137:387, 1973.
16. Gupta S, Safai B, Edelson R, et al. Locomotion of T cells from patients with cutaneous T-cell lymphoma (Sézary syndrome and mycosis fungoides). *Cell Immunol* 50:195, 1980.
17. Kaplow LS. Simplified myeloperoxidase stain using benzidine dehydrochloride. *Blood* 26:215, 1965.
18. D'Amelio R, Rossi P, Le Moli S, Aiuti F. Defective neutrophil chemotaxis in hypogammaglobulinemia and selective IgA deficiency. *Clin Immunol Immunopathol* 16:287, 1980.
19. Steerman RL, Synderman R, Leikin SL, Collen HR. Intrinsic defect of the polymorphonuclear leucocyte resulting in impaired chemotaxis and phagocytosis. *Clin Exp Immunol* 9:839, 1971.
20. Pahwa SG, Smithwick EM, Grimes ER, et al. Chemotactic defects in severe combined immunodeficiency. *J Pediatr* 92:43, 1978.
21. Lazzarin A, Uberti Foppa C, Galli M, et al. Impairment of polymorphonuclear leucocyte function in patients with acquired immunodeficiency syndrome and with lymphadenopathy syndrome. *Clin Exp Immunol* 65:105, 1986.
22. Valone FH, Payan DG, Abrams DI, Goetzl EJ: Defective polymorphonuclear leukocyte chemotaxis in homosexual men with persistent lymph node syndrome. *J Infect Dis* 150:267, 1984.
23. Yeğin O. Chemotaxis in childhood. *Pediatr Res* 17:183, 1983.