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Polyclonal Increases of Serum Immunoglobulins and Increase of Immunoglobulin-Bearing Peripheral Blood Lymphocytes in Children with Kawasaki Disease

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Immunoglobulin-bearing peripheral blood lymphocytes were examined in 20 children with Kawasaki disease and in 13 healthy control children. Routine laboratory tests were also performed. IgG-bearing lymphocytes, IgA-bearing lymphocytes, and IgM-bearing lymphocytes increased in children with Kawasaki disease when compared with those of controls. Measurement of immunoglobulin-bearing cells in peripheral blood may be used as a clinical test in the diagnosis of Kawasaki disease.

(Key Words: Immunoglobulin-bearing Lymphocytes, Circulating Immunecomplex, Vasculitis Disease)

INTRODUCTION

Kawasaki disease is an acute febrile disease in early childhood with various characteristic features such as cervical lymphadenopathy, hyperemic bulbar conjunctiva, erythematous rash, hard and swollen palms and soles, and hyperemic lips. Although the disease is self-limiting in most cases, death due to myocardial infarction occurs in some children affected with this disease. Various aberrations in laboratory tests are observed in patients with Kawasaki disease: increased platelet count, leucocytosis, increased ESR, positive CRP, and increased serum α_2-globulin are present in the majority of patients during the acute phase of the disease. Autopsy findings revealed vasculitis of the coronary artery and, to a lesser extent, of other arteries and arterioles.

Previously, we reported that IgA-bearing peripheral blood lymphocytes were increased in patients with Henoch-Schoenlein purpura, which is one of the most common vasculitis syndromes in the pediatric age group. The purpose of this study was to investigate the aberrations of peripheral blood immunoglobulin-bearing lymphocytes in children with Kawasaki disease.

PATIENTS AND METHODS

Twenty children with Kawasaki disease who were admitted to the

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Tokai University Hospital between 1978 and 1980 were studied. Routine laboratory tests, electrocardiography, and coronary angiography were performed for all children with Kawasaki disease. Among these twenty patients, two had aneurysms in the coronary artery, one had a myocardial infarction, and one had a stricture of the coronary artery. Thirteen age-matched healthy children served as controls. Serum immune-complexes were quantitated by the $C1_q$ solid phase enzyme immunoassay (Special Reference Laboratory, Shinjuku, Shinjuku-ku, Tokyo). Quantitation of immunoglobulin-bearing peripheral blood lymphocytes was performed by the method described previously (1).

RESULTS

The normal range of IgG-bearing peripheral blood lymphocytes was 0-13%, that of IgA-bearing lymphocytes was 0-7%, that of IgM-bearing lymphocytes was 0-17%. IgG-bearing lymphocytes increased in six out of 20 children with Kawasaki disease. IgA-bearing lymphocytes increased in four patients. Serum IgG was elevated in four children with Kawasaki disease at the time of the study. Serum IgA was elevated in eight and serum IgM was elevated in eleven children with Kawasaki disease. Correlations among peripheral blood immunoglobulin bearing lymphocytes, serum immunoglobulin bearing lymphocytes, serum immunoglobulin levels and serum complement levels of children with Kawasaki disease were evaluated by the Mann-Whitney test. Positive correlations were observed between: IgG-bearing lymphocytes and IgA-bearing lymphocytes ($p<0.01$) (Fig. 1), IgA-bearing lymphocytes and IgM-bearing lymphocytes ($p<0.0025$) (Fig. 2), IgM-bearing lymphocytes and IgG-bearing lymphocytes ($p<0.0005$),

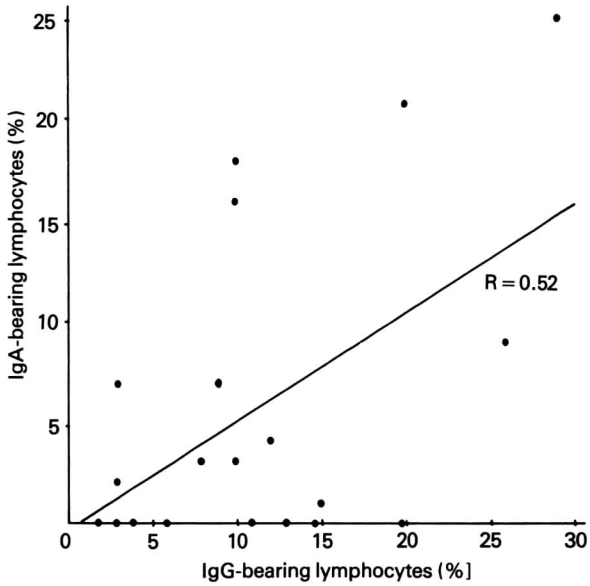

Fig. 1 Correlation between IgG-bearing lymphocytes and IgA-bearing lymphocytes from peripheral blood of children with Kawasaki disease. The R value denotes a correlation coefficient.

serum IgA levels and serum C_3 ($p<0.025$), serum IgA levels and serum C_4 ($p<0.025$), and serum C_3 and serum C_4 ($p<0.01$). A negative correlation was observed between IgM-bearing lymphocytes and serum IgM levels ($p<0.025$). The circulating immune-complex was positive in only one case of Kawasaki disease studied, and in none of the controls.

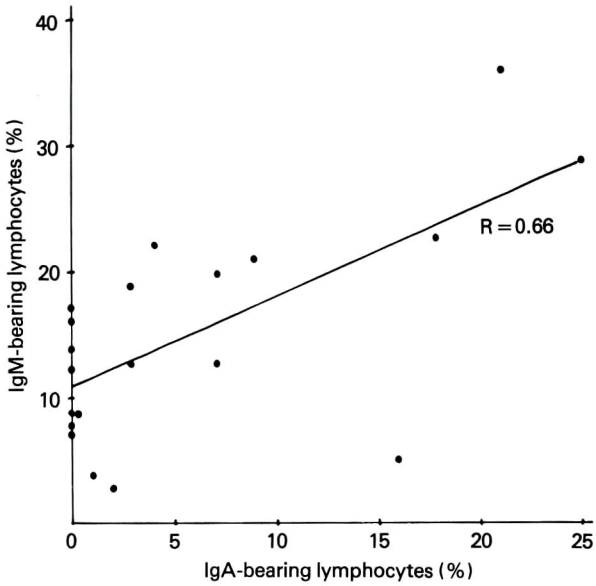

Fig. 2 Correlation between IgA-bearing lymphocytes and IgM-bearing lymphocytes from peripheral blood of children with Kawasaki disease.

DISCUSSION

Increases in immunoglobulin-bearing peripheral blood lymphocytes have been reported in various diseases. There are two groups of such diseases. The first is the group of diseases in which all three classes of immunoglobulin-bearing lymphocytes are increased, i.e., in autoimmune deseases (4). The results obtained in this study indicated that Kawasaki disease is included in this group of diseases. The second is the group of diseases in which a single isotype of immunoglobulin-bearing lymphocytes in increased. IgA-bearing lymphocytes are increased in IgA nephropathy (2) and Henoch-Schoenlein purpura (1). IgM-bearing lymphocytes are increased in membranoproliferative glomerulonephritis (3).

Kawasaki disease and Henoch-Schoenlein purpura are two major vasculitis diseases in the pediatric field in Japan. Polyclonal increases in immunoglobulin-bearing lymphocytes were observed in patients with Kawasaki disease, while isotypic increases in IgA-bearing lymphocytes were observed in Henoch-Schoenlein purpura. The vasculitis of coronary arteries is the major complication in Kawasaki disease, while glomerulonephritis is

the main complication of Henoch-Schoenlein purpura. It is not known, however, whether those vessels are predisposed to develop inflammatory changes, and whether specific immunoglobulin-bearing lymphocytes play some role in the development of vasculitis.

Our preliminary investigation revealed that the increase in peripheral blood lymphocytes was more marked than the increase in serum immunoglobulin levels. Although the mechanism for the polyclonal increases in peripheral blood B lymphocytes is obscure, measurement of immunoglobulin-bearing cells may be useful for the rapid diagnosis of Kawasaki disease or for the screening of Kawasaki disease in patients with subclinical symptoms.

REFERENCES

1) Kuno-Sakai H, Sakai H, Nomoto Y, Takakura T, Kimura M: Increase of IgA-bearing peripheral blood lymphocytes in children with Henoch-Schoenlein purpura. Pediatrics 64: 918—922, 1979.
2) Nomoto Y, Sakai H, Arimori W: Increase of IgA-bearing lymphocytes in peripheral blood from patients with IgA nephropathy. Am J Clin Pathol 71: 158—160, 1979.
3) Sakai H, Nomoto Y, Arimori S, Itoh H, Hasegawa O: Increase of IgM-bearing peripheral blood lymphocytes in patients with idiopathic membranoproliferative glomerulonephritis (MPGN) and their family members. Clin Nephrol 12: 210—215, 1979.
4) Teodorescu M: Characterization and role in autoimmune diseases of the polyclonal B-cell activator produced by T-cells —The helper factor. Immunol Rev 55: 155—178, 1981.