HLA Antigens and Toxoplasmic Retinochoroiditis

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OHNO, S., O'CONNOR, G.R. and KIMURA, S.J. *HLA Antigens and Toxoplasmic Retinochoroiditis*. Tohoku J. exp. Med., 1977, 123 (1), 91-94 — HLA (Human Leukocyte-A) antigens of 20 patients with toxoplasmic retinochoroiditis were determined by the standard microlymphocyte cytotoxicity test to see if these patients have different immunogenetic backgrounds from the normal controls. The results showed that there were no significant differences between the patients and the normal controls. ——— HLA antigens; uveitis; toxoplasmic retinochoroiditis

Since uveitis is multifactorial in origin and may be caused by a number of different immunologic reactions, of which etiology is unknown, in the previous papers we have undertaken an immunogenetical study of HLA antigen patterns in idiopathic uveitis (Ohno et al. 1976, 1977a and b). Toxoplasmosis is caused by invasion of a protozoan parasite, *Toxoplasma gondii*, into various human tissues. It is generally known that toxoplasmosis is an extremely common infectious disease, but in the majority of sero-positive individuals there are no manifest ocular symptoms. A genetically determined predisposition to toxoplasmic disease of the eye, if present at all, may account for the fact that some patients manifest ocular lesions, while others do not. If a susceptible locus for toxoplasmic retinochoroiditis is present within the human major histocompatibility complex on the autosomal chromosome 6, it may have a close association with HLA antigens. It was suggested by Piazza and associates (1973) that adaptive variation of the HLA system, possibly linked to control of immunity against plasmoid infection may exist between "malaric" and "non-malaric" populations.

The present paper deals with the results of our studies on the incidence of HLA antigens in patients with toxoplasmic retinochoroiditis.

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MATERIALS AND METHODS

Twenty patients with toxoplasmic retinochoroiditis and 72 normal healthy controls were typed for HLA antigens. The patients, 8 men and 12 women, ranged in age from 11 to 66 years with a mean of 36.4. The diagnosis of this disease was based on: 1) characteristic ophthalmoscopic findings such as focal exudative necrotizing retinochoroiditis, 2) a positive Sabin-Feldman dye-test for toxoplasmosis, 3) exclusion of other causes of necrotizing retinochoroiditis (O'Connor 1975). HLA typing was performed by the microlymphocyte cytotoxicity test for 10 HLA-A and 14 HLA-B specificities. The frequency of HLA antigens in the patients with toxoplasmic retinochoroiditis was compared with that of normal control subjects, using the chi-square test with the Yates' correction.

RESULTS

The distribution of HLA antigens among 20 Caucasian patients with toxoplasmic retinochoroiditis and among 72 normal control subjects is presented in Table 1. All kinds of HLA antigens, including HLA-A1, A3, and A11, showed no significant difference between the patients with toxoplasmic retinochoroiditis and the controls.

TABLE 1. *Frequency of HLA antigens in toxoplasmic retinochoroiditis*

HLA antigens	Controls (N=72)	Toxoplasmic retinochoroiditis (N=20)
	(%)	(%)
HLA-A1	20(28)	9(45)
HLA-A2	34(47)	8(40)
HLA-A3	16(22)	1(5)
HLA-A9	18(25)	6(30)
HLA-A10	9(13)	4(20)
HLA-A11	10(14)	0(0)
HLA-A28	4(6)	2(10)
HLA-A29	5(7)	2(10)
HLA-AW30	5(7)	1(5)
HLA-AW32	7(10)	2(10)
HLA-B5	6(8)	1(5)
HLA-B7	18(25)	4(20)
HLA-B8	17(24)	6(30)
HLA-B12	19(26)	6(30)
HLA-B13	3(4)	1(5)
HLA-B14	7(10)	2(10)
HLA-B18	4(6)	3(15)
HLA-B27	5(7)	2(10)
HLA-BW15	7(10)	2(10)
HLA-BW16	3(4)	1(5)
HLA-BW17	6(8)	1(5)
HLA-BW22	3(4)	2(10)
HLA-BW35	8(11)	3(15)
HLA-BW40	10(14)	1(5)

DISCUSSION

The present study showed that there is no association between HLA antigen pattern and toxoplasmic retinochoroiditis, although the size of samples is small.

Among many diseases in which an association with HLA antigens was studied, the infectious diseases are especially interesting. In *Yersinia arthritis* (Aho et al. 1974), for example, 88% of the patients with arthritis had HLA-B 27, while only 15% of the patients with *Yersinia* infection but without manifest arthritis had this antigen. Other infectious diseases, such as paralytic poliomyelitis (Morris and Pietsch 1973), leprosy (Thorsby et al. 1973), *H. influenzae* infections (Wisnant et al. 1971), severe streptococcal infections (Krain et al. 1973), asymptomatic Australia antigen disease (Nakayama et al. 1972), infectious mononucleosis (Morris and Forbes 1971), tuberculosis (Rosenthal et al. 1973), herpes labialis (Russel and Schlaut 1975) have been studied in relation to HLA antigens.

Toxoplasma gondii, an intracellular protozoan parasite, is considered to be a near relative of the malarial parasite, *Plasmodium sp.*, and in this connection the study of Piazza and associates (1973) on HLA and malaria seems very interesting. They studied the variation of HLA and 24 other genetic markers in four Sardinian villages, two in the lowlands where malaria was endemic, and two in the highlands which were free of malaria. They found that the frequencies of the alleles at the HLA-B locus differed between the highland and the lowland villages. The difference was significantly greater than that among the neutral markers. Although toxoplasma is not such a strongly selective agent as malaria, it may also be possible for patients with toxoplasmosis to have genetically-determined defense mechanisms which are linked to HLA system. Severe congenital toxoplasmosis sometimes leads to abortion, and some natural selection might have occurred in human evolution as a control mechanism.

In the present study, the antibody titer of the patients with toxoplasmic retinochoroiditis ranged from 1:16 to 1:1024, and the dye test titer of 1:64 was observed most frequently among the patients. There seemed to be no particular correlation between the height of the dye test titers and the HLA antigen pattern.

We did not classify the patients into congenital toxoplasmic retinochoroiditis and acquired toxoplasmosis because of the small size of samples in the present study. It is desirable to study a larger group of patients by the same parameters. It would also be interesting to study the HLA antigens in patients with systemic toxoplasmosis but no retinochoroiditis, in persons who have positive dye tests but no systemic or ocular diseases, and in persons who have no toxoplasmosis (negative dye tests).

Antibody forming responses to various foreign antigens may also be controlled by immune response genes. In influenza A vaccination, for example, it was shown that subjects with HLA-BW 16 had significantly poorer antibody responses than subjects without HLA-BW 16 (Spencer et al. 1976).

Although our preliminary study failed to show any association between toxoplasmic retinochoroiditis and HLA antigens, further extensive studies are needed in order to draw a conclusion in this area.

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