Histocompatibility Antigens in Black Patients with Essential Hypertension

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SUMMARY Essential hypertension is a common disorder with potentially life-threatening sequelae. Hypertension among black persons may have characteristics different from hypertension among white persons. It has been estimated that up to 60% of population variance in blood pressure may be attributable to genetic differences. We studied the distribution of HLA antigens in 100 black hypertensives and 100 normotensive controls. Hypertension was not significantly associated with any of the 25 HLA antigens identified. We conclude that HLA-A and HLA-B locus antigens are not associated with essential hypertension in the black patient.

BLACK PERSONS have a higher prevalence of hypertension and greater morbidity and mortality from hypertensive disease than do white persons. Several lines of evidence support the concept that essential hypertension may have different characteristics in the two racial groups. For example, accelerated hypertension and hypertension associated with suppressed plasma renin activity occur more commonly among blacks than among whites. White hypertensives tend to be more responsive to antihypertensive therapy than do black hypertensives. Evidence indicating variability in the pathophysiology of hypertension in the two races has also been discussed. These differences may be due to environmental or hereditary factors. Epidemiologic surveys have shown that blood pressure may be adversely affected by environmental influences, especially increase in the dietary intake of salt. The association of heredity and essential hypertension seems established, but whether the disparate manifestations of high blood pressure between black and white persons are also due to genetic factors has not been studied. Inherited susceptibility to certain diseases is associated with specific HLA antigens. To examine the possibility that a gene belonging to the major histocompatibility complex may be a predetermining factor in hypertension among black persons, we studied HLA phenotypes in 100 hypertensive black patients.

Materials and Methods

One hundred black patients who regularly attended the Hypertension Clinic of the Martin Luther King, Jr. General Hospital were studied. All were considered to have essential hypertension, i.e., hypertension could not be attributed to a primary cause on the basis of history, physical examination and routine laboratory tests. Intravenous pyelography and plasma cortisol, renin, aldosterone and urinary catecholamines and metanephrines were done when secondary hypertension could not be excluded clinically. Renal arteriography was done whenever the patients had abnormal rapid-sequence i.v. pyelograms. Fifty males (mean age 47 years) and 50 females (mean age 44 years) were studied. All were receiving antihypertensive drugs, including methyldopa, propranolol, clonidine, hydrochlorothiazide and furosemide, either alone or in combination.

One hundred healthy black persons who were either blood donors or employees at the hospital were selected as controls. All were normotensive on three consecutive blood pressure estimations approximately 1 week apart, and none had a positive family history of hypertension. There were 50 males (mean age 44 years) and 50 females (mean age 41 years).

HLA antigens of peripheral blood lymphocytes were studied according to the microlymphocytotoxicity test. Allogeneic anti-HLA antisera were obtained from the Serum Bank, National Institutes of Health, Bethesda. Twenty-five HLA antigens (10 determined by genes belonging to HLA-A locus and 15 to HLA-B locus) were studied. At least two antisera defined each HLA specificity, and all had been closely matched to serum sets used in the various histocompatibility workshops. Examination of lymphocytes of two patients (receiving antihypertensive medications) and several normotensive members of their families did not indicate any interference by antihypertensive drugs on HLA identification.

Results

The HLA phenotype frequencies in our hypertensive patients and normotensive control subjects are shown in table 1. Frequencies of two antigens of the HLA-A locus (HLA-A3 and HLA-A11) and three antigens of HLA-B locus (HLA-B7, HLA-B12, and HLA-B17) were higher by 6–18% in hypertensive patients compared with the controls. By chi-square analysis, this difference was statistically significant only for antigens HLA-A11 (p < 0.02) and HLA-B12 (p < 0.005). When testing for statistical significance in studies involving HLA and disease association, it is recommended that the p value be multiplied by the number of antigens studied at each locus to avoid overestimation of an association. When the p values for HLA-A11 and HLA-B12 were multiplied by 10
and 15, the number of antigens identified at locus A and locus B, respectively, the increased incidence of these antigens in hypertensive patients was no longer statistically significant (table 2). In table 2, our results are compared with those of other investigators. These reports of association of HLA and essential hypertension dealt only with Caucasian subjects. In two studies, HLA and hypertension were significantly associated when the value was uncorrected for the number of antigens studied. In both instances, the association involved different HLA specificities, and in each case the p value was no longer significant when it was corrected for the number of antigens studied.

**Discussion**

The HLA system functions as a marker of disease susceptibility, through both associations and linkages. The mechanisms by which diseases may be associated with HLA is uncertain and has recently been reviewed.

Our studies of black subjects and the studies of Gelthorpe et al. and of Kristensen et al. of Caucasian subjects show that although certain HLA antigens have a higher frequency among hypertensives than among normotensive controls, such differences are not statistically significant when corrected for the number of HLA specificities studied. Therefore, in random subjects, even though studies in hypertension strongly suggest genetic components in the pathogenesis of the disease,
References

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