GROUP DIFFERENTIATION OF THE TISSUES OF THE HUMAN HYPOPHYSIS

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It may now be regarded as proven that the survival and death of homografts is due primarily to immunological reactions arising in the recipient as a result of individual isoantigenic differences between the donor and recipient. In order to elucidate the immunological mechanisms of the phenomena of incompatibility during homoplastic transplantation, it is therefore important to have a clear idea of the antigenic structure of the transplanted tissue.

Various investigators [1-6] have shown that many tissues and organs (liver, kidney, spleen, skin, lung, brain, cornea, etc.) of the human body are, like the erythrocytes, differentiated by group antigens. So far as the isoantigenic differentiation of human hypophyseal tissues is concerned, we have found no information on this subject in the literature. Nevertheless this question has become of definite interest on account of the progress made in the homotransplantation of the hypophysis, the organ regulating the more important functions of the body and, in particular, growth. We have not yet discovered any reliable methods of treatment of diseases such as pituitary dwarfism, in which the process of human growth undergoes serious disturbances. Successful homotransplantation of the hypophysis could prove to be an effective means of treatment of this condition.

It is evident that in seeking methods of overcoming the phenomena of incompatibility during homotransplantation of the hypophysis, especially when selecting the most compatible hypohyseal tissue, some knowledge of the group antigenic properties of this tissue is essential. In the present investigation our object was, therefore, to detect the presence of A, B, M, and N group antigens in the tissues of the human hypophysis.

EXPERIMENTAL METHOD

To determine the presence of A and B isoagglutinogens we used the method of specific absorption of standard sera containing the appropriate antibodies. Specimens of minced hypophyseal tissues obtained from cadavers were thoroughly washed free from traces of blood with physiological saline. The tissue was then ground in a porcelain mortar and physiological saline added in proportion of 10 parts of physiological saline to one part by weight of tissue. The supernatant fluid and residue obtained after centrifugation were used to exhaust standard sera.

In order to detect antigens in the extracts, two drops of standard serum in different dilutions was placed into a series of agglutination tubes, and the same volume of extract was added to each tube. To 100 mg of residue 5 drops of standard serum with a titer of 1:16 were added.

The mixtures of serum with residue and extract were kept for 1 h at room temperature. The exhaustion of the antibodies by the residue and extracts was then tested by titration with corresponding standard erythrocytes (one drop of a 2% suspension of erythrocytes in physiological saline).

As a control of the specificity of absorption of the antibodies, we used tissue from the hypophysis of a human subject of blood group O.

The M and N antigens were determined in the residues by a method described previously [2, 4]. Standard anti-M and anti-N sera were used in a titer of 1:5. In view of the small amount of tissue in each specimen, in the experiments to exhaust specific antibodies we used 4-6 specimens of tissue at a time, obtained from subjects of the same group, as shown by preliminary tests with erythrocytes.

EXPERIMENTAL RESULTS

For determination of the A and B antigens 32 hypophyses were examined, of which 7 belonged to group A, 9 to group B, 5 to group AB, and 11 to group O. A typical experiment is illustrated in Table 1.

It is clear from Table 1 that the group A hypophyseal tissue completely fixed the α-antibodies but practically no β-antibodies. Conversely, group B tissue completely absorbed β-antibodies but did not absorb α-antibodies. Tissue belonging to group AB extracted both α- and β-antibodies from the serum. Tissue of group O had no power to fix either antibodies.

TABLE 1. Determination of A and B Antigens in Hypophysis Tissue

Group of test tissue	Standard serum	Standard erythrocytes	Results of the hemagglutination reaction after absorption of serum by hypophysis tissue in dilution of: whole	1 : 2	1 : 4	1 : 8	1 : 16
A	α	A	—	—	—	—	—
	β	B	+++	+++	+++	+++	++
B	α	A	+++	+++	+++	+++	+(+)
	β	B	+	—	—	—	—
AB	α	A	+	—	—	—	—
	β	B	±	—	—	—	—
O	α	A	+++	+++	+++	++	+
	β	B	+++	+++	+++	++	+
Serum control (before absorption)	α	A	+++	+++	+++	+++	+++
	β	B	+++	+++	+++	+++	+++

TABLE 2. Determination of M and N Antigens in Hypophyseal Tissue

Blocking serum	Standard serum, dilution		Standard erythrocytes	Results of hemagglutination reaction after absorption of serum by hypophysis tissue and erythrocytes: type M, erythrocytes	type M, hypophysis	type N, erythrocytes	type N, hypophysis	type MN, erythrocytes	type MN, hypophysis	Serum control (before absorption)
Anti-M	Anti-N	Whole	N	+++	+++	+	++	—	+++	+++
		1:2		+++	+++	—	±	—	++	+++
		1:3		+++	+++	—	—	—	+	+++
		1:4		++	++	—	—	—	—	+++
		1:5		++	+	—	—	—	—	+++
Anti-N	Anti-M	Whole	M	—	—	+++	+++	—	+++	+++
		1:2		—	—	+++	+++	—	++	+++
		1:3		—	—	+++	+++	—	+	+++
		1:4		—	—	+++	++	—	—	+++
		1:5		—	—	++	++	—	—	+++

It should be noted that the specific exhaustion of antibodies (α, β) from standard sera took place during tests of both the residue and the extracts from tissue of the anterior or posterior lobes of the human hypophysis.

These investigations thus showed that human hypophyseal tissue contains the A and B group antigen identical with the antigens of the erythrocytes.

The M and N antigens in the hypophyseal tissue were studied in 10 series of experiments, and 170 hypophyses were examined. The results of typical experiments are illustrated in Table 2.

It may be seen from Table 2 that type M hypophysis tissue had the ability to extract (like erythrocytes) anti-M antibodies from the serum, but not to extract anti-N antibodies. A similar pattern was observed during absorption of corresponding antibodies by type N hypophysis tissue. Type MN tissue combined with both anti-M and anti-N antibodies, although complete exhaustion of the antibodies was not observed. Consequently, like erythrocytes, the tissues of the hypophysis contained M and N antigens.

These results may be important for the analysis of the mechanism of the immunological incompatibility during homotransplantation of hypophyseal tissue.

SUMMARY

An absorption method was used to investigate the A, B, M and N antigens in the tissues of human hypophysis. The data obtained demonstrate the group differentiation of these tissues with respect to the above-mentioned antigens.

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