TRANSFER OF A FACTOR STIMULATING AMYLOID PRODUCTION FROM MAN TO MICE

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Blood serum and spleen homogenate from patients with amyloidosis stimulate amyloid production in mice. This effect is probably due to the action of a nonspecific factor.

In recent years a special factor accelerating the development of amyloidosis, if transferred into isologous and homologous recipients, has been found in the spleen [1-5, 7, 8] and, less commonly, in other organs [8] and in the blood serum [1, 3, 4] of intensively-immunized mice belonging to different lines. Stimulation of amyloid production in C3H mice by the action of a homogenate of human amyloid spleen has recently been reported [6].

The object of the present investigation was to study the amyloid-producing effect of sera of patients with amyloidosis.

EXPERIMENTAL METHOD

The blood serum and spleen obtained at autopsy from two patients with widespread secondary amyloidosis, from patients with senile amyloidosis of the pancreas and with rheumatic heart disease, and from a clinically-healthy young person dying from trauma, and also the serum from a patient with peptic ulcer and from a woman in labor, obtained while they were admitted to hospital, were investigated (Table 1).

Spleen homogenates were prepared in a glass homogenizer in the proportion of 1 g tissue to 3 ml physiological saline.

Male BALB mice, aged 8 and 10 weeks, were used as donors. Seven series of experiments were carried out on 15-30 mice. In every case the serum was tested, and in some cases (Nos. 1, 3, 4, 6) the spleen homogenate also. In each series, starting from the day after intraperitoneal injection of 1 ml serum or 1 ml homogenate, the mice were given subcutaneous injections of 0.5 ml of 5% casein solution in 0.25% NaOH solution 6 times a week, after which they were sacrificed in groups, usually 5 at a time, at various periods (after 6, 8, and 12 injections of casein).

The first signs of amyloidosis appeared in the control mice, i.e., without preliminary injection of serum or homogenate, not before the 16th injection of casein solution.

The experimental results were assessed on the basis of a histological study of frozen sections of the spleen (in which amyloid is deposited sooner than in other organs), stained with methyl violet, thioflavine-T, and Congo red; the sections were examined in a polarization microscope.

EXPERIMENTAL RESULTS

The principal results are given in Table 1. In the first 3 series, in which both spleen homogenate and serum from patients with amyloidosis were injected, after the 8th injection of casein perifollicular deposi-

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TABLE 1. Stimulation of Amyloid Production in Spleen of BALB Mice by Serum and Spleen Homogenate of Patients with Amyloidosis

Case No.	Primary diagnosis	Material transferred	Number of cases with amyloidosis after injections of casein		
			6 injections	8 injections	12 injections
1	Secondary amyloidosis (pulmonary tuberculosis; 45 years)	Spleen homogenate	0/5	2/5	5/5
		Serum	0/5	2/6	4/6
2	Secondary amyloidosis (lymphogranulomatosis; 38 years)	Serum	0/5	2/5	3/5
3	Senile amyloidosis in pancreas (diabetes mellitis; 71 years)	Spleen homogenate	—	1/5	2/5
		Serum	—	2/5	3/5
4	Control (death from trauma; 31 years)	Spleen homogenate	0/5	0/4	0/4
		Serum	0/4	0/4	0/4
5	Control (rheumatic fever, active phase; 42 years)	Spleen homogenate	—	0/4	0/4
		Serum	—	0/5	0/4
6	Control (gastric ulcer, 30 years)	Serum	—	0/5	0/5
7	Control (normal labor, 30 years)	Serum	—	0/5	0/5

Note. Numerator gives number of cases of discovery of amyloidosis; denominator, total number of cases.

tions and the percentage of animals affected increased in proportion to the number of casein injections, but this relationship was more easily seen in secondary amyloidosis. In the control series, injection of material from patients without amyloidosis (Nos. 5, 6) or from clinically healthy persons (Nos. 4, 7) was ineffective, and the mice did not develop amyloidosis before the 16th injection of casein, as in the case of mice receiving no preliminary treatment.

Hence, not only spleen homogenate, but also the serum of patients with amyloidosis appreciably shortens the time required for amyloid to be formed in mice (8 injections of casein instead of 16).

This phenomenon is perhaps due to the presence of a factor similar to the "amyloid-enhancing factor" [3] or the "amyloid-accelerating substance" [8] of mice, for the manifestation of whose activity it is not essential for the donor and recipient to belong to different species.

The number of experiments in the present series is, of course, far too small to justify any far-reaching conclusions. It is by no means certain that the hypothetical factor is pathognomonic of amyloidosis. Further investigations must be undertaken, using material obtained not only from patients with different types of amyloidosis and animals with experimental amyloidosis,* but also from other pathological conditions.

Such investigations would be not only of theoretical interest, but also of practical importance because identification of the factor in the blood serum could prove a useful diagnostic test for amyloidosis in clinical practice.

LITERATURE CITED

1. V. S. Rukosuev, Arkh. Pat., No. 10, 42 (1970).
2. M. Hultgren, R. Druet, and D. Janigan, Am. J. Path., 50, 943 (1967).
3. D. Janigan and R. Druet, Am. J. Path., 52, 381 (1968).
4. D. Janigan, Am. J. Path., 55, 379 (1969).
5. P. Ranlov, Acta Path. Microbiol. Scand., 70, 321 (1967).

*Still incomplete experiments by the writer have shown that spleen homogenates of rabbits and C3H mice, immunized for long periods, can stimulate the development of amyloidosis in the spleen of BALB mice.

6. T. Shirahama, O. Lawless, and A. Cohen, Proc. Soc. Exp. Biol. (New York), 130, 516 (1969).
7. O. Werdelin, Acta Path. Microbiol. Scand., 72, 23 (1968).
8. J. Willerson, J. Gordon, N. Talal, et al., Arth. and Rheum., 12, 322 (1969).