DNA AND ANTI-DNA ANTIBODIES IN MINK WITH ALEUTIAN DISEASE

V. S. Slugin, N. N. Prozorovskaya,
and D. V. Belokrinitskii

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Free DNA and various types of anti-DNA antibodies were determined in the blood serum and plasma of mink spontaneously developing Aleutian disease (AD) or infected experimentally with it. The control group consisted of healthy mink and other animals: arctic and ordinary foxes and sable. Characteristically the experimental group of animals had a higher frequency of discovery of anti-DNA antibodies of types 2 and 3 in high titers (1:80-1:2560). In addition, free polymer DNA was found more frequently in the experimental group of animals.

KEY WORDS: *Aleutian disease of mink; free DNA; anti-DNA antibodies.*

The reason for the importance of the study of Aleutian disease (AD) of mink is that many of its manifestations are similar to certain human diseases, notably systemic lupus erythematosus (SLE) [12, 15, 16]. Lesions of the kidneys in mink with AD and in SLE in man arise through deposition of a complex of DNA—anti-DNA antibodies—complement in the glomeruli [11, 13, 14].

For this reason, in the investigation described below, an attempt was made to discover DNA and antibodies against it in the serum of mink developing AD spontaneously or infected with it experimentally.

EXPERIMENTAL METHOD

Altogether 55 mink developing the disease spontaneously (150-210 days after presumed infection) and 50 experimentally infected mink (8-9 days after infection) were studied. The control group contained 20 healthy mink. As an additional control, animals of other species were investigated: sable, foxes, and arctic foxes (33 animals), which are not susceptible to AD, both healthy and with some disease other than AD.

The choice of experimental mink was based on epizootologic data, symptomatology, and postmortem changes. Experimental infection of the mink with AD was carried out by intraperitoneal injection of whole blood or a suspension of parenchymatous organs obtained from the mink affected with AD at sacrifice. The blood serum and plasma from the experimental and control animals were tested simultaneously.

The titer and type of anti-DNA antibodies were determined by the passive hemagglutination test (PHT) and the antibody neutralization test (ANT) [6]. Poverennyi's classification [4] was used to establish the type. Precipitating anti-DNA antibodies were determined by counter-immunoelectrophoresis [10]. Preparations of high-polymer thymus DNA (Worthington Biochemical Corporation) were used as antigen in the ANT and

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for immunoelectrophoresis: native, denatured by heating, partially spiralized and denatured by heating in the presence of formaldehyde, and single-stranded. Free polymer DNA was determined by an immunochemical micromethod [5] and by immunoelectroosmophoresis [10]. Serum containing precipitating anti-DNA antibodies was used as the antiserum. To prove the specificity of the reaction, samples of plasma containing free DNA were incubated with a preparation of deoxyribonuclease (Worthington Biochemical Corporation) for 1 h at 37°C in the presence of magnesium ions (0.004 mg deoxyribonuclease to 1 ml plasma).

EXPERIMENTAL RESULTS

Of 55 mink developing AD spontaneously, anti-DNA antibodies were found in the sera of 32 (58%); of 50 mink infected experimentally with AD, anti-DNA antibodies were found in the sera of 20 (40%).

In the control group, anti-DNA antibodies were found in the sera of six of 20 healthy mink (30%) and in 19 sera from 33 other animals (sable, fox, arctic fox) (58%).

Among the sera of mink developing AD spontaneously and containing anti-DNA antibodies, type 1 antibodies were found in 14 (44%) sera, type 2 in seven (22%), and type 3 in 11 (34%) sera. In mink infected experimentally with AD, type 1 anti-DNA antibodies were found in 11 (55%) sera, type 2 in eight (40%) sera, and type 3 in one (5%) serum. In the control groups of animals the sera contained predominantly type 1 anti-DNA antibodies and no type 3 antibodies whatsoever were found.

In the experimental group most of the sera contained anti-DNA antibodies in high titer (1:80-1:2560), but in the control group antibodies were found in the sera predominantly in low titers (1:10-1:40).

On comparison of the frequency of discovery of anti-DNA antibodies in the sera of the experimental group (mink developing AD spontaneously and mink infected experimentally with AD) and the control group (healthy mink and other animals) the difference between them was not statistically significant ($P > 0.05$).* However, if the comparison between these groups was made with reference to the frequency of discovery of type 1 antibodies and of type 2 and type 3 antibodies together, the difference was statistically significant ($P < 0.05$), i.e., antibodies of types 2 and 3 were found more often among animals of the experimental group. The same pattern also was observed with respect to the titer of anti-DNA antibodies: antibodies in higher titer (1:80-1:2560) were found more often in the experimental than in the control group.

Precipitating anti-DNA antibodies were found only in the sera of mink developing AD spontaneously (in 25 of 55 sera tested).

Correlation between the titer of anti-DNA antibodies, the type of antibodies, and the degree of activity of the disease has been established in SLE [2, 3, 7]. If activity in the sera of patients with SLE is high or average, as a rule antibodies of types 2 and 3 are present in high titers. Barnett et al. [9] found a higher titer of anti-DNA antibodies and of free DNA in mink infected experimentally with AD than in the same mink before infection.

On determination of free polymer DNA in the blood plasma of animals of the experimental and control groups, no free DNA was found in the healthy mink and it was found in small quantities in four animals (12%) of the group of "other animals" (sable, fox, arctic fox). Free DNA was present in the blood plasma of 12 (22%) mink developing AD spontaneously, including in seven (13%) mink in a concentration of 3-12 μg/ml and in five (9%) in a concentration of 50-100 μg/ml plasma. Of the experimentally infected animals, free DNA was found in 21 (43%), including in eight (16%) mink in low concentrations and in 13 (27%) in high concentrations. The difference

*Statistical analysis of the results was carried out by means of the chi-square criterion.

between the frequency of discovery of free DNA in the experimental and control groups is significant ($P < 0.01$). The difference between the frequency of discovery of free DNA in the groups of mink developing AD spontaneously and infected with it experimentally also is statistically significant; in the last group free DNA was found more frequently in the blood plasma of the mink.

The suggestion has been made in the literature [8] that circulating free DNA may induce pathogenetic antibodies, i.e., that it may act as an immunogen. The present writers observed previously [1] that free DNA is present in the blood plasma of most patients with SLE, and its concentration depends on the degree of kidney damage.

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