LOCALIZATION OF SPECIFIC ANTIGEN IN ORGANS OF ANIMALS INOCULATED WITH DIFFERENT BATCHES OF LIVE MEASLES VACCINE

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UDC 616.915-085.371-092.9

The location of the specific antigen in the walls of the cerebral blood vessels and in neurons and glial cells was studied by an immunofluorescence method in newborn albino rats and Syrian hamsters inoculated subcutaneously with four different batches of live measles vaccine. Pathomorphological examination of the brain revealed mainly vascular disorders. The results are evidence of the presence of residual neurotropism in attenuated measles virus (strain L-16).

KEY WORDS: *attenuated measles virus; immunofluorescence.*

By means of an immunofluorescence method the writers showed previously that the specific antigen of attenuated measles virus is located in the neurons and cerebral vessels of newborn albino rats and hamsters inoculated subcutaneously with a production batch of live measles vaccine (strain L-16) [5].

Considering differences in the reactogenicity of different production batches of live measles vaccine [6-8], the phenomenon established above was studied in four other sample production batches of live measles vaccine in order to judge the properties of this preparation as a whole.

Besides the study of the localization of the specific antigen in the brain, spinal cord, and organs of animals inoculated with different batches of live measles vaccine, they were also studied pathomorphologically.

EXPERIMENTAL METHODS

Experiments were carried out on 80 newborn albino mice and day-old hamsters. The newborn animals were inoculated subcutaneously with a single vaccination dose of live measles vaccine. Commercial batches (Nos. 244, 401, 419, and 520) of live measles vaccine produced by the Moscow Research Institute of Virus Preparations were used for immunization. The animals were killed by total exsanguination 1, 2, 3, 4, 5, 6, 7, and 8 days after injection of the live measles vaccine. Squash preparations were obtained from the tissue of the brain, lungs, and spleen, fixed with cold acetone, and stained by the indirect Coons' method [4]. Normal human immunoglobulin with a high content of antibodies against measles virus, after preliminary titration, was used as the immune antimeasles serum. The specificity of the immunofluorescence method was confirmed by appropriate controls [4]. For pathomorphological study, the brain, spinal cord, and organs of the animals were fixed in Dubosq–Brasil–Bouin fluid. Changes in the CNS and organs were studied in histological sections stained by the Romanovsky–Giemsa method in the usual way.

EXPERIMENTAL RESULTS

After injection of any of the four batches of live measles vaccine into the newborn mice and Syrian hamsters no animals developed the disease or died. During investigation by the fluorescent antibodies method, after injection of any of the four batches of live measles vaccine specific fluorescence was observed as early as 24 h after inoculation in the walls of the blood vessels of the brain, in glial and nerve cells, and beneath the pia mater. The antigen was located chiefly in the cytoplasm of the glial and nerve cells and was revealed as

Laboratory of Immunopathology, D. I. Ivanovskii Institute of Virology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. M. Zhdanov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 5, pp. 567-569, May, 1978. Original article submitted October 4, 1977.

 0007-4888/78/8505-0620$07.50

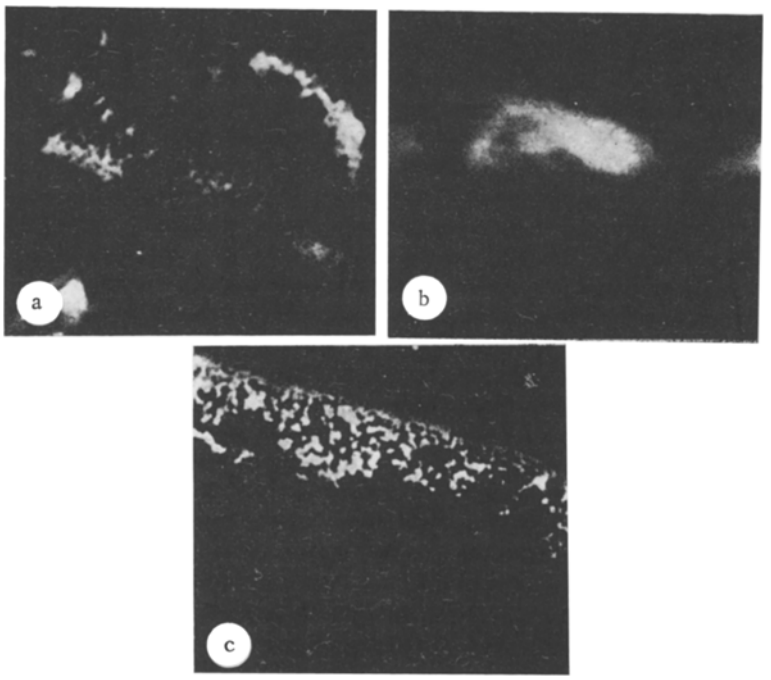

Fig. 1. Localization of specific antigen in brain of newborn Syrian hamsters inoculated with various batches of live measles vaccine, on 1st-3rd days after immunization: a) neuron; b) wall of blood vessel; c) accumulation of antigen beneath pia mater. Indirect Coons' method, 720×.

granular and diffuse fluorescence. The most intensive fluorescence was observed on the 3rd day, when it was seen not only in the cytoplasm, but sometimes in the nucleus also. The antigen could also be found extracellularly in the brain tissue. Fluorescence of the cells was found more frequently and was more intensive in the brain than in the spinal cord (Fig. 1). In animals inoculated with live measles vaccine of batches Nos. 244, 401, and 419 the intensity of fluorescence fell sharply toward the 6th day, whereas in those inoculated with batch No. 520 it was still relatively high. On the 8th day of the investigation, no specific antigen could be found in brain preparations from animals inoculated with any of the four batches tested.

At all times of the investigation no significant difference in the localization of intensity of specific fluorescence could be found in the newborn mice and hamsters.

The pathomorphological study of the organs of the newborn mice after inoculation with these batches of measles vaccine showed a slight degree of edema beneath the pia mater of the brain after 24 h, and vacuolation of the cytoplasm of the neurons of the brain after 48 h. The signs of disturbance of the hemodynamics continued to increase later, to affect all parts of the brain. Hyperplasia of the glial cells, sometimes with shrinking of the neurons of Ammon's horn, also were observed.

Before the 4th-5th days after vaccination the spinal cord showed no pathomorphological changes; not until the 7th day could foci of hemorrhage be observed in the spinal cord of some animals.

The most conspicuous feature revealed by the study of the CNS of the newborn hamsters, like the albino mice, was the hemodynamic disturbances, and no lesions of the neurons were observed. For hamsters, just as for the albino mice, the most reactogenic vaccine was batch No. 520, by the use of which the most intensive fluorescence was observed (see above).

The spleen of all the experimental animals at all times of investigation showed no visible pathology. Investigation of the spleen by the immunofluorescence method revealed specific fluorescence between the 1st and 6th days. The most intensive fluorescence in the cells was observed on the 3rd day. No specific antigen was found in the animals' lungs.

The results of these investigations thus indicate that after inoculation with different production batches of live measles vaccine, attenuated measles virus penetrates into the brain, as shown by specific fluorescence of its various structures. In turn, this indicates that attenuated measles virus of strain L-16 possesses residual affinity for the cellular and vascular structures of the brain and spinal cord of newborn animals. Meanwhile, the absence of the disease in the newborn animals, in the writers' opinion, is an indication that the vaccinal measles virus is sufficiently well attenuated. However, despite this fact, the presence of some degree of neurotropism suggests that under conditions of modified reactivity of the recipient, the attenuated measles virus could give rise to postvaccinal complications. There is evidence in the literature that measles vaccination [1-3] is accomplished not only by the development of vaccination reactions, but also sometimes by the development of postvaccinal lesions of the CNS.

As regards the pathomorphological changes, they can be regarded as due to the direct action of the attenuated virus on brain structures.

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ABILITY OF THERMO- AND ACID-STABLE SERUM SERINE PROTEASE INHIBITOR TO INHIBIT MITOGEN-STIMULATED TRANSFORMATION OF LYMPHOCYTES

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UDC 612.112-06:[612.128:577.152.344.042.2

The ability of a thermostable and acid-stable serine protease inhibitor from rabbit blood serum (TASPI) to inhibit the transformation of human peripheral blood lymphocytes stimulated by phytohemagglutinin (PHA) or concanavalin A (con A) was demonstrated. The degree of inhibition depends on the concentration of the inhibitor and its specific activity. The maximal degree of inhibition was 50-70%. TASPI has no cytotoxicity. Stronger inhibition of transformation is observed if TASPI is added to the culture 24 h after the addition of PHA. Data on the antiprotease activity of human blood serum, either native or inactivated under different conditions, are given. The results suggest that TASPI participates in the control of the biological activity of lymphoid tissue cells.

KEY WORDS: *antiproteases; lymphocyte transformation.*

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Translated from Byulleten' Éksperimental'noi Biology i Meditsiny, Vol. 85, No. 5, pp. 569-572, May, 1978. Original article submitted July 18, 1977.

0007-4888/78/8505-0622$07.50