

EARLY STAGES OF EXPERIMENTAL ALLERGIC POLYNEURITIS PATHOMORPHOLOGICAL AND IMMUNOLOGICAL CHARACTERISTICS

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Few attempts have been made to study experimental allergic polyneuritis (EAP) [1-3], and no systematic investigations have been made of the early stages of this disease. Yet the study of the early course of EAP may give a clearer idea of the order of development of the pathological process and the relationships between the morphological and immunological changes.

The object of this investigation was to make a combined morphological and immunological study of the early stages of EAP at different times after immunization.

EXPERIMENTAL METHOD

Experiments were carried out on 32 female rabbits weighing 2.0-2.5 kg. EAP was produced by intradermal injection of homologous nerve tissue together with Freund's stimulator into the paw [1-3]. During the next 20 days observations were maintained daily on the animals' condition. Every 3-5 days blood samples were taken and the antibodies to homologous peripheral nerve tissue were determined by means of the complement fixation reaction (CFR) in the cold. Microscopic examinations were made of the spinal ganglia and the ganglia of the cranial nerves together with their roots, the nerve trunks, and some sympathetic ganglia. Demyelination was studied by the method of Marchi and Kulchitsky, and the inflammatory reaction by various commonly used histological methods and by Nissl's method.

EXPERIMENTAL RESULTS

The earliest changes were found in the medullated fibers of the sensory ganglia, and to a lesser degree in their roots, in the form of a periaxonal process with disintegration of the myelin into fine granules. In contrast to Wallerian degeneration, the disintegration from the very beginning was of a finely granular character, and the products of disintegration very soon (at the end of the prodromal period and during the first 24 h of the disease) began to be impregnated with osmium. Initially the large and small granules were brown in color after impregnation, but many were black even at this stage. According to some observations, impregnation of the granules of myelin degeneration with osmium to give a black color indicates the formation of cholesterol esters in them. These changes reached their maximum after 3-4 days.

From the 9th to the 12th day after immunization six rabbits were sacrificed. These animals had no signs of the disease or visible morphological changes, and antibodies against peripheral nerve tissue were found in a low titer (1:10) in the serum of only two of them.

Between the 13th and 15th day 10 rabbits were sacrificed. Four of them had no signs of polyneuritis, but microscopically a marked finely granular disintegration of the myelin was observed in three animals of this group. Periaxonal changes in the myelin were usually found only in certain spinal ganglia, and they were absent from the root and nerve trunks. The degenerated myelin had the appearance of large and small granules of different shape, mainly black and brown in color. In three animals of this group low titers of antibodies against peripheral nerve tissue (1:10-1:20) were found, and a titer of 1:80 was found in only one rabbit. The remaining six rabbits by this time had developed symptoms of polyneuritis of varied intensity. All the animals of this group, including those autopsied on the first day of the disease, showed clear morphological changes in the form of granular degeneration, the products of which were

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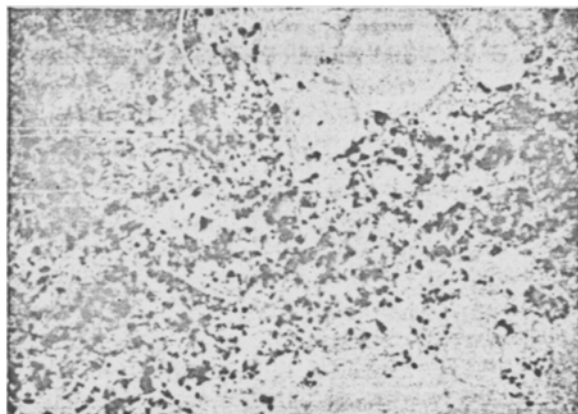


Fig. 1. Marked disintegration of myelin in the nerve fibers of a cervical ganglion of the spinal cord of a rabbit with the appearance of large and small black granules. Taken on the 1st day of the disease from a rabbit with severe symptoms of polyneuritis and a high titer of antibodies in the serum (1:80). Marchi's method. Magnification 240.

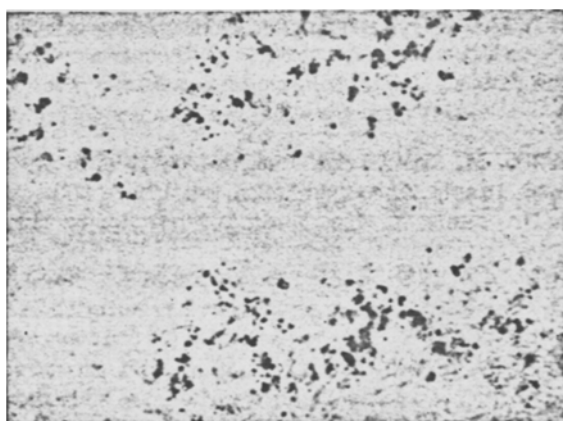


Fig. 2. Slight granular degeneration of myelin in a thoracic spinal ganglion of a rabbit with slight symptoms of polyneuritis. High titer of antibodies in the serum (1:80). Marchi's method. Magnification 240.

mostly impregnated brown and black (Fig. 1). Antibodies against nerve tissue were found in the serum of all six rabbits in titers of 1:10–1:80, regardless of the severity of the disease.

In later periods (from the 16th to the 20th days after immunization) 16 rabbits were sacrificed. Six animals of this group had no symptoms of polyneuritis. Morphological changes were found in only one of these rabbits and severe, advanced degeneration was found only in one ganglion in the lumbo-sacral portion. Antibodies against nerve tissue were found in high titers in five rabbits of this group and in a titer of 1:20 in only one rabbit. Of the remaining 10 sick rabbits, 7 developed severe polyneuritis. Morphological examination of three of these animals, autopsied during the first day of the disease, despite the late onset (16th–20th day after immunization), moderate "early" changes were found (Fig. 2). In the remaining 7 rabbits, autopsied on the 2nd–5th day of the disease, despite differences in the severity of the clinical manifestation, advanced morphological changes were found in the nerve fibers. The products of granular degeneration

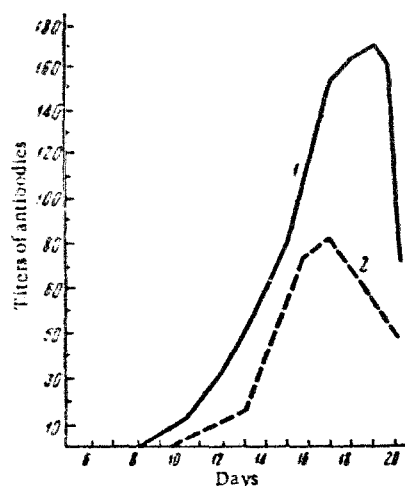


Fig. 3. Titer of antibodies in serum of rabbits immunized with homologous nerve tissue. 1) Rabbits developing disease; 2) rabbits not developing disease.

still does not indicate a pathogenetic role of the antibodies discovered against peripheral nerve tissue in the development of EAP, but it does suggest that they nevertheless play some part in the development of the pathological process.

were impregnated with osmium and appeared gray, forming oval and round clusters in the bodies of the macrophages, and sometimes macrophages were arranged around the vessels. In the blood of all the animals of this group antibodies against peripheral nerve tissue reached high titers.

It is clear from the changes described in the early period of development of EAP in 32 rabbits that a correlation existed between the severity of the disease and the morphological changes in the peripheral nervous system. However, no relationship, however close, could be observed between the symptoms of the disease and the morphological changes, on the one hand, and the dynamics of the increase in the titers of the antibodies, which appeared after the 9th-11th day and increased in all the rabbits subsequently. Because of this, the intensity of the serological changes was compared at times optimal for the development of the disease (16th-20th day after immunization) in five rabbits with no symptoms of the disease and in five rabbits with severe clinical and morphological manifestations of polyneuritis. It is clear from Fig. 3 that maximal antibody formation in all the rabbits took place on the 16th-19th day after immunization, but the mean titers of antibodies were higher in the rabbits developing the disease than in those with no symptoms of polyneuritis. This

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