EFFECT OF EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS ON THE COURSE OF HEAD INJURIES

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UDC 616.832-002.056.3-092.9-06:617.51.001

The characteristic features of head injuries associated with experimental allergic encephalomyelitis in guinea pigs are severe and widespread areas of brain damage marked by intense perivascular cell proliferation and demyelinization in the region of the traumatic focus and also at a distance from it.

The course of a brain injury after trauma of measured intensity depends not only on the magnitude and character of the trauma but also on the state of immunologic sensitivity of the victim to nerve tissue antigens [1, 2]. It is therefore interesting to study the features distinguishing the course of head injuries accompanying demyelinizing conditions of the nervous system, which are characterized by the development of increased sensitivity to brain antigens [3].

In the investigation described below the course of head injuries in experimental allergic encephalomyelitis (EAE) was studied.

EXPERIMENTAL METHOD

Experiments were carried out on 30 male guinea pigs weighing 350-450 g. In the experiments of series I a head injury was inflicted ($2 \times 1.5 \times 1.5$ mm in extent) on 20 guinea pigs by means of a probe, under sterile conditions, on the 10th-12-day after production of EAE by means of a single intradermal injection of monkey brain homogenate with Freund's adjuvant in a dose of 0.1 ml per animal.

In the experiments of series II a similar brain wound was produced in 5 guinea pigs sensitized intradermally with heterologous testicular tissue with Freund's adjuvant. In series III a head injury was inflicted on intact guinea pigs. The animals were decapitated 24-48 h, and 3-4 and 5-7 days after brain injury. Paraffin sections stained with hematoxylin-eosin and by the methods of Nissl, Feulgen, and Brachet were used for histological investigation; control sections were incubated with desoxyribonuclease and with ribonuclease.

EXPERIMENTAL RESULTS

The brain injury inflicted on the animals extended through all layers of the cortex and subjacent white matter, but in most cases it did not damage the wall of the lateral ventricle.

In specifically sensitized animals (experiments of series I) typical features of EAE were observed in the form of multiple foci of infiltration by histiocytes and lymphocytes and corresponding foci of demyelinization, perivascular in their localization and occurring mainly in the white matter, together with signs of meningitis, ependymitis, and choroiditis.

Institute of Neurology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR E. V. Shmidt.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 69, No. 6, pp. 98-102, June, 1970. Original article submitted September 10, 1968.

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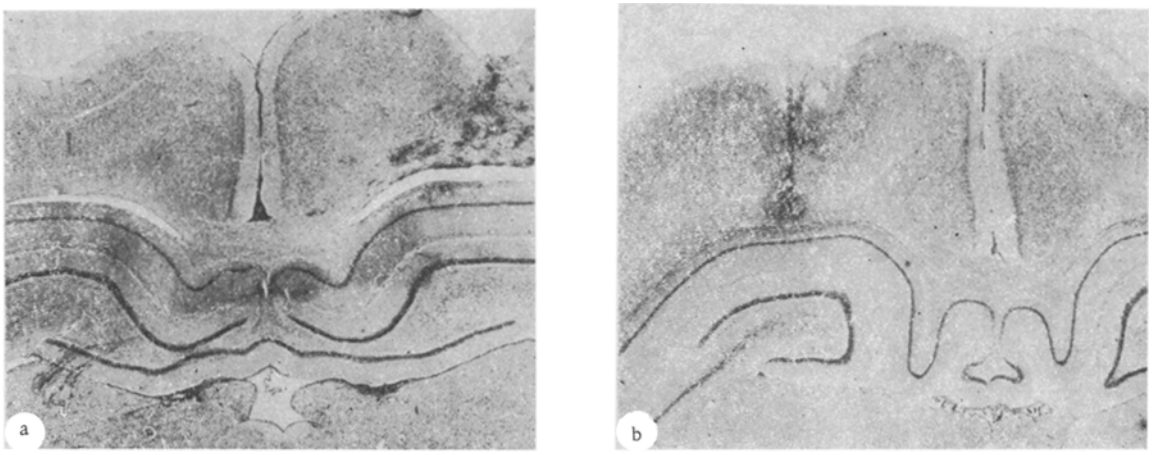

Fig. 1. Brain lesion around site of trauma in a guinea pig with EAE (a) and in a control guinea pig (b). Hematoxylin-eosin, 40×.

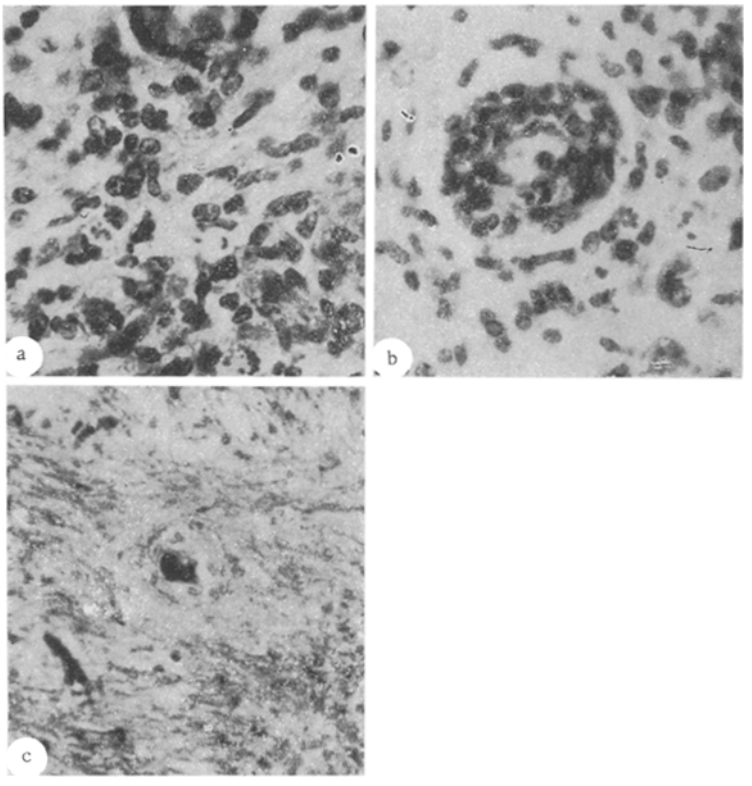

Fig. 2. Polymorphic cellular composition (a) of perivascular infiltration (b) and of demyelinization (c) in perifocal region of trauma. Nissl's (a and b) and Spielmeyer's staining methods, 400×.

At the stage of 24-48 h after brain trauma to the specifically sensitized animals, i.e., in the stage of necrosis of brain tissues, marked edema was observed in the perifocal region, with a fine honeycombed structure in the gray matter and a coarse honeycombed structure in the white. The perivascular and pericellular spaces were grossly dilated. Many of the cavities of the honeycomb in the white matter contained homogeneous spheres formed by acute necrosis of medullated fibers. The nerve cells in the perifocal region were in a state of ischemic degeneration. The injured nerve cells were surrounded by astrocytes, microgliocytes, and polymorphs; pseudoneuronophagy and true neuronophagy were observed. The vessels in the perifocal region were dilated and congested. Stasis was present in many arterioles, capillaries, and

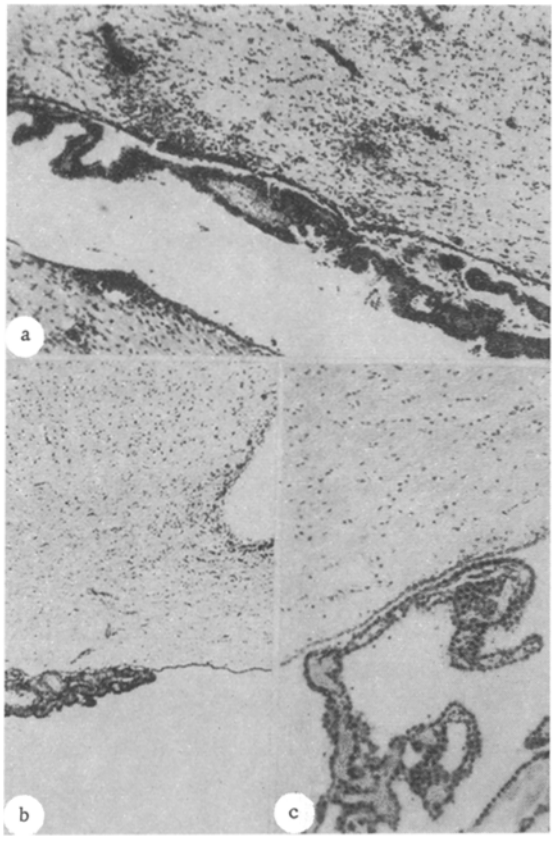

Fig. 3. Reaction of choriod plexus and ependyma close to site of trauma in a guinea pig with EAE (a), a guinea pig sensitized with testicular homogenate (b), and an intact guinea pig (c). Nissl's method, 60× (a and b), 100× (c).

venules. Often the leukocytes, mainly monocytes, were arranged around the periphery of the lumen.

After 5-7 days, i.e., at the stage of elimination of breakdown products and of initial organization of the defect in the brain substance, very intensive proliferation of cells was observed, not only in the perifocal region but also at a considerable distance from it (Fig. 1). No clear line of demarcation could be detected between the traumatic focus and the adjacent brain tissue, for the cell proliferation extended for a considerable distance in the form of bands and islets with a mainly perivascular localization. This process affected the gray and white matter, but it was more marked in the latter, spreading along the entire centrum semiovale and periventricular region. The infiltrating cells were highly polymorphic in composition, including many glial cells, lymphocytes, and histiocytes, and fewer granulocytes and neutrophils, the latter being in a state of karyorrhexis (Fig. 2a). In the oligodendroglia drainage forms of cells and, less often, shrinking of the cells were observed. The microglia was in a state of marked hypertrophy and proliferation. The cell nuclei were enlarged in volume and sometimes curved in shape; sometimes projecting processes of cytoplasm could be seen. The number of cells showed a sharp increase. Foci of demyelinization in the white matter of the brain corresponded to the perivascular zones of infiltration (Fig. 2b, c). Many nerve cells in the cortical gray matter in the perifocal region were in a state of ischemic or severe Nissl's degeneration, and shrunken neurons and ghost cells could be seen. In a few cases neurons in a state of karyorrhexis were visible. The impression was gained that the perifocal region had been sown with the seeds of nuclear destruction on account of both glial cells and leukocytes, on the one hand, and of nerve cells on the other.

The meninges, ependyma, and choroid plexus close to the region of injury were infiltrated with lymphocytes. In most cases the choroid plexus was in close contact with the ependyma facing the traumatic focus (Fig. 3a). Cells infiltrating the choroid plexus were seen to be invading the adjacent white matter and the cells of the ependyma and subependymal layer were proliferating intensively. The signs of meningitis, ependymitis, and choroiditis, typical of EAE, were much more marked on the side of the injured hemisphere (Fig. 1a).

In the experiments of series II on nonspecifically sensitized animals, the changes due to head injury were much less conspicuous after 24-48 h than in the specifically sensitized animals of series I. By the 5th-7th day the region of trauma in these animals was bounded by a narrow barrier of granulocytes, glial cells, and components of the vessel wall. Foci of perivascular infiltration and of demyelinization were not present in the perifocal region. Cellular proliferation was only moderate in intensity and was limited to the perifocal region, not spreading beyond its borders (Fig. 3b).

A similar picture at the stage of necrosis, elimination of breakdown products, and initial organization of the brain substance also was present in the intact guinea pigs of control group III after brain injury (Figs. 1b and 3c).

It must be emphasized that adhesion of the choroid plexus to the ependyma of the ventricle facing the traumatic focus, which evidently reflects the protective, barrier function of the choroid plexus, was observed after brain injury in both the intact and the sensitized animals. However, the intensity of this process was greatest in the specifically sensitized animals (Fig. 3).

The facts described above can be summed up in the statement that brain injury associated with EAE has a number of characteristic distinguishing features due to the presence of a demyelinizing lesion of the nervous system in these animals. The morphological disturbances following brain injury in animals with EAE consist of changes in nerve and glial cells, a leukocytic response, and diapedetic hemorrhages in the stage of necrosis. The characteristic feature distinguishing brain trauma at the stage of elimination of the breakdown products and of initial organization of the defect in the brain substance is intensive perivascular cellular infiltration, proliferation, and demyelinization in the perifocal region of the traumatic focus and also at a considerable distance away from it.

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