SCAR FORMATION IN THE CENTRAL NERVOUS SYSTEM UNDER THE INFLUENCE OF PYROGENAL

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In the modern view, the principal factor preventing the penetration of nerve fibers through the area of a section of the spinal cord is the rapid formation of scar tissue in the cord. The use of a bacterial polysaccharide enabled the American workers Clemente and Windle [3] to obtain a more friable scar and to observe the penetration of intraspinal nerve fibers through it. Other workers, however using the same preparation, obtained negative results [2, 4].

In view of the great importance of this problem, we also made an attempt to prevent the formation of a dense scar between the cut ends of the transected spinal cord in dogs and also to investigate the possible regeneration of the nerve fibers. As a substance to inhibit scar formation we used the Soviet preparation pyrogenal – a complex polysaccharide of baterial origin, prepared in the N. F. Gamaleya Institute of Epidemiology and Microbiology of the AMN SSSR.

In the present communication we describe the results showing the influence of pyrogenal on the formation of scar tissue.

METHOD

Experiments were carried out on 21 dogs aged from 1 to 2 years. Twelve were experimental animals and nine controls. The spinal cord was transected in the region of the 8th-10th thoracic segment. A longitudinal incision was made in the dura mater, the cord was lifted out on a hook and divided with a fine, pointed scalpel so that the hook was lifted out through the cut. The ends of the spinal cord were placed together and its surface covered with a fibrin film. Pyrogenal was administered systematically at intervals from the second day until nine months after operation, in a dose of 5-10 μg/kg. The animals were sacrificed 14 days and 1, 3, 6, 13 and 26 months from the beginning of the experiment. The spinal cord in all these cases was examined histologically. Serial sections were cut from the area of transection of the cord in a dorso-ventral direction. The sections were stained with hematoxylin–eosin, hematoxylin-picrofuchsin, Spielmeyer's hematoxylin and thionin, and were also impregnated with silver on the argyrophilic fibers of the scar by Foot's method and on the glia by the methods of Cajal and Stern-Beletskii. The nerve fibers were also impregnated with silver by different methods.

RESULTS

Two weeks after operation we observed no marked differences in the structure of the scar tissue in the experimental and control dogs. In the first of these the defect in the cord was replaced by loose connective tissue containing thin, isolated bands of collagen fibers. The wide intervals between the bands were filled with fibroblasts of various degrees of differentiation, histiocytes and numerous macrophages. The scar contained many thin-walled vessels. The scar in the control dogs showed basically thesame structural features, but the bands of collagen fibers in the controls were somewhat wider.

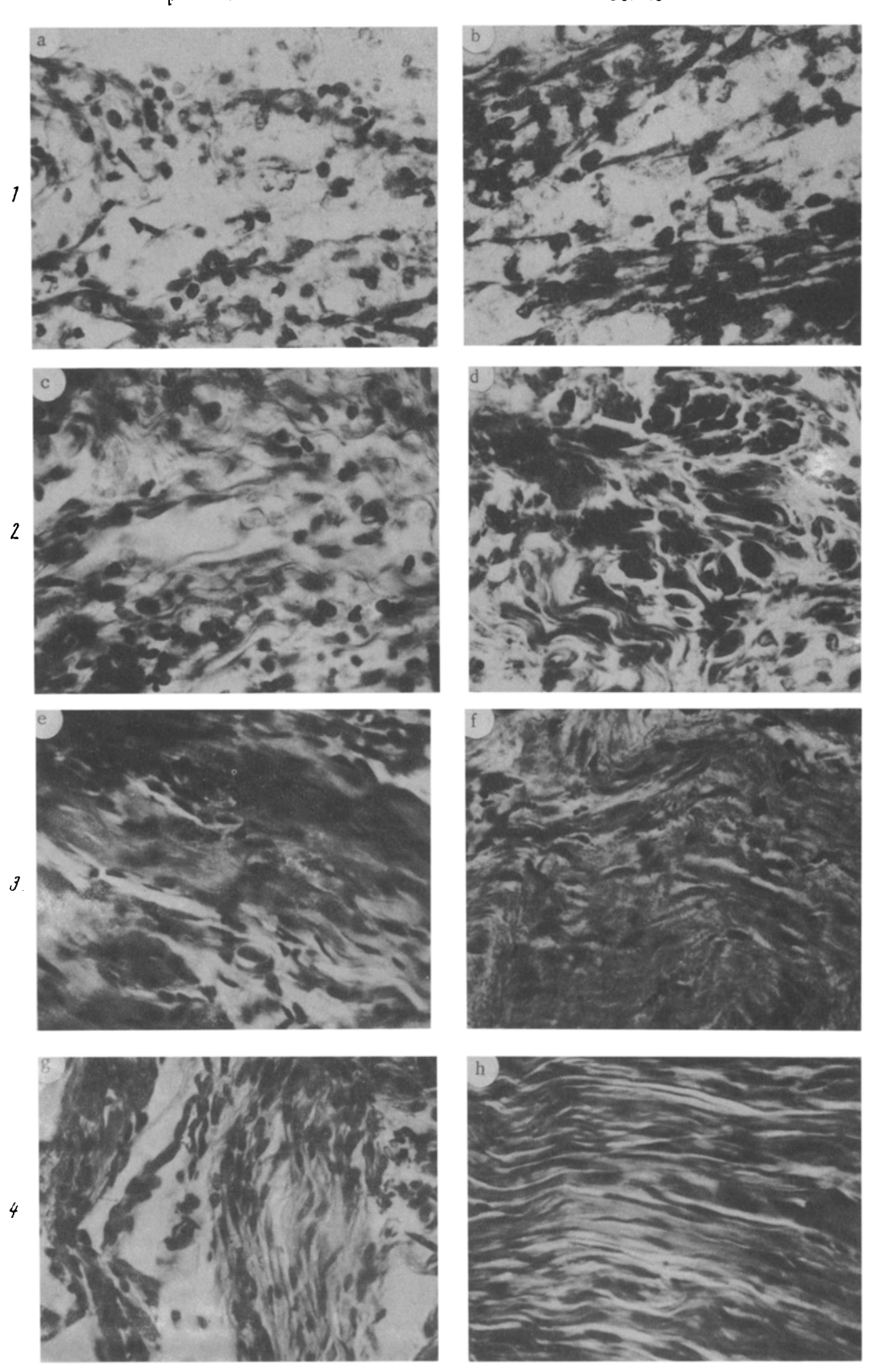

Fig. 1-4. Structure of the scar tissue at the site of transection of the spinal cord in experimental and control dogs. Magnification 400 : 1. Stained with hematoxylin-picrofuchsin and hematoxylin–eosin. 1) 1 month after operation; 2) 3 months after operation; 3) 13 months after operation; 4) 26 months after operation.

One month after operation the character of the scar in the experimental animal had undergone little change (Fig. 1a) and the structural signs found in the scar of the dog examined two weeks after operation were largely preserved. As in the latter case the thin bands of collagen fibers were separated by wide zones of cells, containing as before large numbers of macrophages. The scar contained a fairly dense network of thin-walled vessels.

In contrast to the experimental dog, in the control animal one month after operation the process of scar formation had been carried much further (Fig. 1b). For instance, the bands of collagen fibers had become thicker and were separated by correspondingly narrower zones of cells.

The difference in the tempo of formation of the scar structure was even more obvious at the later periods of observation. Three months after operation the structure of the scar differed sharply in the experimental and control dogs. In the first (Fig. 2c) a slowing of the development of organization of the cord defect was clearly found. Although the number and thickness of the bundles of collagen fibers were slightly increased, the intervals between them remained wide and were filled with connective tissue cells, among which were many macrophages. Considerable numbers of thin- and thick-walled vessels were found in the scar.

The scar formed at this time in the control animal (Fig. 2d) consisted of thick, spirally twisted and haphazardly interwoven bands of collagen fibers. In contrast to the scar in the experimental dog, in which the collagen fibers stained a pink color with picrofuchsin, in the scar in the control dog they were bright red in color. In places very narrow zones of loose connective tissue were found, in which macrophages were absent. Few blood vessels were present in the scar.

Slowing of the tempo of organization of the scar in the experimental animals was also observed at later periods after operation. This could clearly be observed 6, 13, and 26 months after operation (Figs. 3e, and 4g). In the scar in these animals relatively wide zones of loose connective tissue were seen, containing fibroblasts in various stages of differentiation, histiocytes and always a few macrophages. In every case in which pyrogenal was given, thin- and thick-walled blood vessels passed in the loose tissue zones among the bundles of collagen fibers and along the bundles themselves.

In the control animals at these periods (Figs. 3f and 4h) the scar had become even poorer in cells, the intermediate areas of loose connective tissue had disappeared, the bundles of collagen fibers had become adherent to each other and the nuclei of the fibroblasts had acquired an extremely flattened shape. Vessels had almost completely disappeared from the scar, and only a few thick-walled vessels remained near the meninges. In the last case to be observed, signs of hyalinosis of the scar could be observed here and there.

Having noted the well marked influence of pyrogenal on the formation of the structure of the scar, attention must be drawn to the fact that this influence mainly extended to the central area of the scar and had little effect on its peripheral part, in immediate contact with the meninges.

It is thus clear from the pathomorphological findings described above that the administration of pyrogenal influences scar tissue formation in the region of transection of the spinal cord in dogs. In all the animals receiving pyrogenal, at both early and later periods, even after 26 months, we could observe a looser structure of the scar, delay in the maturation of fibroblasts, the presence of macrophages, and better vascularization of the scar tissue. The action of pyrogenal was demonstrated especially clearly by depression of the formation of collagen fibers.

Our findings are in agreement with the observations of Clemente and Windle [3] on the influence of pyromen on the development of a scar in brain tissue. The delayed formation of such a scar facilitates the penetration of nerve fibers along the vessels and the collagen fibers proceeding along the long axis of the spinal cord [1, 5].

We consider that the early use of pyrogenal in the case of injuries to brain tissue may be of practical value in clinical practice, by preventing the rapid formation of a dense scar, with its attendant serious complications.

SUMMARY

Pyrogenal was used in 21 dogs in an attempt to prevent rapid scar formation between the stumps of the severed spinal cord. Pathomorphological studies of the medullary scar were undertaken 14 days, 1, 3, 6, 12, and 26 months after the operation. It was shown that pyrogenal interferes with scar formation at the site of section of the spinal cord. In all cases, even at later dates, the scar of the experimental animals was of a looser structure, the maturation of the fibroblasts was delayed, macrophages were present and the tissues were better vascularized.

Pyrogenal had a more marked effect on the inhibition of formation of collagen fibers.

LITERATURE CITED

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