HISTOPATHOLOGICAL CHANGES IN MUSCLES IN EXPERIMENTALLY PRODUCED OSTEOMYELITIS

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Published papers on osteomyelitis following gunshot wounds deal chiefly with the study of morphological changes in the muscles situated in the immediate vicinity of the inflammatory focus [11], and in the sciatic nerve [7]. Descriptions of morphological changes in the nervous apparatus of the muscles are to be found in only two case reports of this type of osteomyelitis [1].

In view of the general resemblance of this type of osteomyelitis to the experimentally produced form, we undertook the investigation of changes in the reactivity of the organism, including within this term also the morphological equivalents of reactivity, in experimental osteomyelitis proceeding in the presence of additional factors affecting the central and peripheral nervous systems.

Seven series of experiments were performed on 105 rabbits and 10 dogs.

EXPERIMENTAL METHOD

Osteomyelitis of the long bones of rabbits and dogs was produced by making an incision, 1-2 cm in length, under local anesthesia, at the medial surface of the left shin, and reaching to the bone. An opening 0.2 cm in diameter was then bored into the tibia, extending into the marrow cavity. We then introduced, through a cannula inserted into the borehole, 0.3 ml of a *Staphylococcus aureus* culture (250 million organisms per ml) per kg body weight of the animal.

In the first series of experiments the left sciatic nerve was divided and sutured, three to four weeks after appearance of osteomyelitis of the left tibia.

In the second series the left sciatic nerve was divided at a high level, after development of osteomyelitis symptoms, and vitamin B_1 was introduced into the peripheral stump, at a dosage level of 0.01 per kg body weight of the animal, after which the severed ends of the nerve were united.

In the third series the left sciatic nerve was not divided, but vitamin B_1 was injected into it at the same dosage.

In the fourth series we applied sleep therapy after the onset of osteomyelitis; this consisted in giving the animals subcutaneous injections of 2% Barbamyl (5 ml per kg body weight), twice daily for ten days.

In the fifth series we induced osteomyelitis ten days after division and repair of the left sciatic nerve.

The same was done in the sixth series, with the difference that sleep therapy was instituted simultaneously with induction of osteomyelitis.

The seventh (control) series consisted of animals with uncomplicated experimental osteomyelitis.

The experimental and control animals were killed three or six months after induction of osteomyelitis.

We made a histological examination of preparations of the gastrocnemius muscle, impregnated with silver by the Bielschowsky-Gross-Lavrent'ev procedure.

EXPERIMENTAL RESULTS

Histological examination of the left gastrocnemius muscle three months after operation of the animals of the first series showed atrophic changes in the muscle fibers, manifested by proliferation of the cell nuclei, with signs of irritation in the nerve structures, such as varicosities, excessive sinuosity, vacuolization, and irregular caliber of the nerve fibers. Deviations from the normal were not seen in the right gastrocnemius.

Six months after operation we found atrophic changes in the left gastrocnemius, with proliferation of muscle and connective tissue cell nuclei and large numbers of leucocytes, lymphocytes, and polyblasts were present in the muscle tissue; fairly marked evidence of irritation was seen in some nerve bundles and in individual axons, which were highly convoluted, of irregular caliber, often with clubbing, and coarsely impregnated with silver (Figure 1). Proliferation of muscle and connective tissue cell nuclei was seen in the right gastrocnemius, with coarse and incomplete impregnation with silver.

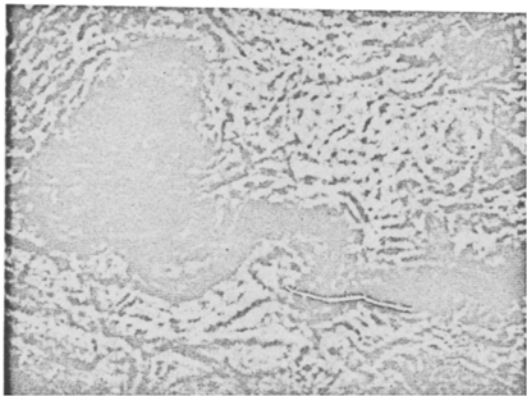

Fig. 1. Morphological changes in nerve structures of a dog's gastrocnemius, after induction of osteomyelitis, with subsequent division of the sciatic nerve. Excessive tortuosity of nerve bundles is seen 6 months after the operation. Impregnated according to Bielschowsky-Gross-Lavrent'ev.

In the second series of experiments we found atrophy of the muscle fibers, with proliferation of nuclei, three months after operation. In some of the sections perivascular round-cell infiltration, with an admixture of polyblasts, was seen. The nerve supply of the muscle was well developed, and large, medium, and small bundles of fibers were seen, consisting mostly of medium and small axons. Motor endings could not be seen. The nerve structures frequently showed signs of irritation, and were coarsely impregnated with silver. The right gastocnemius showed proliferation of muscle and connective tissue cell nuclei, and the nerve fibers were coarsely impregnated. Round-cell infiltration was seen sporadically.

Six months after the operation the left gastrocnemius showed increasing atrophy of muscle fibers, although the muscle was well supplied with nerves. The signs of irritation of the preterminal and terminal axons were less marked than at three months. Signs of irritation of the nerve fibers of the right gastrocnemius were evident, as well as proliferation of muscle and connective tissue cell nuclei.

Thus, the experiments of the first series showed fairly pronounced signs of irritation of the nerve fibers of the left gastrocnemius, which became more marked with the passage of time. These changes were more pronounced than in the second series of experiments.

The experiments of the third series showed that three months after the operation only coarse staining with silver could be seen in the nerve bundles, with only slight evidence of irritation of the preterminal and terminal axons of the left gastrocnemius. The motor nerve endings were clearly seen. The right gastrocnemius showed large foci of round-cell infiltration, chiefly around the blood vessels.

Atrophy of the fibers of the left gastrocnemius, with proliferation of muscle and connective cell nuclei, was seen six months after the operation. Motor nerve endings were visible. Signs of irritation were evident in some bundles of nerve fibers and in individual axons, such as irregular caliber, excessive convolution, edema-

Fig. 2. Morphological changes in nerve structures of a dog's gastrocnemius, after induction of osteomyelitis, with subsequent injection of vitamin B_1 into the intact sciatic nerve. An edematous condition of the neuroplasma of the preterminal axons is seen 6 months after the operation. Impregnated according to Bielschowsky-Gross-Lavrent'ev.

Fig. 3. Morphological changes in the nerve structures of a dog's gastrocnemius, after division of the sciatic nerve, followed by its repair. The preparation is from a dog with experimental osteomyelitis, and sleep therapy had been applied. A neuroma of a motor nerve ending had developed 3 months after the operation. Impregnated according to Bielschowsky-Gross-Lavrent'ev.

tous neuroplasm, and separation of fibers (Figure 2). Proliferation of muscle and connective tissue cell nuclei was seen in the right gastrocnemius, with only slight evidence of irritation of the preterminal axons.

Three months after the application of sleep therapy to the animals of the fourth series the preterminal axons of the left gastrocnemius showed only slight evidence of irritation. Proliferation of muscle and connective tissue cell nuclei was seen in the right gastrocnemius, and slight irritation of the nerve fibers was evident.

After six months only an insignificant degree of atrophy of the muscle fibers of the left gastrocnemius could be seen. No deviations from the normal were evident in the right gastrocnemius.

The experiments of the third and fourth series thus revealed a mild irritation of the nerve structures of both gastrocnemius muscles. Atrophy of muscle fibers was more pronounced in the later stages of the experiments of the third series.

Three months after the operation, and after induction of experimental osteomyelitis, acute atrophy of the muscle fibers was evident in the left gastrocnemius of animals of the fifth series, with increase in the number of muscle and connective tissue cell nuclei; the transverse striation of the muscle fibers could not be distinguished. Numerous streaks of fat were seen in some of the sections, with dilatation and thickening of the vessels. There were signs of acute irritation and fragmentation of the nerve structures of the muscle; excessive growth of nerve fibers was less frequently encountered. The nerve bundles consisted mainly of fine nerve fibers. Motor nerve endings could not be perceived. The nerve structures of the right gastrocnemius were coarsely impregnated, and the fibers were of uneven caliber. Preterminal and terminal axons sometimes formed loops.

Three months after operation of the animals of the sixth series muscle fiber atrophy was seen in the left gastrocnemius, with proliferation of muscle and connective tissue cell nuclei, and frequently with extensive foci of round cell infiltration. The blood vessels were very dilated, and had thickened walls. The nervous structures of the muscle showed signs of irritation and degeneration, such as varicosities, excessive convolution, edema of the neuroplasma, spiral fibers within bundles, neuromata of motor endings, and fragmentation (Figure 3). The right gastrocnemius showed coarse impregnation with silver, and proliferation of muscle and connective tissue cell nuclei.

After three months, the animals of the seventh series (controls) were found to have parts of the left gastrocnemius replaced by fatty tissue. Individual parts of the muscle showed granular degeneration. Extensive round-cell infiltration was seen in some of the sections. Evidence of medium irritation and degeneration of nerve fibers was seen in the form of blurred contours and fragmentation. Proliferation of muscle and connective tissue cell nuclei was seen in the right gastrocnemius, while its nervous structures gave evidence of irritation and of low grade degenerative changes in the fibers, which were convoluted, of irregular caliber, twisted spirally, edematous, and fragmented.

After six months signs of inflammation were seen in the left gastrocnemius muscle, the nervous structures of which showed signs of irritation, and were only weakly impregnated. The only change found in the right gastrocnemius was in the coarse impregnation of its nervous structures with silver.

A comparison of the results of histological examination of the muscles of the animals of the first and second groups with those of the seventh (control) series shows that the signs of irritation of the nervous structures of the left gastrocnemius were more pronounced in the former two series than in the control series.

In the third and fourth series of experiments the signs of irritation of the nervous structures of this muscle were less marked than in the control series.

In the fifth and sixth series of experiments the signs of irritation and degeneration of the nervous structures of the left gastrocnemius were more pronounced than in the control series.

We consider that our observations confirm the view that there are two types of nerve regeneration processes; an adequate and an inadequate type [1, 5, 8].

The most severe forms of experimental osteomyelitis were found in the animals of the fifth and sixth series of experiments. Deep trophic ulceration of the heel developed sooner in these animals than in those of the first and second series, and they showed less tendency towards healing. X-ray examination showed that a considerable part of the tibia was affected by the destructive process. The histopathological changes in the gastrocnemius muscles and their nervous structures were also more acute. These findings suggest that preliminary division of the sciatic nerve, followed by its immediate repair, lowers the reactivity of the animals towards the pathogenic agent of osteomyelitis, and aggravates the subsequent pathological process; not even sleep therapy improved their condition.

Osteomyelitis took a much milder form in the animals of the third and fourth series of experiments. These animals showed no motor or trophic disturbances, the osteomyelitic process proceeded sluggishly, only small destructive lesions of the bone were seen, and only low-grade histopathological changes appeared in the muscle.

Introduction of vitamin B_1 into the intact nerve, and sleep therapy applied after infection both had a favorable effect on the animals, by creating conditions favorable for the strengthening of the compensatory capabilities of the organism.

The manifestations of a state of irritation of the nervous structures of the gastrocnemius muscles, observed by us, may be considered as being one of the manifestations of the compensatory action of the nervous system.

SUMMARY

This work was devoted to the study of histological changes in the gastrocnemius muscles and their nerve apparatus in experimentally induced osteomyelitis of the tibia. It was revealed in experiments with rabbits that a number of changes take place both on the affected side and in the healthy extremity. These changes are manifested in stimulation and degeneration of the nerve apparatus of the muscles which are more pronounced on the side of the lesion. Bilateral atrophies, deformations and inflammatory changes of the muscle fibers are observed. Changes on the healthy extremity are apparently of reflex origin. Excessive regenerative processes in the nerve apparatus of the muscles enhance dystrophic changes. Sleep induced by drugs and vitaminization of the nerves were applied in the third and fourth series of experiments. It was demonstrated that the change of the functional condition of the peripheral and the central portions of the nervous system increase the compensatory adaptation of the organism and decrease the tissue dystrophy. This evidently points to the reflex mechanism of the pathological changes described above and of the compensatory phenomena as well.

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