MORPHOLOGY AND PATHOMORPHOLOGY

Experimental Study of the Etiology and Pathogenesis of Sciatic Neuropathy under Conditions of Therapy for Ischium Fractures

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Surgical (with external fixation device; series I) and conservative (series II) treatment of experimental unilateral transverse fracture of the body and ramus of ischium was carried out in 35 mongrel dogs. Roentgenometry, pathological, and histological studies showed sciatic nerve injury in both series, a complication of the fracture emerging at the moment of primary lesion. Further damage to the nerve due to its compression in an anatomical narrowings with fibrous degenerative tissues and bone fragments under conditions of conservative therapy, tunnel neuropathy, was paralleled by more pronounced destructive changes persisting for one year after the experiment.

Key Words: *sciatic nerve; tunnel neuropathy; fracture*

Closed fractures of skeletal bones are usually associated with peripheral nerve lesions and serve as a factor predisposing to tunnel neuropathies, which rank second among diseases of the peripheral nervous system [2,4-6]. Pelvic traumas are often accompanied by sciatic nerve injuries leading to lasting and sometimes stable disability [7,9,10]. We found no published data about the etiology and pathogenesis of sciatic neuropathies in fractures of the ischium essential for solution of the therapeutic and strategic problems.

Here we studied the etiology and pathogenesis of sciatic neuropathy, specifically, pathomorphological changes in the sciatic nerve in experimental fracture of the ischial bone treated by surgical and conservative methods.

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MATERIALS AND METHODS

Unilateral transverse fracture of the ischial bone body and ramus was created similarly in mongrel dogs (n=35) of medium weight aged 1-5 years. In experimental series I (n=18), the fracture was treated surgically using external fixation device [3]. In experimental series II (n=17), conservative therapy was carried out, consisting in mobility limitation (the animals were kept in cages) and therapy with non-narcotic analgesic and antihistaminic drugs. The animals were sacrificed by anesthetic overdosage 14, 28, 35, 65, 215, and 400 days after surgery. The animals were handled, operated on, and sacrificed in accordance with Regulations for Studies on Experimental animals, approved by the Order No. 755 of August 12, 1977, of the Ministry of Health of the USSR and the Helsinki Declaration of the World Association on Humane Handling of Animals (1996).

The angle of the ischial bone fragment dislocation was evaluated on the roentgenograms. After sacrifice,

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the fragments of damaged and contralateral areas of the pelvic and femoral bone were examined layer by layer and macroscopic changes were described. Sciatic nerve fragments were taken at the level of the trauma and embedded in araldite. Semithin cross-sections were stained with methylene blue and basic fuchsin. The diameters of myelinated fibers were measured in digitally processed images of semithin sections on a DiaMorph complex using VideoTest Master–Morphology 4.0 software. The mean diameters of myelinated nerve fibers (D_{mf}) was calculated, their numerical densities (NA_{mf}) per mm^2, and percentage of their reactive and degenerative forms (Deg%) were calculated. Sciatic nerves of 4 intact mongrel dogs served as the control. The resultant digital material was analyzed by nonparametrical statistical methods by Kolmogorov–Smirnov's test (test-based software by I. P. Gaidyshev [1] added to dynamically attached library for Microsoft Excel 97).

RESULTS

No dislocation of the bone fragment was seen in X-ray images of series I animals; minor macroscopic changes were seen during the early periods of the experiment. The sciatic nerves retained their anatomic continuity throughout the experiment.

Microscopy of specimens from series I showed an increase in the counts of fibroblasts and mast cells, appearance of macrophages and leukocytic plasmocytic infiltration in the epineurium on days 14 and 28 of the experiment. The walls of epineural microvessels were thick and the lumens were dilated. The perineurium retained fine lamellar structure; subperineural edemas were negligible. In contrast to the control, endoneural microvessels had wide lumens. Some myelinated fibers had signs of axonal and wallerian degeneration.

After 35 days, the number of microvessels in the epineurium increased and collagen depositions developed. Moderate subperineural edemas persisted in large bundles. The majority of fibers had normal structure (Fig. 1, *a*), NA_{mf} index virtually did not differ from that in intact nerve (Table 1), while Deg% was higher ($p<0.001$) than in the control (Fig. 2). New conductors (D≤2 μ) were found, their relative content being 1% (just solitary in the control <1%). The percentage of fibers thicker than 10 μ (indicator of effective regeneration of the nerve) was normal (33-44% *vs.* 33-53% in the control). The D_{mf} index was significantly (by 7.2%; $p<0.01$) lower than that of the intact nerve (Table 1).

After 65 days, the nerves just slightly visually differed from the intact ones. NA_{mf} index decreased by 10.5% ($p<0.01$), Deg% increased by 1.5 times and was 2.1-fold higher than in the control ($p<0.001$; Fig. 2). Similarly as during the previous period, the percentage of fibers with D≤2 μ was 1%, while the percentage of conductors with D>10 μ was virtually normal (37-55%) and D_{mf} was restoring (Table 1). After 215 and 400 days of the experiment, the morphology was virtually the same as that of the intact nerve and the majority of the parameters virtually did not differ from the control, except NA_{mf}, which remained by 12.8% below the normal ($p<0.01$) after 215 days.

In experimental series II, roentgenography showed displacement of the ischial bone fragment in the ventral direction in the sagittal plane with the formation of an angle of 32.5±12.5° in 13 of 17 animals. Dislocation of the fragment in the segmental plane with internal or external rotation was detected in 4 cases (Fig. 3).

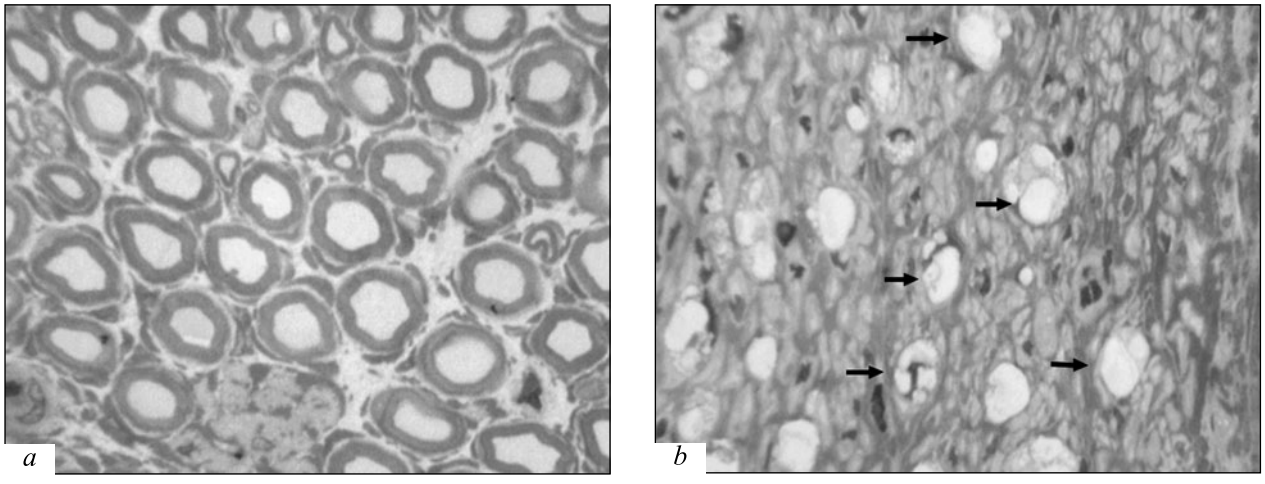

Fig. 1. Microscopic picture of the sciatic nerve under conditions of surgical and conservative treatment. *a*) sciatic nerve during surgical treatment, day 35 of the experiment; the majority of pulpous and pulp-free nerve conductors retain the normal structure; *b*) sciatic nerve during conservative therapy, day 28 of the experiment, myelinated fiber degradation products (arrows). Transverse semithin sections stained with methylene blue and basic fuchsin, objective 40, ocular 12.5×.

TABLE 1. Numerical Density (NA_{mf}) and Mean Diameter (D_{mf}) of Myelinated Nerve Fibers in the Sciatic Nerve of Experimental Limb at Different Stages of Experiment and in Intact Sciatic Nerve

Experiment period	NA_{mf}/mm^2		D_{mf}, μ	
	series I	series II	series I	series II
Intact nerve	11,791±0.604		8.61±0.10	
35 days	11,991±4920	11,994±3839	7.99±0.10*++	7.00±0.10**
65 days	10,726±1120*++	15,531±1499**	8.31±0.19++	7.34±0.11**
215 days	10,281±484*+	11,612±716	8.40±0.12	8.52±0.15
400 days	12,000±483+	8583±495*	8.43±0.15	8.52±0.25

Note. *p<0.01, **p<0.001 between the values in intact sciatic nerve and values in series I and II. +p<0.01, ++p<0.001 between values in series I and II (by Kolmogorov–Smirnov's test for independent samples).

Hematomas between the bone fragments were found in preparation of the injured area on days 14, 28, and 35. The femoral alveus of the sciatic nerve was stenosed because of dislocation of the ischial bone fragment and callus growth, this leading to fibrosis of tissues surrounding the nerve. The color of the femoral caudal muscles changed, their volume and elasticity decreased. The sciatic nerve retained its continuity throughout the experiment.

Microscopy of the nerve (series II) during the early period (days 14-28) of the experiment showed a significant increase in the epineural cell count and appearance of plasmocytic and leukocytic infiltration. The lumens of epineural microvessels were dilated. The internal elastic membrane was fragmented and somewhere absent in some of these vessels. The tunica media was thick, some smooth muscle cells had vacuolated cytoplasm and small nuclei. The perineurium was thick, perineural cells hypertrophic, some of them with vacuolated cytoplasms. Extensive subperineural edemas were seen. Numerous inflammatory cells and neurolemmocytes were found in the endoneurium. Overall destruction of fibers was seen in some places of large bundles (Fig. 3, *B*), presented by demyelination, axonal and wallerian degeneration, while in other places regeneration was seen. After 35 days, compensatory hypervascularization of the epineurium and collagen depositions were found. The perineurium remained thick, the counts of perineural cells increased. NA_{mf} virtually did not differ from the control (Table 1), Deg% was 3.0 and 2.2 times higher (p<0.001) than in the intact nerve and in series I, respectively. The new fibers were solitary (1-2%) and were within regeneration clusters. The relative count of conductors with D>10 μ was low in two animals (1 and 18%) and reached the lower normal value (34%) in one. D_{mf} was 18.7 and 12.4% lower than in the intact nerve and series I, respectively. After 65 days, NA_{mf} and Deg% were 24.1 and 30.9%, 2.5 and 1.2 times higher (p<0.001) than the control and the parameters in series I, respectively. The majority of myelinated fibers looked morphologically mature, but new conductors with D≤2 μ were still sometimes found (1%); the relative content of large fibers increased to 29-31%, but did not reach the level in the control. Regeneration clusters were still found among mature fibers of the sciatic nerve after 215 and 400 days, as well as fibers with signs of axonal and wallerian degeneration. NA_{mf} returned to normal after 215 days; after 400 days it decreased by 27.2 and 28.5% in comparison with the control and series I, respectively. Deg% increased after 215 and 400 days surpassing the control level by 4.0 and 4.2 times (p<0.001) and the

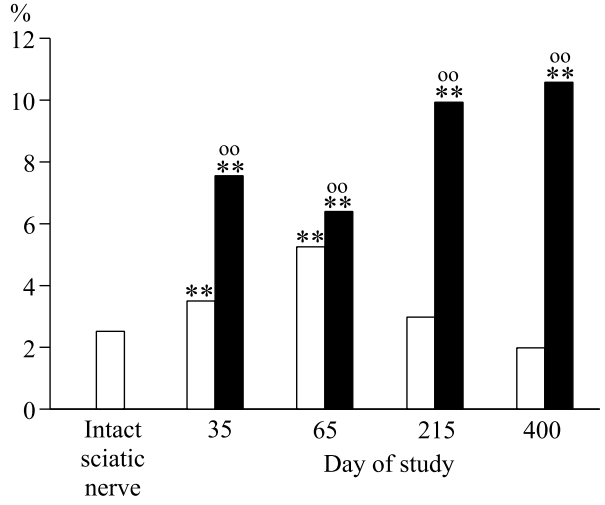

Fig. 2. Percentage of destroyed myelinated fibers in the intact sciatic nerve and in sciatic nerve in surgical (series I) and conservative (series II) treatment. **p<0.001 between the values in intact sciatic nerve and values in series I and II (Kolmogorov–Smirnov,s test for independent samples): oo$p$<0.001 between values in series I and II (Wilcoxon's test for independent samples). Light bars: series I; dark bars: series II.

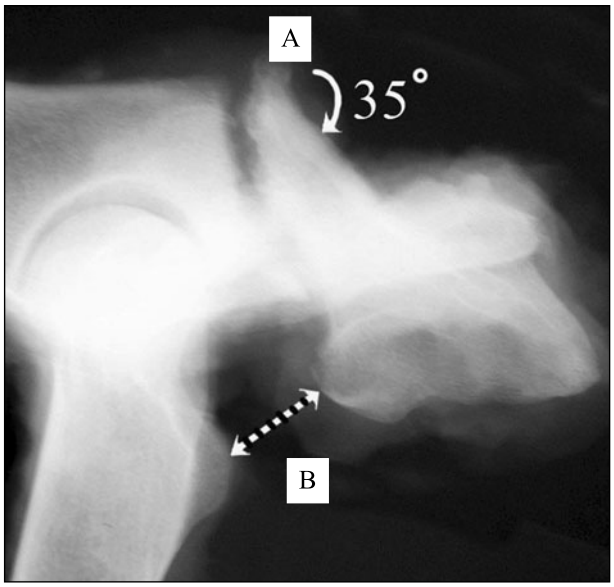

Fig. 3. Relationships between the dog pelvic and femoral organ complex under conditions of conservative therapy of the ischial bone fracture on day 65 after the injury. *A*: angle of ischial bone fragment dislocation in sagittal plane; *B*: short distance between femoral bone greater trochanter and tuber of the ischium. Roentgenogram of the dog pelvic caudal part in lateral projection.

parameter in series I by 3.3 and 5.3 times, respectively. After 400 days, Deg% in one animal was similar to the control due to lesser dislocation of the bone fragment. The large conductor fraction was restored, D_{mf} reached the normal level (Table 1).

Hence, the data indicate that the ischial bone fracture is associated with the sciatic nerve neuropraxia and axonotmesis. This type of the peripheral nerve injury is more incident in closed traumas and is caused by nerve stretching and compression in the damaged region [7]. Despite the creation of favorable conditions (surgical treatment, providing stable fixation of bone fragments), the nerve restoration takes a long time. Conservative treatment is associated with further damage to the sciatic nerve, paralleled by overall destruction of the myelinated fibers at the early stage of the experiment. A great number of conductors with signs of axonal and wallerian degeneration was retained until the end of the experiment (their level after 400 days surpassed the normal level 5.3 times and their number reduced). This phenomenon was characterized as tunnel neuropathy [4] caused by the nerve compression in anatomically stenosed sites formed by the bones, fibrous degenerative tissues, and bone fragments.

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