Pathomechanisms of Sciatica in Lumbar Disc Herniation. Ultrastructural Analysis of Periradicular Adhesive Tissue

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Introduction: Sciatic pain is a frequent clinical problem. An important manifestation of the degenerative lumbar spine is pain radiating to the legs, also called sciatica. The straight-leg-raising (SLR) test is one of the most significant signs for making a clinical diagnosis of lumbar disc herniation [1]. Our previous study showed that intraradicular blood flow and electrophysiological values apparently disturbed during the SLR test in patients with disc herniation [2,3]. This study is to investigate the relationships between nerve root movement and the electrophysiological values during an intraoperative SLR test in vivo. And also, the mechanisms responsible for the adhesive nerve root were studied by examining herniated tissue collected at operation from patients with lumbar disc herniation.

Methods: The subjects were 18 patients with lumbar disc herniation who underwent microdiscectomy (11 men and 7 women, aged 40.3 years on averag [range, 17-59]). The details of this study were explained to the patients in obtaining their informed consent in advance. Regarding operated disc levels, 10 patients were operated on L4/5 disc and 8 patients on L5/S1 disc. The preoperative SLR test revealed that 12 patients experienced sciatica below an angle of 30 degrees and 6 patients from 30 to 60 degrees. First, we confirmed that the nerve roots were compressed by the hernia by observation under an operating microscope, and then performed an intraoperative reverse SLR test by hanging down the patients' leg on the affected side from the operating table with the knees extended while the nerve roots were observed under the microscope. If there was mild adhesion of the hernia to the dura mater that were easily removed by a micro-dissector, this was classified as type 1 (Fig. 1A), and severe adhesions that were difficult to remove by a micro-dissector were classified as type 2 (Fig. 1B). Then, the nerve root function was evaluated electrophysiologically using the action potentials from the nerve root after tibian nerve stimulation at the popliteal fossa. The tibian nerve was stimulated with 0.1-ms square-wave voltage pulses at a rate of 2.0/s using a surface electrode. The stimulus intensity was adjusted to 20-35 mA and 100 responses were summated. The amplitude of action potential was recorded directly from the nerve root. The patients' legs were allowed to hang down to the angle at which sciatica was experienced before the operation and kept at that position for 30 seconds while the changes of amplitude were measured. After removal of the hernia, the SLR test was conducted up to 60 degrees in all patients. The periradicular specimens collected during surgery were examined by light and electron microscope.

Results: Nerve root movement was clearly disturbed, being only 0 ~ 1 mm (0.2 ± 0.5 mm on average) during intraoperative SLR test. After removal of the hernia, the nerve roots showed smooth gliding in all patients, with the gliding distance of the nerve root being 1 ~ 4 mm (2.1 ± 0.9mm) at an angle of 60 degrees. During the SLR test, amplitude was decreased by 8.0 ~ 65.3% (34.2 ± 18.7% on average) after initiating the test. When the angle of the legs was returned to zero degrees, amplitude showed an immediate improvement and the value recovered to that obtained before the SLR test. After removal of the hernia, the SLR test conducted showed no significant decrease of amplitude, and confirmed that discectomy had improved nerve conduction function. When the SLR test was performed at 1 week after the operation, all the patients were negative and did not develop sciatica, unlike the results obtained preoperatively. We permitted the correlation between nerve root motion and amplitude from the results of SLR test before and after removal the hernia (Fig.1).

During the operation, microscopic observation revealed that a hernia mass was adhered to dura mater of the nerve roots in all the patients. Regarding the severity of adhesion of the hernia to the dura mater, 8 patients showed type 1 adhesions and 10 patients showed type 2 adhesions. In particular, transligamentous and sequestrated hernias were associated with severe adhesions to the dura mater. In the histological examination, type 2 adhesions showed the severe inflammatory changes with granulation in the periradicular and herniated tissue (Fig.2A). In the electron micrograph, high endothelial venules [HEV] (Fig.2B), development capillaries (Fig.2C), and lymphatic vessels (Fig.2D) and were present in the periradicular adhesive tissue. Examination at high magnification showed many pinocytotic vesicles in the vascular endothelial cells. Many macrophages and fibroblasts infiltration observed adjacent to the dura mater of nerve root (Fig.3), and many fibroblasts producing collagen fibers were observed in the periradicular adhesive tissue (Fig.3A). On the other hand, many macrophages also observed adjacent to the herniated tissue of nucleus pulposus showed the presence of phagocytic vacuole(phagosome) that phagocyteze collagen fibers, as well as primary lysosomes that are important in the digestion and degradation of substances (Fig.3B).
**Discussion**: Vascularization and HEV with high endothelial cells were observed in the periradicular adhesive tissue around the site of herniation. HEV are found in virtually all peripheral lymph tissue, except the spleen [4]. Formation of new HEV is also said to occur in inflammatory lesions, and HEV are believed to be closely involved in the adhesion and migration of inflammatory cells (especially macrophages and lymphocytes) mobilized locally. Briefly, HEV do not appear to be specific to lymph tissue but instead appear to differentiate, even if only temporarily, from ordinary venules in any part of the body, thereby regulating the local immune response by allowing local lymphocyte infiltration. Thus, vascularization will occur at site of inflammation by some chemical factors of herniated disc and will make the periradicular adhesive tissue around disc herniation. In previous our study, nerve root motion was clearly disturbed and there was a sharp decrease of intraradicular blood flow and amplitude during SLR test [2,3]. After removal of the hernia, the nerve roots showed smooth gliding in all patients and the SLR test showed no significant decrease of blood flow and amplitude. The presence of periradicular adhesions will compound the nerve root pain by fixing the nerve in one position and thus increasing the susceptibility of the nerve root to tension or compression. Periradicular adhesion led to severe tension or compression on the nerve root, thus causing disturbance of intraradicular blood flow and breakdown of the blood-nerve barrier, resulting in intraradicular inflammatory changes such as edema and demyelination [5]. On the other hand, it is apparent from the natural history of lumbar disc herniation that an inflammatory reaction around the hernia is essential for spontaneous involution of the mass.

**Significance**: Control of the periradicular inflammatory reaction is an important challenge when treating patients with disc herniation.

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Fig. 1. Changes of action potentials during SLR test
Fig. 2. Light (A) and electron (B-D) micrographs of periradicular adhesive tissue. B. High endothelial venule, C. Development capillary, D. Lymphatic vessel.
Fig 3. Electron micrographs of periradicular adhesive tissue adjacent to the dura mater of nerve root (A) and around disc herniation (B). [F: fibroblast, H: herniated tissue, M: macrophage, P: periradicular adhesive tissue]