INTRODUCTION: Degenerative changes of the cervical spine, such as cervical spondylotic myelopathy (CSM), ossification of posterior longitudinal ligaments (OPPL), ossification of yellow ligaments (OYL), are very common causes for cervical myelopathy. Chronic myelopathy, caused by degeneration of the cervical spine, impairs motor and sensory functions insidiously and progressively. One of characteristics of chronic compression of spinal cord, not so in acute spinal cord injury, is to have spinal plasticity.

The exact mechanisms of chronic spinal cord compression are not fully understood. Attempts have been made to reproduce the chronic cervical cord compression in animal models; however the characteristic temporal profile, which is the hallmark of the clinical condition, had not been adequately reproduced. An appropriate model for the pathophysiology of this condition should exhibit a latency period after induction of compression with insidious onset of neurological dysfunctions, followed by a phase of progressive disturbance[1,2]. Furthermore, it was also important to make the model without direct surgical stress to the spinal cord. The purpose of this study was to produce a new model of chronic cervical cord compression satisfying these clinical conditions, while assessing through the evaluation of motor and sensory functions, MRI image and histopathological examination.

METHODS: 17 Sprague-Dawley 4 weeks-old male rats were anesthetized with an intraperitoneal injection of 35 mg/kg pentobarbital sodium. With the rats prone, C4 laminas were exposed, and bilateral C4 and C5 roots were identified. The polyethylene line (PE, catch, Tole, Japan) was inserted against the ventral aspect of the vertebral body of C4 and a plastic plate (1mm×2mm×0.5mm, Japan) was inserted against the ventral aspect of the vertebral body of C4. Polyethylene line was fastened with three laps. The CCS (Cervical Canal Stenosis) model rats and the sham rats, whose polyethylene line were fastened and immediately removed, were kept for 12 months in ordinary laboratory conditions.

Neurological motor and sensory functions in each group were assessed at 3, 6 and 12 months after surgery following the Basso Beattie and Bresnahan (BBB) Locomotor Rating Scale and Von Frey filament test. In the radiograph assessment, the anteroposterior (A-P) diameter of spinal canal and vertebral body from C2 to C6 were measured at 3, 6, 12 months after surgery. MRI imaging studies were performed at 12 months after surgery on a 0.4T permanent magnet. Transverse areas of C4/C5 disc spinal cord level in T1-weighted axial views were obtained. Signal-difference-to-noise ratios (SDNRs) of all sequences were evaluated for the cervical spinal cord to assess the contrast of the spinal cord to the surrounding tissue of the spinal canal. All animals were sacrificed 12 months after surgery for histopathological examinations. The light microscopy specimens were sliced to a thickness of 5-μm and stained with Nissl-stain. The motoneurons were counted in each segment.

The experiment was carried out under the control of the local animal ethics committee in accordance with guidelines on animal experiment in our university, Japanese government animal protection and management law, and Japanese government notification on feeding and safekeeping of animals.

RESULTS: Postoperatively, the rats were in good, healthy condition without any infections. The body weight increased rapidly from 51.0±1.1g at surgery to 481.7±14.7g (control rat) or to 465.0±19.8g (CCS model rat) at 3 months after surgery. Afterward, body weight increased gradually in both groups (control rat was 883.3±43.2g and CCS model rat was 848.9±43.9g at 1 year after surgery), and no difference was detected between the two groups in that course.

BBB scale of CCS model (17.3±1.6 points) rat was lower than control rat (20.8±0.4 points) after 12 months; however there were no differences between each group until 6 months after surgery. In the von Frey filament test, the response frequency of CCS model had no differences between control rats until 6 month after surgery, but the decreasing response frequency of CCS model appeared after 12 months.

The mean A-P diameter of spinal canal at C4 compression level of CCS model was progressively narrowed, and after 12 months, which was about 65% of control rat. At 12 months after surgery, compression of the spinal cord was evident with flattening of the cross-section view in CCS model rat. The transverse area of the spinal cord was 10.57±1.9mm² in the control rat and 7.98±1.7mm² in CCS model rat (Fig.1 A, B). The SDNR of CCS model rat (31.4±13.6) was significant higher than normal rat (20.4±5.5), and a high-intensity area in T2-weighted MRI spinal cord image was observed in the CCS model rat.

In the CCS model rat, the spinal cord was compressed along the whole circumference, and the neurons were flatter, smaller, and decreased in number of motoneurons in the gray matter (Fig. 1C, D).

DISCUSSION: In previous studies, various methods have been undertaken to induce spinal cord compression. These include transplantation of tumor cells, placement of screws with gradual tightening, implantation of an expanding sheet, a combination of vascular ligation plus screw compression, and the tip-toe-walking Yoshimura (twy/twy) mouse. These models had various difficult problems; the time course of these tumor models was too rapid, epidural tissues were injured during the direct implantation of the sheet or screws placement, and the compression site of twy-mouse could not select without C1–C2 vertebral level.

In this model, the polyethylene line cuts into the dorsal wall of the spinal canal following the growth of the spinal canal and vertebral body, and gradually compressed the spinal cord. After 12 months from surgery, spinal canal of CCS model rat was narrowed to 65%, and spinal cord was compressed to 74% of control rat. This model was unique because of the slow disease’s course, the lack of surgical damage in spinal epidural tissues or direct damage to spinal cord. Additionally, behavioral assessment was helpful and meaningful to accurately know specific functions of spinal cord.

In our model, rats with polyethylene line presented motor deficits and sensory disturbances 12 months after surgery, however no clinical manifestation took place until 6 months after surgery. This insidious and delayed onset of symptoms is one of the most typical characteristics of chronic compression of spinal cord.

CONCLUSION: The present study produced new model of chronic cervical cord compression without direct injury on cord in the rat.

REFERENCES: