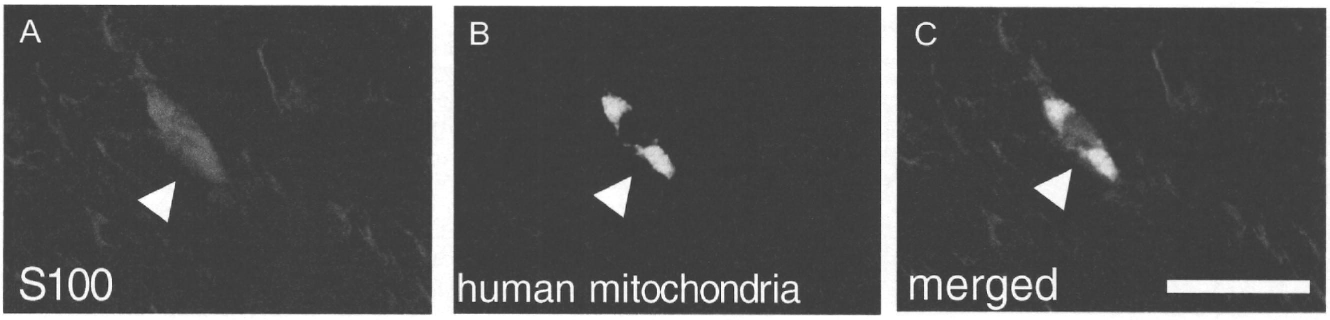

Fig. 5 Double immunofluorescence study for cell marker in the Schwann cells induced from human bone marrow stromal cells (hBMSC-SC) group 5 weeks after transplantation. (A) S-100 (B) human mitchondria (C) merged view; arrowhead indicates S-100 and human mitchondria double-positive cell. Bar = 50 μm.

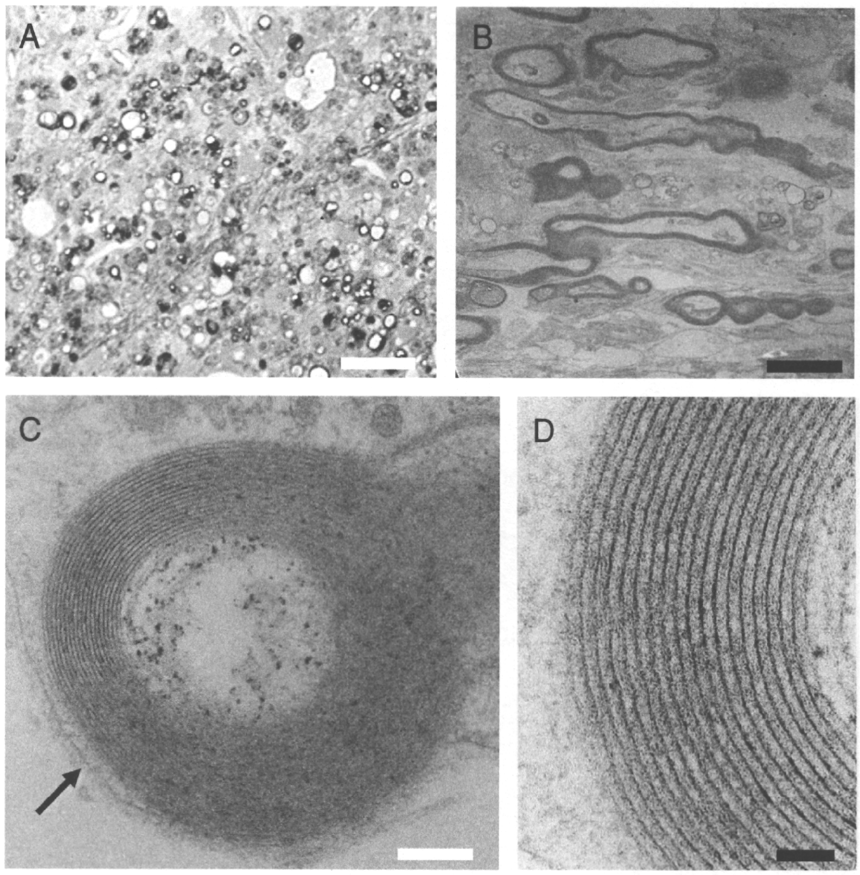

Fig. 6 Electron microscopic findings in the Schwann cells induced from bone marrow stromal cells (BMSC-SC) group. (A) Photomicrograph of Epon-embedded semi-thin transverse sections stained with toluidine blue. (B) Lower-magnification view and (C, D) higher-magnification views. (A, B) Large numbers of myelin sheaths were observed near the injured site. (C, D) Higher-magnification image revealing lamellar formation with basement membrane, which is characteristic of peripheral-type myelin (arrow in (C)). Bars = 10 μm in (A), 1 μm in (B), 500 nm in (C) and 100 nm in (D).

between the reduction of cystic cavity volume and hind limb functional recovery has been reported.[21–23] Thus the reduction of the area of cystic cavity reflects spinal cord tissue sparing, reflecting neuroprotective effects of the treatment. The present results showed that transplantation of hBMSC-SC significantly reduced the area of cystic cavity, showing the neuroprotective property of hBMSC-SC. Second, hBMSC-SC has a potential to enhance axonal regeneration similar to those of rat BMSC-SC.[7,8] The present results showed that transplantation of hBMSC-SC increased the number of GAP-43-positive fibers at the lesioned site and the adjacent sites. Similarly, hBMSC-SC increased the number of TH- and serotonin-positive fibers at the caudal site in contused adult rat spinal cord, both descending fibers of which contribute to motor function.[15–18] GAP-43-positive fibers may include not only regenerating fibers but also local sprouting. TH-positive fibers may include not only descending fibers but also peripheral fibers derived from sympathetic nerves as well.[24] Thus it is hard to distinguish between regenerating central

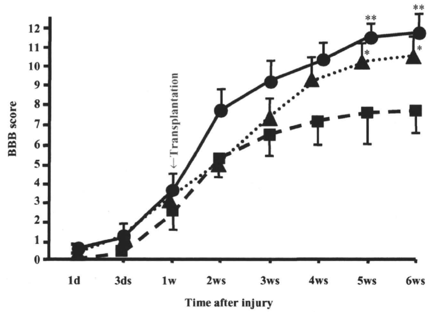

Fig. 7 Hind limb functional recovery. Hind limb function recovered significantly in the Schwann cells induced from human bone marrow stromal cells (hBMSC-SC) (triangle, $*P < 0.05$) and hBMSC-SC (square, $**P < 0.01$) groups from 4 weeks after transplantation, and a significant difference from the Matrigel alone (MG) group (circle) was maintained until 5 weeks after transplantation. The average recovery score in the hBMSC group was 10.5, which indicates occasional weight-supported plantar steps without fore limb–hind limb coordination, and the average recovery score in the hBMSC-SC group was 11.7, which indicates frequent and consistent weight-supported plantar steps and occasional fore limb–hind limb coordination, whereas that in the MG group it was 7.67, which indicates all three joints of hind limbs had extensive movement. $*P < 0.05$ and $**P < 0.01$. Bars = ± SE.

axons from local sprouting and/or peripheral-derived axons. However, recent reports showed that local sprouting can contribute to functional recovery.[25,26] Therefore, the increased number of several types of nerve fibers might associate with functional recovery.

In the present study, injured rats showed a tendency to recover at a relatively early stage after transplantation of transplanted cells, and also only a small number of transplanted cells survived in the injured spinal cord. Thus, it is more likely that the soluble factors secreted from transplanted hBMSC-SC influenced the course of improvement than that integration of transplanted cells into host neural circuit contributes to functional recovery. Our hypothesis is supported by the recent findings that BMSC can secrete several neurotrophic factors and these factors would have the potential to work effectively toward the recovery of spinal cord injury.[9,27,28] To elucidate the soluble factors secreted from hBMSC-SC, we performed cytokine antibody array. The results of cytokine antibody array revealed that several kinds of growth factors are potentially neurotrophic. For example, VEGF is known to suppress secondary degeneration and promote functional recovery after spinal cord injury,[29] TIMP-1 and 2 were reported to suppress the apoptosis of neurons[30] and TIMP-2 has been reported to promote neurite outgrowth of PC-12 cells.[31]

In addition to these mechanisms, hBMSC-SC may enhance re-myelination as shown by the findings of electronic microscopy in the present study. The fact that only a few hBMSC-SC could survive in the lesioned spinal cord suggests that transplantation of hBMSC-SC promoted migration of endogenous Schwann cells into the lesioned site and they re-myelinated axons in the injured spinal cord together with the transplanted hBMSC-SC.[32]

We suggest that one of the possible merits of Schwann cell induction is the promotion of survival after transplantation into the lesioned spinal cord, which was shown in our previous report.[8] However, the present results showed that only a small number of transplanted hBMSC-SC could survive in the injured spinal cord regardless of immunosuppression. Immunological rejection may occur for certain xeno-grafted cells. We expect if the transplanted hBMSC-SC could survive and integrate into lesioned spinal cord, axonal regeneration and functional recovery might be more obviously accelerated.

The principal findings of the present study were that hBMSC-SC could be successfully induced from hBMSC and they could restore injured spinal cord tissue in the contusion injury model. Although more precise characterization of hBMSC-SC is needed, the present results showed that hBMSC-SC is morphologically and phenotypically identical to Schwann cells. It encourages us to step forward hBMSC-SC transplantation for clinical application that hBMSC-SC has a potential to restore lesioned spinal cord.

In conclusion, transplantation of Schwann cells derived from bone marrow stromal cells is a potentially useful treatment for spinal cord injury. Although further exploration is needed to establish optimal conditions for more effective functional recovery, our study advances us toward using cell transplantation therapy for treatment of spinal cord injury.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Fig. S1 Cytokine array analysis of hBMSC-SC-conditioned media. hBMSC-SC-conditioned media was incubated with cytokine antibody arrays following manufacturer's instruction (RayBio® human cytokine antibody array 6 and 7 (RayBiotech, Inc., Norcross, GA, US). The following factors were detected in hBMSC-SC-conditioned media: macrophage chemoattractant protein-1 (MCP-1), interleukin-6 (IL-6), insulin-like growth factor binding protein 2 and 4 (IGFBP-2 and 4), tissue inhibitor of metalloproteinase-1 and 2 (TIMP1 and 2) vascular endotherial growth factor (VEGF), urokinase receptor (uPAR), soluble tumor necrosis factor alpha receptor-1 (sTNF-αR) and interleukin-8 (IL-8) (Supporting Fig. S1). Positive control spots were indicated by asterisks.

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Fig. 2. Axial T1-weighted MRI at the same level shows hyperintensity of the left lentiform nucleus.

theories have been proposed to explain the imaging findings including calcium deposition, petechial haemorrhage, ischaemia, infarction, cytotoxic oedema and myelin breakdown. It is of note that this focal abnormality is induced by hyperglycaemia, a systemic disturbance. Pre-existing basal ganglia disease, such as focal small vessel ischaemia, may be present in these diabetic patients, with hyperglycaemia tipping the balance in these regions into cellular dysfunction. Hyperglycaemia impairs cerebral autoregulation, which may explain hypoperfusion on imaging, and causes gamma-aminobutyric acid (GABA) depletion in basal ganglia neurons as a result of anaerobic metabolism.[6] It may be the GABA depletion, the main inhibitory neurotransmitter in the basal ganglia, which results in chorea. Although much further investigation is needed, the pathological and radiological findings suggest that non-ketotic hyperglycaemic crisis induces ischaemia and metabolic disturbance resulting in basal ganglia dysfunction.

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Postoperative paralysis following posterior decompression with instrumented fusion for thoracic myelopathy caused by ossification of the posterior longitudinal ligament

Masashi Yamazaki *, Akihiko Okawa, Chikato Mannoji, Takayuki Fujiyoshi, Takeo Furuya, Masao Koda

Spine Section, Department of Orthopaedic Surgery, Chiba University Graduate School of Medicine, 1-8-1 Inohana, Chuo-ku, Chiba 260-8677, Japan

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ABSTRACT

A 60-year-old man presented with thoracic myelopathy due to ossification of the posterior longitudinal ligament (OPLL). His spinal cord was severely impinged anteriorly by a beak-type OPLL and posteriorly by ossification of the ligamentum flavum at T4/5. He underwent surgical posterior decompression with instrumented fusion (PDF). Immediately after surgery, he developed a Brown-Séquard-type paralysis, which spontaneously resolved without requiring the addition of OPLL extirpation. This example highlights that the risk of postoperative neurological deterioration cannot be eliminated even when PDF is selected as the surgical procedure for thoracic OPLL, especially in instances in which the spinal cord is severely compressed.

1. Introduction

Despite the variety of surgical procedures for treating thoracic myelopathy due to ossification of the posterior longitudinal liga-

* Corresponding author. Tel.: +81 43 226 2117; fax: +81 43 226 2116.
E-mail address: masashiy@faculty.chiba-u.jp (M. Yamazaki).

ment (OPLL), postoperative paraplegia remains a major risk.[1,2] Twenty years ago, we hypothesized that stabilizing the spine with instrumentation could yield a certain degree of neurological recovery even without complete OPLL extirpation. Based on this hypothesis, in 1989 we introduced the surgical procedure of posterior decompression with instrumented fusion (PDF) for patients with thoracic OPLL. In our earlier study of 17 patients who underwent PDF for thoracic OPLL, all of the patients had a considerable degree of neurological recovery and no postoperative paralysis occurred.[3] Based on the results of that study, we have employed PDF for all instances of thoracic OPLL treated surgically at our institute since 2003. Subsequently, however, we had our first encounter with postoperative paralysis in our 23rd PDF patient.

2. Case report

A 60-year-old man had thoracic myelopathy with a Japanese Orthopaedic Association (JOA) score of 4.5, on a scale from 0 to 11. He complained of bilateral motor weakness of his lower extremities and was unable to walk without a cane. Lateral radiographs showed T4–9 OPLL. MRI scans showed severe narrowing of the spinal cord at T4/5. Reconstruction images from a CT myelogram showed impingement of the spinal cord anteriorly by a beak-type OPLL (Fig. 1) and posteriorly by ossification of the ligamentum flavum (OLF) (Fig. 1A) at T4/5. The image showing a beak-type OPLL also showed a non-ossified area between the ossified masses at T4/5 (Fig. 1A), indicating that the spinal column still had some mobility at the cord compression level.

We performed a T4–7 laminectomy and a T2–10 posterior instrumented fusion using pedicle screws as anchors at the T2, T3, T4, T8, T9 and T10 levels. An intraoperative spinal ultrasonography after the laminectomy showed continuing anterior impingement of the spinal cord by the beak-type OPLL at T4/5 and an absence of the subarachnoid space on the ventral side of the spinal cord (Fig. 2).

Immediately after surgery, the patient suffered a severe motor loss of his right lower limb (muscle strength at grade 0 out of 5) and analgesia of his left lower extremity and left trunk below the umbilicus, indicative of a Brown-Séquard-type paralysis. We immediately administered a 1000 mg bolus of methylprednisolone sodium succinate intravenously. One hour after surgery, we detected muscle contraction in the patient's right lower limb. The morning following surgery, his right lower limb showed a slight recovery of motor function (muscle strength at grade 1 to 3 out of 5). By the end of the day, the sensory loss in his left lower

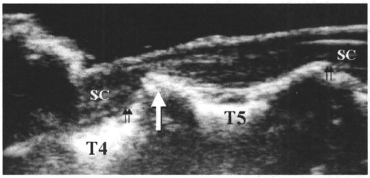

Fig. 2. Intraoperative spinal ultrasonography in the midsagittal plane after laminectomy showing anterior impingement of the spinal cord (SC) by the beak-type ossification of the posterior longitudinal ligament at T4/5 (arrow) and the absence of the subarachnoid space on the ventral side of the spinal cord from T4/5 to T5/6 (double arrows).

extremity and trunk had begun to diminish, showing hypalgesia at grade 5 to 8 out of 10. His neurological recovery gradually progressed from that point on. Three months after surgery, the patient could walk with a cane. Six months after surgery, his JOA score had risen to 7, and his recovery was 38.5%. At the final follow-up 5 years and 3 months after surgery, the patient could walk without a cane and his recovery remained at 38.5%.

3. Discussion

During PDF, we pay maximal attention to avoid injury to the spinal cord.[3] In spite of such efforts, neurological deterioration occurred immediately after surgery in this patient. This incident suggests that the decompression procedure itself entails a risk of postoperative paralysis in patients with a severely compressed spinal cord. It is possible that when the spinal cord is severely compressed by OPLL and OLF from both anterior and posterior directions, as in our patient, the risk of intraoperative injury to the spinal cord may increase. In instances with a severely pinched spinal cord, the risk of postoperative neurological deterioration evidently cannot be completely eliminated, even when PDF is selected as the surgical procedure for thoracic OPLL.

An alternative treatment option for this patient would have been single-stage anterior and posterior decompression for combined thoracic OPLL and OLF. Several authors have previously reported excellent clinical results using this procedure.[1,4] However, in the same papers, these authors also reported several examples of postoperative paralysis after single-stage anterior and posterior compression, which suggests that the overall outcomes of single-stage anterior and posterior decompression are not necessarily superior to the outcomes of PDF.[1,4]

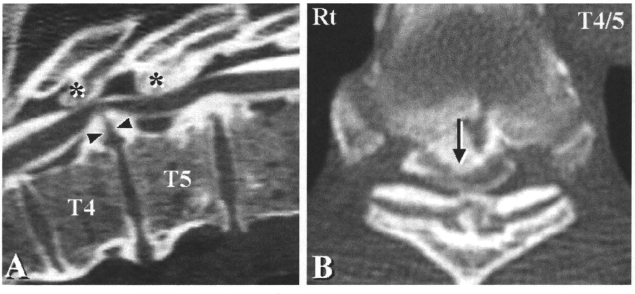

Fig. 1. Preoperative midsagittal (A) and axial (B) reconstruction images from a CT myelogram showing impingement of the spinal cord anteriorly by a beak-type ossification of the posterior longitudinal ligament (OPLL) (A, B, arrow) and posteriorly by ossification of the ligamentum flavum (A, asterisks) at T4/5. The mid-portion of the beak-type OPLL contains a non-ossified area (A, arrowheads).

Published studies have also shown that anterior decompression through thoracotomy does not necessarily produce favorable results when performed as rescue surgery on thoracic OPLL and OLF patients whose myelopathy worsens after laminectomy.[5,6] Of particular concern is the possibility that worsening myelopathy might indicate severe damage to the spinal cord resulting from the laminectomy, in which case the spinal cord may likely not further tolerate an anterior decompression procedure. Because of this risk, we did not choose anterior extirpation of OPLL through thoracotomy as rescue surgery in our patient.

Fortunately, our patient's paralysis spontaneously resolved without requiring us to add OPLL extirpation. In light of what appears to be a higher risk of postoperative paralysis following other surgical procedures such as laminectomy alone and OPLL extirpation,[1,2] we suggest that PDF is still the safest surgical procedure among the surgical treatment alternatives for thoracic OPLL. To further improve the safety of PDF for thoracic OPLL, however, we will need to further modify the treatment protocol to reduce the risk of damage to the spinal cord during PDF. One promising possibility is neuroprotective therapy with preoperative administration of neural growth factors.

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Fourth-ventricular immature teratoma

Sunil V. Furtado *, Nandita Ghosal, Vishal B. Rokade, Alangar S. Hegde

Department of Neurosurgery, Sri Sathya Sai Institute of Higher Medical Sciences, EPIP Area, Whitefield, Bangalore 560066, Karnataka State, India

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ABSTRACT

Teratomas account for 3% of all childhood tumors. This group of non-germinomatous germ cell tumors exhibit cellular and structural characteristics associated with the three germ layers. The immature cells can differentiate into more malignant neoplasms. We report the presentation and management of a 4-year-old girl with an immature teratoma of the fourth ventricle. The outcome of this intracranial immature teratoma was poor, due to the patient's age, the extensive lesion at presentation and the grade of the tumor.

1. Introduction

Intracranial teratomas represent 2% to 5% of all teratomas in infancy and account for 0.3% to 0.6% of all intracranial neoplasms.[1,2] They are seen involving midline intracranial structures; are more commonly reported in the pineal region, third ventricle and suprasellar region; and present with obstructive hydrocephalus.[1,3,4] Teratomas are extremely rare in the posterior fossa and are seldom reported in children beyond 2 years of age. We present a rare, large immature teratoma based exclusively in the fourth ventricle.

2. Case report

A 4-year-old girl with a 2-month history of headaches and vomiting presented with two episodes of hydrocephalus. She had left-side abducens palsy and florid papilledema. Her head circumference was normal for her age. A CT scan of her head revealed an isodense lesion in the posterior fossa occupying the entire fourth ventricle and causing obstructive hydrocephalus, for which she underwent an emergency ventriculoperitoneal shunt (Fig. 1a). A MRI brain scan showed a lesion in the fourth ventricle arising from the vermis with mixed intensity on T1- and T2-weighted images, with cystic areas and exhibiting non-homogeneous contrast enhancement. The patient underwent a midline suboccipital craniotomy and decompression of the tumour through the vermis (Fig. 1b,c,d). The tumor was grey and soft to firm in consistency with areas of calcification. It was infiltrating the floor of the fourth ventricle and was merging imperceptibly with the vermis. Near-total decompression was achieved because of brainstem infiltration. A postoperative MRI scan showed residual tumor along the ventricular floor with minimal blood in the operative cavity (Fig. 2). Histopathological examination revealed an immature teratoma of the posterior fossa having glial components with immature neural

* Corresponding author. Tel.: +91 80 2841 6837; fax: +91 80 2841 1503.
E-mail address: sunilvf@gmail.com (S.V. Furtado).

Posterior Decompression with Instrumented Fusion for Thoracic Myelopathy caused by Ossification of the Posterior Longitudinal Ligament : Clinical Results and Mechanisms for the Improvement of Myelopathy

Masashi Yamazaki, Akihiko Okawa, Tsuyoshi Sakuma, Hiroshi Takahashi,
Kei Kato, Mitsuhiro Hashimoto, Masao Koda, Kazuhisa Takahashi

Key words : thoracic myelopathy, ossification of posterior longitudinal ligament, kyphosis, spinal mobility, instrumented fusion

Introduction

To treat thoracic ossification of the posterior longitudinal ligament (OPLL), surgeons have employed a variety of surgical procedures ; however, postoperative paraplegia has remained a major risk[1,2]. At our institute, two patients experienced transient postoperative paraparesis after laminectomy, which resolved after the addition of posterior instrumented fusion without OPLL extirpation[3,5]. On the basis of these two cases, we hypothesized that stabilizing the spine with instrumentation could yield a certain degree of neurological recovery even without complete OPLL extirpation. Based on this hypothesis, in 1989 we first introduced the surgical procedure of posterior decompression with instrumented fusion (PDF) for patients with thoracic OPLL, in whom OPLL extirpation entailed a risk of neurological deterioration[4]. In the present study we analyzed the process of neurological recovery after PDF in patients we have treated at our institute. In addition, we analyzed the contribution of thoracic kyphosis correction following PDF to the neurological recovery.

Materials and Methods

1 . Patient Population

From May 1989 through February 2007, a total of 29 patients with thoracic myelopathy because of OPLL underwent PDF at our institute. The group comprised 8 men and 21 women. The mean age at surgery was 55.1 years, ranging from 32 to 74 years. The mean follow-up period was 6 years and 10 months, ranging from 2 years to 20 years and 5 months.

2 . Surgery

We principally performed a laminectomy at sites where preoperative radiographic and magnetic resonance images showed loss of the subarachnoid space on the dorsal side of the spinal cord. After confirming the adequacy of the posterior decompression with intraoperative spinal ultrasonography, we performed posterior spinal fixation using a hook and pedicle screw-rod system. We usually did not correct kyphosis at the rod setting, but performed the fixation *in situ*.

3 . Clinical Assessment

Surgical outcomes were evaluated using the Japanese Orthopaedic Association (JOA) score (full score = 11 points), and recovery rate was calculated[4]. We assessed the JOA score before surgery, at 3, 6, 9, 12 months after surgery, and at the final follow-up.

4 . Radiographic Assessment

In six consecutive patients (Cases 19 through 24), we preoperatively measured the kyphotic angles at the

Department of Orthopaedic Surgery, Chiba University Graduate School of Medicine〔1-8-1 Inohana, Chuo-ku, Chiba 260-8677, Japan〕

instrumented fusion levels in the supine, prone, and sitting positions. To calculate the kyphotic angle, we measured the sagittal Cobb angle between the upper endplate of the uppermost vertebra and the lower endplate of the lowest vertebra at the instrumented fusion levels.

5. Statistical Analysis

Statistical analysis was performed using a Mann-Whitney *U* test. A *p*-value$<$0.05 was considered statistically significant.

Results

1. Surgical Outcome

The JOA score before surgery was 3.6±1.4. All patients showed neurological recovery at the final follow-up ; the JOA score at final follow-up was 7.8±2.0, and the mean recovery rate was 57.0%.

The JOA score was 6.3±1.9 at 3 months after surgery, 7.2±2.0 at 6 months after surgery, 7.6±2.0 at 9 months after surgery, and 7.8±2.0 at 12 months after surgery. The JOA score 3 months after surgery and later was significantly higher than that before surgery. In addition, the JOA score 9 months after surgery and later was significantly higher than that 3 months after surgery. The mean recovery rate was 37.5% at 3 months after surgery, 48.6% at 6 months after surgery, 53.8% at 9 months after surgery and 56.4% at 12 months after surgery. The recovery rate 9 months after surgery and later was significantly higher than that 3 months after surgery. The time at which the JOA score reached its peak value was 9±4.8 months (range : 3-24) after surgery.

One patient chose additional anterior decompression surgery via thoracotomy 1 year and 11 months after PDF.

No patient developed persistent paralysis after surgery, but two patients (6.9%) had transient paralysis immediately after surgery.

2. Kyphotic Angles at Instrumented Fusion Levels

The difference between the kyphotic angle in the supine position and the kyphotic angle in the sitting position ranged from 8 to 20 degrees, indicating that some mobility remained in the thoracic spine in spite of the presence of OPLL. The mean spinal mobility per disc was 1.3 degrees, ranging from 0.9 to 2.0 degrees.

In all six patients, the postoperative kyphotic angle at the instrumented fusion levels was greater than the preoperative kyphotic angle in the supine position, but less than the preoperative kyphotic angle in the sitting position. Evaluating the correction of kyphosis after surgery with respect to the preoperative kyphotic angle in the sitting position demonstrated some correction of the kyphosis, with a mean change in the kyphotic angle of 3.2 degrees.

Discussion

The present results demonstrated that the surgical outcome of PDF was superior to the surgical outcome of laminectomy alone[1,4]. When laminectomy alone is performed for thoracic OPLL, the posterior shift of the spinal cord is often restricted because the thoracic spine is physiologically kyphotic, leading to persistent anterior impingement of the spinal cord by OPLL. Despite this insufficient decompression of the spinal cord, PDF resulted in considerable neurological recovery, indicating that posterior instrumented fusion has some positive effect on myelopathy after laminectomy for thoracic OPLL.

In this study, we also demonstrated that in patients with thoracic OPLL, the spinal column still showed some mobility at the cord compression level in spite of the presence of massive heterotopic vertebral ossification. We suggest that the remaining mobility of the spinal column at the cord compression level correlates with the development and aggravation of myelopathy in patients with thoracic OPLL.

We measured kyphotic angles in six consecutive cases to determine the extent of correction of kyphosis by the posterior instrumented fusion. Even when we based our calculation of the correction of kyphosis upon the preoperative kyphotic angle in the sitting position, the mean correction was still only 3.2 degrees, indicating that our posterior instrumented fusion procedure did not sufficiently correct our patients' kyphosis. In turn, these results suggest that correction of kyphosis is not a major factor contributing to the neurological improvements observed after PDF.

In the present study, myelopathy in our patients slowly improved. After PDF, anterior impingement of the spinal cord by OPLL persists, but the stabilization of the spine may decrease the damage to the spinal cord at the cord compression level, enabling a slow neurological recovery to commence.

In this study, we encountered two cases of postoperative paralysis after PDF. Fortunately, the paralysis spontaneously resolved without any additional requirement for OPLL extirpation. These incidents suggest that the decompression procedure itself in patients with a severely compressed spinal cord entails a risk of postoperative paralysis, such that even the selection of PDF as our surgical procedure for thoracic OPLL cannot completely eliminate the risk of postoperative paralysis. However, in light of what appears to be a higher risk of postoperative paralysis following other surgical procedures such as laminectomy alone and OPLL extirpation[1,4], we suggest that PDF is the safest surgical procedure among the alternatives for thoracic OPLL.

When neurological recovery after PDF is insufficient, addition of anterior OPLL extirpation surgery should be considered. The present findings demonstrating gradual neurological recovery after PDF, indicate that additional anterior surgery during the early stage of recovery after PDF generally is not desirable. Instead, we should follow postoperative neurological recovery in patients for at least nine months before arriving at a decision regarding additional anterior surgery.

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Outcome of Posterior Decompression Surgery for Cervical OPLL Patients of the K-line (−) Group : Laminoplasty versus Posterior Decompression with Instrumented Fusion

Takayuki Fujiyoshi*[1,2], Masashi Yamazaki*[1], Akihiko Okawa*[1], Takeo Furuya*[1], Masao Koda*[1], Kazuhisa Takahashi*[1], Hiroaki Konishi*[3]

Key words : cervical myelopathy, ossification of posterior longitudinal ligament, dynamic factor

Introduction

We have recently reported a concept for making decisions regarding the surgical approach for cervical ossification of the posterior longitudinal ligament (OPLL) : the K-line, or line that connects the midpoints of the spinal canal at C2 and C7. When the OPLL exceeds the K-line, the patient is classified into a K-line (−) group[1)]. Our studies using intraoperative spinal ultrasonography showed that sufficient posterior shift of the spinal cord was not obtained after posterior decompression surgery in the K-line (−) group, leading to poor surgical outcome[1)]. We have also reported that hypermobility of vertebrae at the maximum cord compression level is a risk factor for poor surgical outcome after laminoplasty for patients with cervical myelopathy because of OPLL[5)]. Moreover, our analyses of asymptomatic OPLL patients have shown that patients with massive OPLL barely developed myelopathy when the mobility of their cervical spine was highly restricted[2)]. From these findings, we hypothesized that the key for the development of cervical myelopathy because of OPLL would be a dynamic factor, and that by controlling the instability, better neurological recovery could be obtained. In the present study, we analyzed the efficacy of posterior decompression with instrumented fusion for cervical OPLL patients of the K-line (−) group.

Methods

1. Patient Population

From January 2000 through March 2007, a total of 14 OPLL patients of the K-line (−) group underwent posterior decompression surgery in our institute. Laminoplasty was performed in 7 patients (LMP group) and posterior decompression (laminoplasty or laminectomy) with instrumented fusion in 7 patients (PDF group). Regarding surgical indication, we performed laminoplasty for all OPLL patients of the K-line (−) group from January 2000 through August 2002. From September 2002, we principally performed PDF for all OPLL patients of the K-line (−) group.

2. Surgery

Our surgical cervical laminoplasty procedure was a C3-7 en block laminoplasty (Itoh's method)[5)]. We principally performed a bilateral open door laminoplasty or laminectomy at C3-7 for the PDF surgical procedure. We initially used pedicle screws at C2 and C7 and lateral mass screws at C3, C4, and C5, and connected 3.2mm or 3.5mm diameter rods to the instrumented fusion anchors. We did not usually correct the kyphosis at the rod setting, but performed the fixation *in situ*. For bone grafting, we used spinous processes that we had extirpated before laminoplasty or laminectomy and grafted them onto the facets.

*[1]Department of Orthopaedic Surgery, Chiba University Graduate School of Medicine〔1-8-1 Inohana, Chuo-ku, Chiba 260-8677, Japan〕
*[2]Department of Orthopaedic Surgery, Kimitsu Chuo Hospital
*[3]Department of Orthopaedic Surgery, Nagasaki Rosai Hospital

Table 1 Clinical data for laminoplasty group and posterior decompression with fusion group

Surgical groups	LMP group [$n=7$]	PDF group [$n=7$]
Age at surgery (yrs)*	65.6 ± 11.6 (48-81)	67.7 ± 10.1 (54-80)
Follow-up period (mths)*	48.1 ± 35.3 (18-100)	43.1 ± 19.4 (21-72)
JOA score (points)*		
Before surgery	9.8 ± 3.5 (5.5-16)	6.7 ± 1.9 (4.5-9.5)
After surgery	9.3 ± 3.9 (5-16)	10.8 ± 3.4 (4.5-13)
Recovery rate (%)*	−7.3 ± 26.9 (−50-21.7)	41.3 ± 23.1** (0-61.9)
Occupation ratio of OPLL (%)*	63.8 ± 16.7 (38-90)	65.1 ± 16.9 (45-92.7)
SRM (degrees)*	7.8 ± 3.7 (3-12)	10.5 ± 6.1 (1.6-19.4)

LMP : laminoplasty, PDF : posterior decompression with instrumented fusion, JOA : Japanese Orthopaedic Association, SRM : segmental range of motion at the maximum spinal cord compression level.
*Values are expressed as mean ± standard error, with the range in parentheses.
**Statistically different from the LMP group ($p<0.05$).

3. Clinical Assessment

We noted age at surgery, and investigated the length of the follow-up period, and pre- and post-operative Japanese Orthopaedic Association (JOA) scores for cervical myelopathy (full score = 17 points)[5], and recovery ratio[5].

4. Radiographic Assessment

Using cervical lateral radiographs, we measured the occupation ratio of the spinal canal by OPLL[5]. The segmental range of motion at the maximum spinal cord compression level (SRM) was measured from cervical flexion and extension radiographs[5].

5. Statistical Analysis

We used a Mann-Whitney *U* test to determine differences between the PDF and LMP patient groups. A p-value <0.05 was considered statistically significant.

Results

Age at surgery was 65.6 ± 11.6 years old in the LMP group and 67.7 ± 10.1 years old in the PDF group. The follow-up period was 48.1 ± 35.3 months in the LMP group and 43.1 ± 19.4 months in the PDF group. No significant difference was seen between the ages and the follow-up periods (Table 1).

Pre- and post-operative JOA scores were 9.8 ± 3.5 points and 9.3 ± 3.9 points in the LMP group and 6.7 ± 1.9 points and 10.8 ± 3.4 points in the PDF group. In LMP group, 3 out of 7 patients were neurological deteriorated after surgery. The recovery ratio was −7.3 ± 26.9% in the LMP group and 41.3 ± 23.1% in the PDF group ($p<0.05$) (Table 1).

The OPLL occupation ratio was 63.8 ± 16.7% in the LMP group and 65.1 ± 16.9% in the PDF group. The SRM was 7.8 ± 3.7 degrees in the LMP group and 10.5 ± 6.1 degrees in the PDF group. No significant difference was seen in the OPLL occupation ratio and the SRM (Table 1).

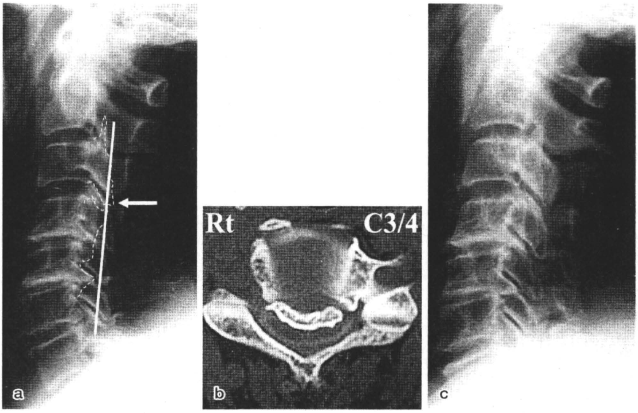

Fig. 1 Case 1

a : Preoperative cervical lateral radiograph.

b : Axial CT image at C3/4.

c : Postoperative cervical radiograph after C3-7 laminoplasty.

Case Presentation

Case 1 : LMP group

An 81-year-old woman presented with cervical myelopathy, and her preoperative JOA score was 9 points. Cervical lateral radiograph at neutral position demonstrated a C2-6 OPLL (Fig. 1a). Maximum occupation ratio of the spinal canal by OPLL was 70% at C3/4 (Fig. 1b). By the K-line classification, this case was classified as K-line (−) (Fig. 1a, arrow). Flexion and extension cervical radiographs showed the SRM at C3/4 was 12 degrees. A C3-7 laminoplasty was performed (Fig. 1c). Postoperatively, the patient had a poor neurologic recovery. Her JOA score 23 months after surgery was 5 points, indicating postoperative deterioration (recovery rate : −50%).

Case 2 : PDF group

A 67-year-old man presented with cervical myelopathy, and his preoperative JOA score was 5.5 points. Cervical lateral radiograph demonstrated C5-6 OPLL (Fig. 2a), and the maximum OPLL occupation ratio was 93% at C6 (Fig. 2b). This case was classified as K-line (−) (Fig. 2a, arrow). The SRM at C5/6 was 10 degrees. A C3-7 laminectomy and C3-T1 posterior instrumented fusion was performed (Fig. 2c). Postoperatively, the patient had a sufficient neurologic recovery. His JOA score 21 months after surgery was 12 points (recovery rate : 57%).

Discussion

Iwasaki et al. reported that the surgical outcome after laminoplasty was insufficient and inferior to anterior decompression with spinal fusion in patients with an OPLL occupation ratio >60%[3,4]. Tani et al. reported that anterior decompression surgery was superior to laminoplasty in cervical OPLL patients when the occupation ratio was >50%[9]. The main reason for such a poor surgical outcome after laminoplasty has been considered to be that posterior shift of the spinal cord is insufficient in patients with massive OPLL. We previously showed that posterior shift of the spinal cord after laminoplasty was insufficient even when the OPLL was small if patients' cervical alignment was kyphotic. Thus, we have

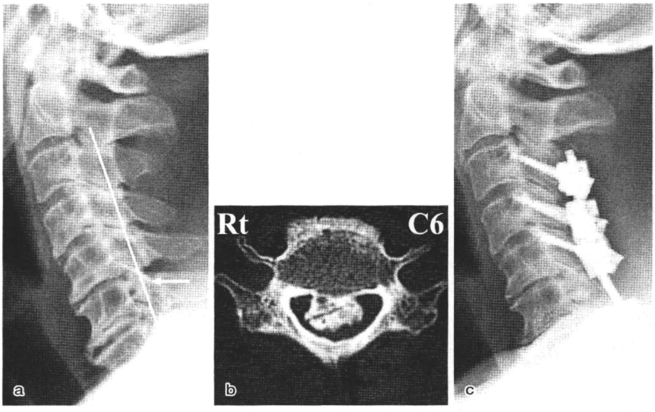

Fig. 2 Case 2

a : Preoperative cervical lateral radiograph.

b : Axial CT image at C6.

c : Postoperative cervical radiograph after C3-T1 posterior decompression with instrumented fusion.

advocated the concept of the K-line, which can evaluate OPLL size and cervical alignment in one parameter[1]. Because surgical outcome after laminoplasty was poor in cervical OPLL patients of the K-line (−) group, we recommend anterior decompression surgery for these patients[1]. In spite of such informed consent, some patients still chose laminoplasty, because the postoperative course of anterior surgery is difficult to tolerate.

Previous reports have described the importance of dynamic factors in the development of myelopathy in cervical OPLL patients[6,8]. We also reported that larger SRM is a risk factor leading to the development of myelopathy and the poor surgical outcome in patients after laminoplasty for cervical OPLL[2,5]. This finding suggests that SRM, rather than static compression factors, preferentially contributes to the development and the aggravation of myelopathy.

In the present study, we added posterior instrumented fusion to laminoplasty or laminectomy for cervical OPLL patients of the K-line (−) group. The results showed that the addition of the posterior fusion caused considerable neurological recovery compared with laminoplasty alone. We suggest that the addition of posterior instrumented fusion can eliminate the dynamic factor and achieve a better surgical outcome even in cervical OPLL patients of the K-line (−) group. The other possible positive effect of posterior instrumented fusion is a prevention of progression of cervical kyphosis after posterior decompression surgery. Analyses on the cervical alignment of LMP group and PDF group will clarify the effect.

We believe that complete excision of the ossified mass using an anterior approach is theoretically the best procedure[7]. However, when laminoplasty is selected for such cases, the addition of posterior instrumented fusion is desirable to stabilize the spine and decrease damage to the cord.

Conclusion

The present results demonstrate that, for cervical OPLL patients of the K-line (−) group, better surgical outcome can be obtained by posterior decompression with instrumented fusion when compared with laminoplasty alone.

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ORIGINAL ARTICLE

C5 palsy following anterior decompression and spinal fusion for cervical degenerative diseases

Mitsuhiro Hashimoto · Macondo Mochizuki · Atsuomi Aiba · Akihiko Okawa · Koichi Hayashi · Tsuyoshi Sakuma · Hiroshi Takahashi · Masao Koda · Kazuhisa Takahashi · Masashi Yamazaki

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Abstract Postoperative C5 palsy is a common complication after cervical spine decompression surgery. However, the incidence, prognosis, and etiology of C5 palsy after anterior decompression with spinal fusion (ASF) have not yet been fully established. In the present study, we analyzed the clinical and radiological characteristics of patients who developed C5 palsy after ASF for cervical degenerative diseases. The cases of 199 consecutive patients who underwent ASF were analyzed to clarify the incidence of postoperative C5 palsy. We also evaluated the onset and prognosis of C5 palsy. The presence of high signal changes (HSCs) in the spinal cord was analyzed using T2-weighted magnetic resonance images. C5 palsy occurred in 17 patients (8.5%), and in 15 of them, the palsy developed after ASF of 3 or more levels. Among ten patients who had a manual muscle test (MMT) grade ≤ 2 at the onset, five patients showed incomplete or no recovery. Sixteen of the 17 C5 palsy patients presented neck and shoulder pain prior to the onset of muscle weakness. In the ten patients with a MMT grade ≤ 2 at the onset, nine patients showed HSCs at the C3–C4 and C4–C5 levels. The present findings demonstrate that, in most patients with severe C5 palsy after ASF, pre-existing asymptomatic damage of the anterior horn cells at C3–C4 and C4–C5 levels may participate in the development of motor weakness in combination with the nerve root lesions that occur subsequent to ASF. Thus, when patients with spinal cord lesions at C3–C4 and C4–C5 levels undergo multilevel ASF, we should be alert to the possible occurrence of postoperative C5 palsy.

Keywords C5 palsy · Cervical spine · Anterior surgery · Decompression · Fusion

M. Hashimoto · M. Mochizuki · A. Aiba
Department of Orthopaedic Surgery,
Numazu City Hospital, 550 Harunoki,
Higashi-Shiiji, Numazu, Shizuoka 410-0302, Japan

A. Okawa · K. Hayashi · T. Sakuma · H. Takahashi · M. Koda · K. Takahashi · M. Yamazaki (✉)
Spine Section, Department of Orthopaedic Surgery,
Chiba University Graduate School of Medicine,
1-8-1 Inohana, Chuo-ku, Chiba 260-8677, Japan
e-mail: masashiy@faculty.chiba-u.jp

Introduction

Postoperative C5 palsy is well known as a common complication after decompression surgery at the cervical spine [12]. Previous reports have indicated that C5 palsy occurs not only after posterior cervical decompression surgery, such as laminoplasty [1, 2, 5, 6, 8, 10, 13, 16–19], but also after anterior surgery [3–5, 7, 14, 15, 18, 19]. However, the number of studies analyzing C5 palsy after anterior cervical surgery is smaller than that for after posterior cervical surgery. Thus, the incidence, prognosis, and etiology of the C5 palsy after anterior cervical surgery have not yet been fully established. The aim of the present study was to investigate the incidence and prognosis of C5 palsy after anterior cervical surgery and discuss the mechanism of development of this disorder.

Materials and methods

Patient population

Between 1996 and 2004, 199 patients underwent anterior decompression surgery and spinal fusion (ASF) for cervical degenerative diseases in our institute (Table 1). Their

Table 1 Cervical lesions and incidence of postoperative C5 palsy

Cervical lesions	No. of cases	Cases of palsy (%)	Patients with MMT grade ≤2 (%)
Cervical spondylotic myelopathy	113	9 (7.9)	5 (4.4)
OPLL	62	6 (9.7)	5 (8.1)
Disc herniation	2	0	0
Cervical spondylotic amyotrophy	16	2 (12.5)	0
Cervical spondylotic radiculopathy	6	0	0
Total	199	17 (8.5)	10 (5.0)

MMT Manual muscle test, *OPLL* ossification of posterior longitudinal ligament

cervical lesions were cervical spondylotic myelopathy (CSM) in 113 cases, cervical ossification of the posterior longitudinal ligament (OPLL) in 62 cases, cervical spondylotic amyotrophy (CSAM) in 16 cases, cervical spondylotic radiculopathy in 6 cases, and disc herniation in 2 cases. The number of fused levels was 1 for 33 cases, 2 for 40 cases, 3 for 46 cases, 4 for 71 cases, and 5 for 9 cases (Table 2). One level fusion surgery was performed by anterior cervical discectomy and fusion, and two or more levels of fusion surgery were performed by anterior cervical corpectomy and arthrodesis. Autologous iliac bone was grafted for one- or two-level fusions and an autologous fibula strut was grafted for fusion surgery of three or more levels [11]. In cases of one or two level fusion, a cervical collar was used postoperatively. In cases where three or more levels were fused, patients were immobilized with a halo vest for 8 weeks after surgery. No spinal instrumentation such as an anterior cervical plate system was used in the present series.

Clinical assessment

We defined C5 palsy as when patients showed a deterioration in muscle power of the deltoid or biceps brachii by at least one grade in the manual muscle test (MMT) without aggravation of lower extremity function. We evaluated the laterality of C5 palsy, onset of pain, onset of weakness, and time course of any MMT grade change. The Japanese Orthopaedic Association (JOA) score was used to evaluate the severity of myelopathy [9].

Table 2 Fused levels and C5 palsy incidence

No. of levels fused	Fused level	No. of patients	Cases of palsy (%)	Patients with MMT grade ≤2 (%)
1	C3–C4	13	0	0
	C4–C5	5	0	0
	C5–C6	11	0	0
	C6–C7	3	0	0
	C7–T1	1	0	0
	Subtotal	33	0	0
2	C3–C5	14	0	0
	C4–C6	14	2 (14.3)	1 (7.1)
	C5–C7	12	0	0
	Subtotal	40	2 (5.0)	1 (2.5)
3	C2–C5	1	0	0
	C3–C6	27	4 (14.8)	2 (7.4)
	C4–C7	15	0	0
	C5–T1	3	0	0
	Subtotal	46	4 (8.7)	2 (4.3)
4	C2–C6	6	2 (33.3)	2 (33.3)
	C3–C7	63	9 (14.3)	5 (7.9)
	C4–T1	2	0	0
	Subtotal	71	11 (15.5)	7 (9.9)
5	C2–C7	9	0	0

Radiological assessment

Using lateral cervical radiographs and images from computed tomography (CT), CT myelography, and magnetic resonance (MR), we identified the most stenotic level of the spinal column. High signal changes (HSCs) of spinal cord were assessed on preoperative and postoperative T2-weighted MR images. Anterior shift of the spinal cord after surgery at the most stenotic level of the spinal column was calculated on axial images from preoperative and postoperative CT myelography (Fig. 1a). Lateral tilting of grafted bone was assessed on postoperative cervical anterior–posterior radiographs (Fig. 1b).

Statistical analysis

Fisher's exact probability test was applied for statistical analysis. $P < 0.05$ was considered significant.

Results

Postoperative C5 palsy was found in 17 of 199 cases (8.5%). In CSM cases, 9 of 113 patients (7.9%) developed C5 palsy. Similarly, 6 of 62 OPLL patients (9.7%) and 2 of 16 CSAM patients (12.5%) developed C5 palsy. No patients with cervical spondylotic radiculopathy and disc herniation developed C5 palsy (Table 1). When the degree of paralysis was restricted to MMT grade ≤2, ten patients (5.0%) showed paralysis. They included five CSM cases (4.4%) and five OPLL cases (8.1%) (Table 1).

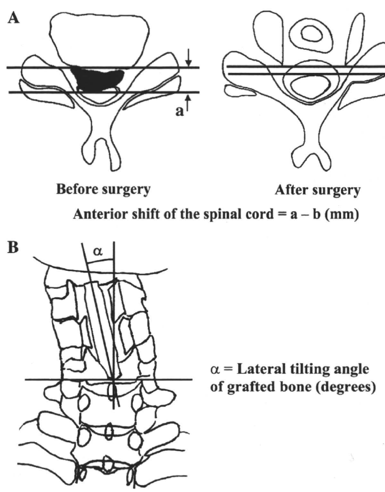

Fig. 1 Schematic drawings of anterior shift of the spinal cord (**a**) and lateral tilting of the grafted bone (**b**)

No patient showed an incidence of C5 palsy where there was only one level fusion. C5 palsy was found in 2 (5.0%) of 40 patients who underwent 2 level fusion, 4 (8.7%) of 46 patients with 3 level fusion, and 11 (15.5%) of 71 patients with 4 level fusion. No case of C5 palsy was found in nine patients with 5 level fusion (Table 2). To summarize, 2 of 73 patients (2.7%) developed C5 palsy after fusion at 1 or 2 levels, while 15 of 126 patients (11.9%) developed the palsy after 3 or more levels of fusion. The incidence of the palsy after fusion at three or more levels was significantly higher than that when only one or two levels were fused.

No additional surgery was performed for the postoperative C5 palsy cases. When C5 palsy developed, we stimulated the patient's deltoid muscle using low-frequency sound waves and performed both active and passive shoulder range of motion (ROM) exercises to prevent contracture of the patient's shoulder.

JOA scores of 17 patients who developed C5 palsy are shown in Table 3. All of the 17 patients showed a recovery from their myelopathy. Their extent of recovery ranged from 27.6 to 100% (average 71.2%) (Table 3).

The onset and prognosis of C5 palsy in the 17 patients are summarized in Table 4. Sixteen of 17 patients had radiating neck and shoulder pain prior to their muscle weakness. Pain was recognized 1–7 days (average 3.6 days) after surgery. Muscle weakness developed 2–23 days (average 7.2 days) after surgery. Twelve patients completely recovered from their C5 palsy. However, the recovery was incomplete in three patients, and two patients with OPLL showed no recovery. No patient showed preoperative weakness of the deltoid or biceps brachii. All seven patients who had an MMT grade ≥3 at the onset of their C5 palsy showed full recovery. Among ten patients with MMT grade ≤2 at the onset, five showed recovery to MMT grade 5, and three to MMT grade 4; two patients did not show any recovery and still had an MMT grade ≤2 at their follow-up. There was 0.8–15 months to maximum recovery (average 2.8 months). No patient with C5 palsy developed a new sensory deficit at the C5 dermatome area.

The radiological characteristics of the 17 patients are summarized in Table 5. In all of the 17 patients, the most stenotic level of their spinal column included the C3–C4 or C4–C5 levels. On MR images, HSCs were found at C3–C4 or C4–C5 levels in 12 patients. When restricted to the ten patients who had an MMT grade ≤2 at the onset, nine of the ten had such HSCs (Table 5). Anterior shift of the spinal cord ranged 0.8–5.2 mm. Tilting of the grafted bone ranged from 0° to 14° (Table 5).

Table 3 JOA score of 17 patients who developed C5 palsy

Patient no.	Age (years)/sex	Lesion	Levels fused (*n*)	FU period	JOA score						Recovery rate (%)
					Pre-op			At FU			
					Total	M-UE	M-LE	Total	M-UE	M-LE	
MMT grade ≤2											
1	37/F	CSM	C4–C6 (2)	9y 3m	16	4	4	17	4	4	100
2	26/M	CSM	C3–C6 (3)	10y 10m	13	3	3	17	4	4	100
3	50/M	CSM	C3–C6 (3)	1y	13	3	3	15	3	4	50
4	73/F	CSM	C2–C6 (4)	9y 10m	8	1	1	15	4	3	77.8
5	62/M	OPLL	C3–C7 (4)	4y 4m	7	1	1	16	4	3	90
6	52/M	CSM	C3–C7 (4)	5y 1m	10	2	3	15	3	4	71.4
7	61/M	OPLL	C3–C7 (4)	1y	2.5	0	0	6.5	1	1	27.6
8	70/F	OPLL	C3–C7 (4)	5y 6m	10	3	2	12.5	3.5	2.5	35.7
9	71/M	OPLL	C2–C6 (4)	5y 6m	8.5	2	1.5	13	4 (−2)	2	64.7
10	64/M	OPLL	C3–C7 (4)	10y	10.5	2.5	2	13	4 (−2)	3	38.5
MMT grade ≥3											
11	73/M	CSAM	C4–C6 (2)	9y 10m	15	4 (−2)	2	17	4	4	100
12	70/M	CSAM	C3–C6 (3)	5y 2m	16	4 (−1)	4	17	4	4	100
13	65/F	CSM	C3–C7 (4)	10y 3m	12	4	4	17	4	4	100
14	44/F	CSM	C3–C7 (4)	10y	13	3	3	15	4	4	50
15	64/M	CSM	C3–C7 (4)	5y 5m	10.5	2	2	13	3	2	38.5
16	48/M	CSM	C3–C7 (4)	4y 6m	14	3	3	16	4	4	66.7
17	65/M	OPLL	C3–C7 (4)	4y 2m	13.5	3	3	17	4	4	100
Mean ± SD					11.3 ± 3.5	2.4 ± 1.1	2.5 ± 1.1	14.8 ± 2.7	3.4 ± 0.9	3.3 ± 1.0	71.2 ± 27.0

JOA score Japanese Orthopaedic Association score for cervical myelopathy, *FU* follow-up, *M-UE* motor function score of upper extremity, *M-LE* motor function score of lower extremity, *CSM* cervical spondylotic myelopathy, *CSAM* cervical spondylotic amyotrophy

Case presentation

Case 2

A 26-year-old man presented with myelopathy due to cervical spondylosis and a preoperative JOA score of 13 points. A preoperative roentgenogram showed kyphotic alignment of his cervical spine (Fig. 2a). Anterior corpectomy of C4 and C5 and arthrodesis at C3–C6 were performed using an autologous fibula strut. After surgery, the fibula strut tilted toward his right side. The lateral tilt angle of the grafted fibula was 5° immediately after surgery (Fig. 2b), and 14° on the seventh day (Fig. 2c). On the seventh day, subluxation of the right uncovertebral joint of C4–C5 was shown on an anterior–posterior roentgenogram (Fig. 2c, arrow). Postoperative CT 8 weeks after surgery showed foraminal stenosis of C4–C5 on the right side (Fig. 2d, e, arrows). On the third day after surgery, he had neck and right-shoulder pain. On the fourth day, his right deltoid muscle began to deteriorate to MMT grade 2. On the 70th postoperative day, the palsy naturally recovered to MMT grade 5. In this case, we speculated that the cause of the C5 palsy was foraminal stenosis at the right C4–C5.

Case 9

A 71-year-old man presented with cervical myelopathy caused by OPLL. A preoperative roentgenogram showed mixed type OPLL from C1 to C6 (Fig. 3a). His preoperative JOA score was 8.5 points. Preoperative T2-weighted MR images showed compression of the spinal cord and HSCs at C3–C4 and C4–C5 levels (Fig. 3b). He underwent anterior corpectomy of C3, C4, and C5 and arthrodesis using an autologous fibula strut from C2 to C6 (Fig. 3c). On the first day after surgery, he complained of left shoulder pain. On the fifth day, his left deltoid muscle power had deteriorated to MMT grade 2. On the 22nd postoperative day, his right deltoid muscle power had deteriorated to MMT grade 2. Eight months later, muscle power in his right upper extremities recovered to MMT grade 5. However, his left deltoid did not show any recovery, and was still MMT grade 2 at a final follow-up of 5 years and 6 months after surgery. Postoperative T2-weighted MR images showed HSCs at C3–C4 and C4–C5 levels (Fig. 3d, e). High intensity signal changes were detected in the gray matter of the spinal cord. Axial views of a CT myelogram revealed an excessive 5.2 mm

Table 4 Onset and prognosis of C5 palsy

Patient no.	Impaired muscle	Laterality	Onset of pain (days)	Onset of weakness (days)	MMT grade			Months to recovery	Degree of recovery
					Pre-op	At onset	At FU		
MMT grade ≤2									
1	D, B	Rt	2	13	5	2	5	3	Complete
2	D, B	Rt	3	4	5	2	5	1.8	Complete
3	D, B	Blt	3	8	5	2	5	0.8	Complete
4	D, B	Rt	3	6	5	2	5	2	Complete
5	D, B	Lt	3	4	5	2	5	1	Complete
6	D, B	Lt	7	12	5	2	4	6	Incomplete
7	D, B	Rt	3	4	5	2	4	1.8	Incomplete
8	D, B	Lt	–	2	5	2	4	15	Incomplete
9	D, B	Blt	1	5	5	2	2	NR	No
10	D, B	Lt	5	5	5	1	1	NR	No
MMT grade ≥3									
11	D, B	Rt	3	7	5	4	5	1	Complete
12	D, B	Lt	2	3	5	3	5	1.3	Complete
13	D, B	Rt	7	23	5	4	5	2	Complete
14	D, B	Lt	1	2	5	4	5	1	Complete
15	D, B	Lt	3	10	5	3	5	0.8	Complete
16	D, B	Lt	5	5	5	4	5	1	Complete
17	D, B	Rt	7	10	5	3	5	3	Complete
Mean ± SD			3.6 ± 2.0	7.2 ± 5.3	5.0 ± 0	2.6 ± 0.9	4.4 ± 1.2	2.8 ± 3.6	

D Deltoid, *B* biceps, *Rt* right, *Lt* left, *Blt* bilateral, *NR* not recovered

Table 5 Radiological characteristics of 17 patients who developed the C5 palsy

Case no.	Most stenotic level	T2W HSC	Anterior shift of spinal cord (mm)	Lateral tilting of grafted bone (°)
MMT ≤2				
1	C4/5	–	NA	1
2	C4/5, C5/6	C4/5	1.9	14
3	C3/4	C3/4	3.4	2
4	C4/5	C4/5	NA	11
5	C4/5	C4/5	3.6	2
6	C3/4, C4/5	C3/4, 4/5	1.0	1
7	C4/5, C5/6	C4/5, 5/6	NA	NA
8	C3/4	C3/4	1.2	0
9	C3/4, C4/5	C3/4, 4/5	5.2	2
10	C3/4	C3/4, 4/5	1.0	6
MMT ≥3				
11	C4/5	–	2.0	1
12	C4/5	–	1.9	1
13	C4/5, C5/6	–	NA	6
14	C4/5, C5/6	C4/5, 5/6	0.8	0
15	C4/5	C4/5	1.9	1
16	C3/4	C3/4	4.3	1
17	C3/4, C4/5	–	3.6	2

T2W HSC High signal change in T2-weighted magnetic resonance images, *NA* not assessed