Table 4 Number of patients with high signal changes in T2-weighted MR imaging

	CSM patients over 70 y/o group(n=27)	CSM patients under 50 y/o group(n=27)
C3-4	11(p<0.05)	2
C4-5	14(p<0.05)	3
C5-6	4(p<0.05)	16
C6-7	0	2

Discussion

Penning placed great importance on retrolisthesis with respect to the pathogenesis of spinal cord compression in spondylotic myelopathy, especially when marked narrowing of the osseous spinal cord in extension is present. Under these conditions, the spinal cord is compressed between bony pincers formed by the anterior aspect of the arch of the inferior vertebra on one side and the posterioinferior aspect of the body of the superior vertebra on the other side, leading him to suggest that this mechanism of compression be referred to as the pincers mechanism[4].

Tani et al. reported that a high incidence (95%) of focal conduction block at C3-4 or C4-5 with normal conduction at C5-6 and C6-7 was characteristic of CSM in elderly people[6]. In another study of elderly CSM patients, Tani et al. found a significant association between degenerative spondylolisthesis and conduction block in the face of a relatively wide spinal canal and concluded that this association indicates the functional importance of degenerative spondylolisthesis in elderly patients with CSM. The authors also consider the higher incidence of both degenerative spondylolisthesis and focal conduction block at the upper cervical levels (C3-4 or C4-5) in this age group to be of clinical interest[5].

Hayashi et al. reported that spondylotic changes such as narrowing of intervertebral discs and osteophytes predominated at the lower disc levels of C5-6 and C6-7, while the upper disc levels of C3-4 and C4-5 exhibited comparatively greater mobility and vertebrolisthesis, especially retrolisthesis in extension. They also reported that pathologic changes at the upper disc levels of C3-4 and C4-5 tended to occur more frequently in aged patients than in younger ones[2]. Hayashi et al. reported in another paper that although their CSM patients did have spinal canal stenosis, the development of myelopathy in their study group did not entirely correlate with AP canal diameter, indicating that other factors besides a narrowed spinal canal might be involved[1].

In our study the cervical spinal canal diameter was wider in the elderly CSM group than that in the younger CSM group, a finding consistent with the results of the study by Hayashi et al. cited above[1]. Moreover our discovery of spondylolisthesis at C3-4 and C4-5 in the elderly group is consistent with the two studies by Tani et al. cited above[5,6]. Consequently we would identify the following radiological findings in the elderly CSM group, compared with the younger CSM group, as characteristic of the elderly CSM group : 1) spinal canal diameter was wider ; 2) spondylolisthesis at C3-4 was more frequently observed ; 3) a higher percentage of patients had HSCs in the spinal cord on T2-weighted MR imaging at C3-4 and C4-5.

Hosono et al. reported that the prevalence of postoperative axial symptoms was significantly higher after laminoplasty than after anterior fusion among their study patients (60% *vs.* 19% ; p<0.05). In 18 patients (25%) from the laminoplasty group, the chief complaints after surgery were related to axial symptoms for more than 3 months, whereas in the anterior fusion group, no patient reported having such severe pain after surgery[3]. Indeed, none of the patients in our study experienced severe pain following anterior cervical surgery. These two studies together thus provide evidence that with respect to axial symptoms, anterior cervical surgery appears superior to laminoplasty.

Conclusions

Our study findings identified the following etiologic factors as characteristic of CSM in elderly patients, compared with the younger CSM patients : 1) spinal canal diameter was wider : 2) spondylolisthesis at C3-4 was more frequently observed : and 3) a higher percentage of patients had HSCs at C3-4 and C4-5. Anterior cervical surgery for CSM in elderly patients was less invasive in terms of OR time and blood loss and was associated with few perioperative complications and a satisfactory JOA score recovery rate. In light of these findings, anterior cervical surgery is a reasonable procedure for elderly people with CSM. Furthermore, because of its very low rate of postoperative axial symptoms, anterior surgery that does not cause muscle injury may be preferable to laminoplasty.

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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).

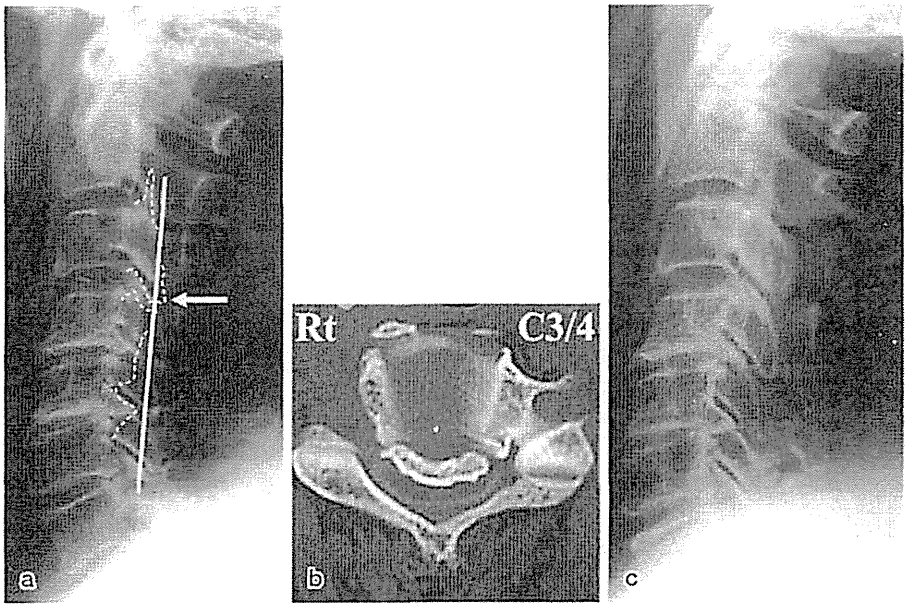

Fig. 1 Case 1
a : Preoperative cervical lateral radiograph.
b : Axial CT image at C3/4.
c : Postoperative cervical radiograph after C3-7 laminoplasty.

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

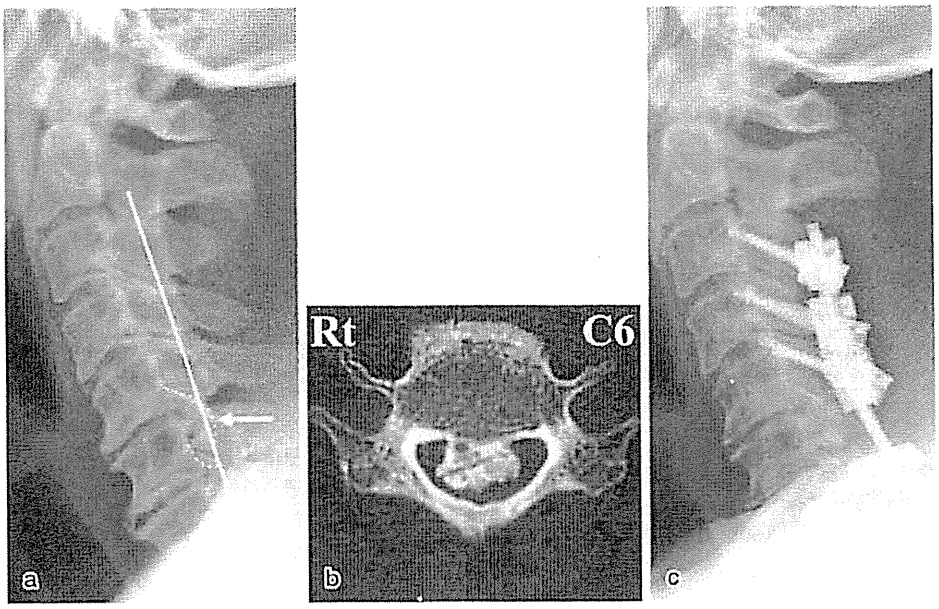

Fig. 2 Case 2

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[3]. 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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C5 Palsy after Anterior Cervical Decompression and Spinal Fusion for Cervical Degenerative Diseases

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Key words : C5 palsy, cervical spine, anterior surgery

Introduction

Postoperative C5 palsy is one of the major complications after cervical decompression surgery. According to Sakaura et al., the average incidence of C5 palsy was 4.3% (range 1.6-12.1%) in the anterior cervical decompression and spinal fusion (ASF) group, and 4.7% (range 0-30.0%) in the cervical laminoplasty group[8]. However, since fewer studies have analyzed C5 palsy after ASF than after cervical laminoplasty, the clinical and radiological characteristics of C5 palsy after ASF have not been as well defined. The aim of this study was to investigate the incidence and prognosis of C5 palsy after ASF and to discuss the mechanisms behind its development.

Materials and Methods

1. Patient Population

Between 1996 and 2004, consecutive 199 patients underwent ASF for cervical degenerative diseases, including 133 patients with cervical spondylotic myelopathy (CSM), 62 patients with cervical ossification of the posterior longitudinal ligament (OPLL), 16 patients with cervical spondylotic amyotrophy (CSA), 6 patients with cervical spondylotic radiculopathy, and 2 patients with disc herniation. The average age of them was 57.0 years old ranging from 25 to 88 years old. One hundred and forty patients were male and 59 patients were female. The number of fused levels was as follows : one level (33 patients), two levels (40 patients), three levels (46 patients), four levels (71 patients), and five levels (9 patients).

One level fusion 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 autologous fibula strut was grafted for fusion surgery of three or more levels. In cases where three or more levels were fused, patients were immobilized with a halo vest for 8 weeks after surgery. No additional surgery was performed for the postoperative C5 palsy cases.

2. Clinical Assessments

We defined C5 palsy as deterioration in muscle power of the deltoid or biceps brachii by at least one grade, as assessed by the manual muscle test (MMT), without aggravation of lower extremity function. We retrospectively reviewed their records and evaluated the following clinical measures : onset of radiating neck and shoulder pain, onset of weakness, time course of any MMT grade change, and severity of myelopathy [Japanese Orthopaedic Association (JOA) score].

3. Radiological Assessments

Using lateral cervical radiographs plus computed tomograms (CT) after myelography and magnetic resonance (MR) images, we identified the most stenot-

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Table 1 Onset and prognosis of C5 palsy

Case no.	Lesion	Levels fused (n)	Impaired muscle	Laterality	MMT grade			Months to recovery	Degree of recovery
					Pre-op.	At onset	At follow-up		
(MMT≤2)									
1	CSM	C4-6(2)	D, B	Rt	5	2	5	3	Complete
2	CSM	C3-6(3)	D, B	Rt	5	2	5	1.8	Complete
3	CSM	C3-6(3)	D, B	Blt	5	2	5	0.8	Complete
4	CSM	C2-6(4)	D, B	Rt	5	2	5	2	Complete
5	OPLL	C3-7(4)	D, B	Lt	5	2	5	1	Complete
6	CSM	C3-7(4)	D, B	Lt	5	2	4	6	Incomplete
7	OPLL	C3-7(4)	D, B	Rt	5	2	4	1.8	Incomplete
8	OPLL	C3-7(4)	D, B	Lt	5	2	4	15	Incomplete
9	OPLL	C2-6(4)	D, B	Blt	5	2	2	NR	No
10	OPLL	C3-7(4)	D, B	Lt	5	1	1	NR	No
(MMT≥3)									
11	CSA	C4-6(2)	D, B	Rt	5	4	5	1	Complete
12	CSA	C3-6(3)	D, B	Lt	5	3	5	1.3	Complete
13	CSM	C3-7(4)	D, B	Rt	5	4	5	2	Complete
14	CSM	C3-7(4)	D, B	Lt	5	4	5	1	Complete
15	CSM	C3-7(4)	D, B	Lt	5	3	5	0.8	Complete
16	CSM	C3-7(4)	D, B	Lt	5	4	5	1	Complete
17	OPLL	C3-7(4)	D, B	Rt	5	3	5	3	Complete

D = deltoid, B = biceps brachii, Rt = right, Lt = left, Blt = bilateral, NR = not recovered

ic level of the spinal column. We also looked for the presence of high signal changes (HSCs) in the spinal cord on preoperative and postoperative T2-weighted MR images.

Results

Overall 17 cases (8.5%) of all 199 cases developed postoperative C5 palsy. The average age of them was 58.5 years old ranging from 26 to 73 years old. Twelve patients were male and 5 patients were female. Stratifying by disease, 9 (7.9%) of the 113 CSM patients, 6 (9.7%) of the 62 OPLL patients, and 2 (12.5%) of the 16 CSA patients developed C5 palsy ; none of the radiculopathy or disc herniation patients developed C5 palsy. Stratifying by number of fused levels, none of the one-level fusion patients, 2 (5.0%) of the 40 two-level fusion patients, 4 (8.7%) of the 46 three-level fusion patients, 11 (15.5%) of the 71 four-level fusion patients and none of the five-level fusion patients developed C5 palsy.

All 17 patients showed some recovery from their myelopathy, the extent of which ranged from 27.6 to 100% (mean 71.2%). Sixteen of these 17 patients presented with radiating neck and shoulder pain prior to their muscle weakness. Pain was recognized 1-7 days (mean 3.6 days) after ASF, and muscle weakness developed 2-23 days (mean 7.2 days) after ASF. No patient had preoperative weakness of the deltoid or biceps brachii. Among the 10 patients with MMT grade ≤2 at the onset, 5 improved to MMT grade 5, 3 improved to MMT grade 4, and 2 with OPLL did not recover at all. Time to maximum recovery ranged from 0.8-15 months (mean 2.8 months) (Table 1). Among all 17 patients, the most stenotic level of the spinal column was either C3-4 or C4-5 disc level ; T2-weighted MR images identified HSCs at C3-4 or C4-5 disc levels in 12 of all 17 patients and 9 of the 10 patients with an MMT grade ≤2 at the onset (Table 2).

Table 2 Radiological chracteristics of 17 patients who developed C5 palsy

Case no.	Most stenotic level	T2W HSC
(MMT≤2)		
1	C4-5	—
2	C4-5, C5-6	C4-5
3	C3-4	C3-4
4	C4-5	C4-5
5	C4-5	C4-5
6	C3-4, C4-5	C3-4, C4-5
7	C4-5, C5-6	C4-5, C5-6
8	C3-4	C3-4
9	C3-4, C4-5	C3-4, C4-5
10	C3-4	C3-4, C4-5
(MMT≥3)		
11	C4-5	—
12	C4-5	—
13	C4-5, C5-6	—
14	C4-5, C5-6	C4-5, C5-6
15	C4-5	C4-5
16	C3-4	C3-4
17	C3-4, C4-5	—

T2W HSC = high signal change in T2-weighted magnetic resonance images

Discussion

There does not seem to be any unified definition of postoperative C5 palsy in previous reports. Hasegawa et al. described that inclusion criteria were deterioration of motor function by at least 1 level in a standard MMT without aggravation of lower extremity function, the appearance of a new sensory disturbance between postoperative day 0 and 2 months after surgery, or both deterioration of motor function and the appearance of a new sensory disturbance between postoperative day 0 and 2 months after surgery, or both deterioration of motor function and the appearance of a new sensory disturbance and that exclusion criteria were pain without change in motor or sensory function, or deterioration of lower extremity function, including tetraparesis[3]. Imagama et al. described that C5 palsy was defined as a paresis of deltoid (MMT grade 0 to 2), with or without involvement of the biceps, but no loss of strength in other muscles[7]. There were reports on postoperative C5 palsy that did not mention the clear definition of C5 palsy[1,2,5,6,9,10]. Only five large studies on C5 palsy have analyzed more than 100 cases of ASF[2,3,6,9,10], among which the incidence of C5 palsy after ASF ranged from 3.2 to 9.1%. One of the major factors responsible for this range seems to be the absence of a unified definition of C5 palsy. In our study, although we observed an 8.5% incidence of postoperative C5 palsy under our criteria, further restricting our definition of palsy to MMT grade ≤2 at the onset yielded an incidence of 5.0%. Providing a clear definition of C5 palsy in one's reports therefore is essential.

Regarding the correlation between the number of fused levels and the incidence of postoperative C5 palsy, Ikenaga et al. reported that no patient developed C5 palsy after fusion of one or two levels, whereas 18 of 362 patients (5.0%) developed C5 palsy after fusion of three or more levels[6]. Similarly, Greiner-Perth et al. reported that 3 of 65 (4.6%) patients developed C5 palsy after fusion of one or two levels in contrast with 7 of 56 patients (12.5%) who developed C5 palsy after fusion of three or more levels[2]. In our study, we identified 2 of 73 patients (2.7%) who developed C5 palsy after fusion of one or two levels *versus* 15 of 126 patients (11.9%) who developed C5 palsy after fusion of three or more levels. Thus our results in conjunction with previous reports collectively indicate that the likelihood of developing C5 palsy increases as ASF involves more corpectomy levels.

Sakaura et al. reported that patients with postoperative C5 palsy generally had a good prognosis for functional recovery[8]. However, irreversible cases of C5 palsy after ASF have been reported. Ikenaga et al. reported 7 cases of partial recovery among 18 patients with C5 palsy[6], and Greiner-Perth et al. reported two cases of partial recovery in ten patients[2]. Among our 17 C5 palsy patients, three patients recovered incompletely, and two patients showed no recovery. For the two palsy patients with no recovery, both had OPLL, and deteriorated to MMT grades 1 and 2 at the onset, had HSCs on T2-weghted MR images at both

C3-4 and C4-5 disc levels. This suggests that, when patients with compression myelopathy and an ossified mass at C3-4 and C4-5 disc levels develop C5 palsy with an MMT grade ≤2 after ASF, favorable recovery from their palsy may not necessarily be expected.

Over the past years, various hypotheses have been advanced regarding the etiology of postoperative C5 palsy, which together fall into two basic groups. The first focuses on nerve root lesions as the primary cause, either from direct injury to the nerve root[5] or in association with shifts in the spinal cord and nerve root[6,9]. The other group of hypotheses implicates spinal cord disorders as the source of C5 palsy. For instance, Chiba et al.'s analysis of C5 palsy after cervical laminoplasty indicated that upper extremity paresis might be caused by a deterioration of grey matter, with local reperfusion injury in the spinal cord as the pathomechanism[1].

Sixteen of the 17 patients in our study presented with neck and shoulder pain prior to the onset of muscle weakness, a finding that supports the hypothesis that nerve root lesions may have been the cause of postoperative C5 palsy, just as Saunders stated that a delayed painful weakness of one shoulder was thought to be a C5 radiculopathy[9]. Moreover, the most stenotic level of the spinal canal for all 17 of our C5 palsy patients was C3-4 or C4-5 disc levels. HSCs were detected at the C3-4 or C4-5 disc levels in 12 of these 17 cases and in 9 of the 10 cases with an MMT ≤2. These findings indicate that asymptomatic damage of anterior horn cells within the grey matter of the spinal cord was pre-existing in severe postoperative C5 palsy cases. Taking all these findings into account, we would propose a "double lesion" hypothesis for the development of C5 palsy after ASF for cervical lesion as follows : the pre-existing asymptomatic damage at the anterior horn cells may contribute to the development of postoperative C5 palsy, in combination with nerve root lesions after the anterior cervical corpectomy and spinal fusion procedure.

Conclusions

The overall incidence of C5 palsy after ASF among our study patients was 8.5% and higher among those who had multilevel corpectomy and spinal fusion cases. Our findings also suggest that in most of our patients with severe C5 palsy after ASF, pre-existing asymptomatic damage of anterior horn cells at the C3-4 or C4-5 disc levels may have participated in the development of motor weakness in combination with nerve root lesions occurring subsequent to ASF. Our study results thus indicate that clinicians need to be alert to the possible development of postoperative C5 palsy in patients with spinal cord lesions at the C3-4 and C4-5 disc levels who undergo multilevel ASF.

The data listed in Table 1 and Table 2 was cited from the Hashimoto et al.'s published paper[4].

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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

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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.

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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).

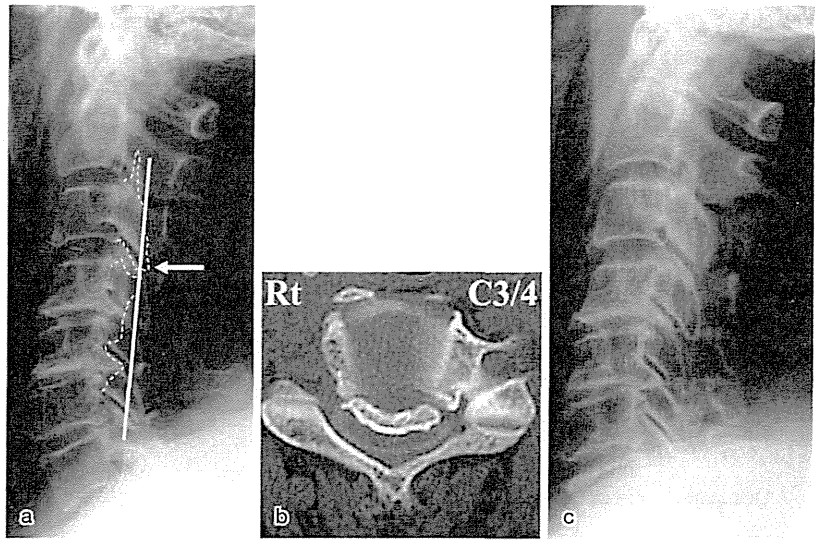

Fig. 1 Case 1
a : Preoperative cervical lateral radiograph.
b : Axial CT image at C3/4.
c : Postoperative cervical radiograph after C3-7 laminoplasty.

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

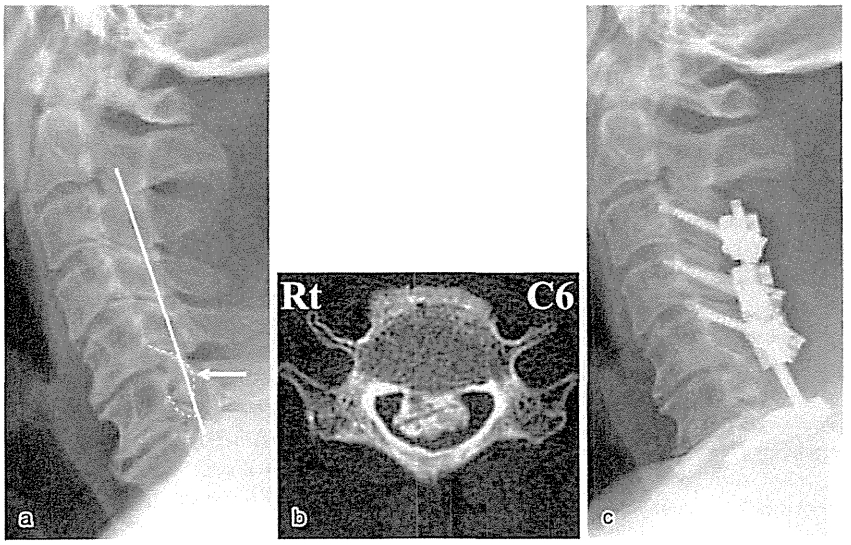

Fig. 2 Case 2

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

Association between serum leptin and bone metabolic markers, and the development of heterotopic ossification of the spinal ligament in female patients with ossification of the posterior longitudinal ligament

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Abstract Obesity is a risk factor for ossification of the posterior longitudinal ligament (OPLL) of the spine, which is characterized by heterotopic bone formation in the posterior longitudinal spinal ligament. Hyperleptinemia is a common feature of obese people and leptin is believed to be an important factor in the pathogenesis of OPLL. However, the association between leptin and bone metabolism and the development of OPLL is not understood fully. The objective of the present study was to determine the association between serum leptin concentration and bone metabolic markers and the extent of heterotopic ossification of the spinal ligament in patients with OPLL. The serum concentrations of leptin, insulin, fructosamine, bone-specific alkaline phosphatase, and carboxyterminal propeptide of type I procollagen, urine deoxypyridinoline levels, and the number of vertebrae with OPLL involvement were measured in 125 (68 males and 57 females) patients with OPLL. The correlation between leptin and these other factors was then examined. Serum leptin and insulin concentrations were increased significantly in OPLL females compared to non-OPLL female controls. In the females with OPLL, serum leptin concentrations corrected for body mass index correlated positively with the number of vertebrae with OPLL involvement. In females, serum leptin levels were significantly higher in patients in whom OPLL extended to the thoracic and/or lumbar spine than in patients in whom OPLL was limited to the cervical spine. Our results suggest that hyperleptinemia, in combination with hyperinsulinemia, may contribute to the development of heterotopic ossification of the spinal ligament in female patients with OPLL.

Keywords Leptin · Ossification of the posterior longitudinal ligament (OPLL) · Insulin · Gender · Bone metabolic markers

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Introduction

Ossification of the posterior longitudinal ligament (OPLL) of the spine is characterized by heterotopic bone formation in the spinal canal and is considered to belong to the same pathological entity as ankylosing spinal hyperostosis. Enlarged OPLL often compresses the spinal cord and causes severe neurological disorders [33].

The Zucker fatty (*fa/fa*) rat, a model for hereditary obesity, exhibits hyperglycemia, hyperinsulinemia, hyperlipidemia, and heterotopic ossification of the spinal

ligament [13, 20, 39]. A missense mutation (Gly269Pro) in the leptin receptor gene (Ob-R) was found in this rat where leptin-binding affinity was reduced and signal transduction was attenuated, leading to a compensatory elevation in circulating leptin levels [10, 17, 21, 28]. Since heterotopic ossification of the spinal ligament in the *fa/fa* rat is quite similar to that found in human OPLL, researchers in the field of spinal surgery consider the *fa/fa* rat as a useful animal model for studying the pathophysiology of OPLL [28, 36].

Leptin, a product of the obese (*ob*) gene, is secreted primarily by adipocytes and plays an important role in regulation of food intake and energy expenditure [30]. Peripheral administration of leptin increases bone growth and indices of bone formation [26, 37]. Leptin can also act directly on stromal cells to enhance their differentiation into osteoblasts and inhibit their differentiation into adipocytes [3]. On the other hand, intracerebroventricular infusion of leptin leads to rapid bone loss [32], implying that leptin regulates bone mass through alternate pathways, one involving a direct stimulatory effect on bone growth when administered peripherally and another acting indirectly via a hypothalamic relay that suppresses bone formation, when administered centrally [4]. As leptin has the potential to drive stromal cells into osteogenic differentiation, serum leptin may be associated with the development of heterotopic ossification of the spinal ligament. However, to date, the association between leptin and heterotopic ossification of the spine, particularly in OPLL, has been largely unstudied.

In this study, we hypothesized that serum leptin levels are elevated in patients with OPLL and may be associated with bone metabolic markers and the extent of OPLL development. We measured serum leptin concentrations in OPLL patients and non-OPLL controls and corrected these levels using individual body mass index (BMI). We then analyzed the association between the leptin/BMI ratio and bone metabolic markers, and the number of vertebrae with OPLL involvement. Based on these results, we discuss the possible role(s) of leptin in the development of OPLL.

Subjects and methods

The study subjects (Table 1) were 125 Japanese patients with OPLL (68 males and 57 females) and 62 non-OPLL control subjects (35 males and 27 females, the majority of who had spinal degenerative disorders other than OPLL). All patients were followed at the Department of Orthopedic Surgery of Chiba University Hospital between 1995 and 2008.

Based on previous data that circulating leptin concentrations are significantly higher in females than in male subjects [14, 17, 22], we subdivided the OPLL and non-OPLL groups according to gender. The mean age of OPLL females, non-OPLL females, OPLL males, and non-OPLL males was 58.6 ± 9.0, 61.7 ± 8.7, 61.2 ± 8.1, and 56.5 ± 11.2 years, respectively. The mean BMI (weight in kilograms divided by the square of height in meters) of OPLL females, non-OPLL females, OPLL males, and non-OPLL males was 25.2 ± 4.4, 22.9 ± 3.1, 24.0 ± 2.7, and 23.1 ± 2.5 kg/m^2, respectively. All the patients were informed that data on the blood or urine samples would be submitted for publication and the

Table 1 Clinical characteristics of OPLL (ossification of the posterior longitudinal ligament) patients and non-OPLL controls

	Female OPLL versus non-OPLL		
	OPLL (n = 57)	Non-OPLL (n = 27)	p (Student's t)
Age (year)	58.6 ± 9*	61.7 ± 8.7	<0.05
Height (cm)	152.9 ± 6.7	150.3 ± 6.7	N.S.
Weight (kg)	59 ± 9.8*	51.9 ± 7.8	<0.01
BMI (kg/m^2)	25.2 ± 4.4*	22.9 ± 3.1	<0.05
Serum leptin (ng/ml)	9.67 ± 5.1*	6.55 ± 3.67	<0.01
Leptin/BMI	0.368 ± 0.169*	0.275 ± 0.122	<0.01
	Male OPLL versus non-OPLL		
	OPLL (n = 68)	Non-OPLL (n = 35)	p (Student's t)
Age (year)	61.2 ± 8.1*	56.5 ± 11.2	<0.05
Height (cm)	163.8 ± 5.8*	166.6 ± 5.6	<0.05
Weight (kg)	64.6 ± 9.2	64.4 ± 7.8	N.S.
BMI (kg/m^2)	24 ± 2.7	23.1 ± 2.5	N.S.
Serum leptin (ng/ml)	3.85 ± 2.2	3.2 ± 1.4	N.S.
Leptin/BMI	0.156 ± 0.079	0.136 ± 0.055	N.S.

N.S. not significant, *BMI* body mass index

* Significantly different from non-OPLL

patients volunteered freely to participate in this study. This study was approved by the ethics committee of Chiba University Hospital.

A blood sample was collected from each subject between 11:00 and 13:00 h after overnight fasting and the serum immediately frozen at –80°C until analysis. For a urine analysis, the 2-h morning urine after the first void urine was tested. Serum leptin concentrations were measured using a commercially available radioimmunoassay (RIA) kit (Linco Research, Inc., St. Charles, MO). As gender and adipose tissue volume influence leptin production, the serum leptin levels were corrected for BMI, a measure of obesity, and then compared within each gender group. The minimum detection limit of serum leptin levels was 0.5 ng/ml with a 4.5% coefficient of variation. Serum insulin levels were also measured using a microparticle enzyme immunoassay (EIA) (AxSYM insulin assay kit, Dainabot Co., Ltd., Tokyo, Japan). The minimum detection limit of serum insulin levels was 0.8 μU/ml with a 5.5% coefficient of variation. The serum concentrations of bone formation markers, bone-specific alkaline phosphatase (BAP) and the carboxyterminal propeptide of type I procollagen (PICP) were measured using an EIA (Takara, Tokyo, Japan) and a RIA (Orion Diagnostica, Espoo, Finland) kit, respectively. Urine deoxypyridinoline (DPD) was measured with an EIA kit (DS Pharma Biomedical, Osaka, Japan) as a marker of bone resorption.

Radiographic evaluation of the number of vertebrae and segments with OPLL involvement in individual patients was evaluated by at least two different authors, all of whom were senior spinal surgeons. Patients with ossification of the yellow ligament of the spine, which is often seen as heterotopic ossification of the spinal ligament at the thoracic spine, were excluded from the study.

Statistical methods

Previous studies have shown that circulating leptin levels correlate positively with BMI [14, 31]. To eliminate the influence of obesity, we calculated the leptin/BMI ratio for individual patients. Comparison of age, height, body weight, BMI, serum leptin levels, and leptin/BMI ratios between OPLL patients and non-OPLL controls was performed using Student's *t* test. In female OPLL patients, correlations between leptin/BMI ratios and serum BAP, PICP, insulin, and fructosamine (FRA) levels, urine DPD levels, and the number of vertebrae with OPLL involvement were analyzed using Pearson's correction analysis.

In addition, the OPLL patients were divided into two subgroups according to the extent of OPLL development, with patients in whom OPLL was limited to the cervical spine being designated as type C-OPLL, while subjects in whom OPLL extended to the thoracic and/or lumbar spine being designated as type TL-OPLL (Fig. 1). Type C-OPLL included 63 patients (48 males and 15 females) while type TL-OPLL included 62 patients (20 males and 42 females) (Table 2). Student's *t* test was then performed to analyze differences in age, height, body weight, BMI, leptin/BMI ratios, and serum insulin and FRA levels between type C-OPLL and type TL-OPLL patients. The correlation between leptin/BMI ratios and serum BAP, PICP, insulin, and FRA levels, urine DPD levels, and the number of vertebrae with OPLL involvement in both female type TL-OPLL and female type C-OPLL patients were analyzed using Pearson's correlation analysis. All these analyses were performed with the significance level being set at $p < 0.05$.

Results

Serum leptin concentrations and leptin/BMI ratios in OPLL and non-OPLL patients

The characteristics of the four subgroups are presented in Table 1. Both OPLL and non-OPLL groups exhibited

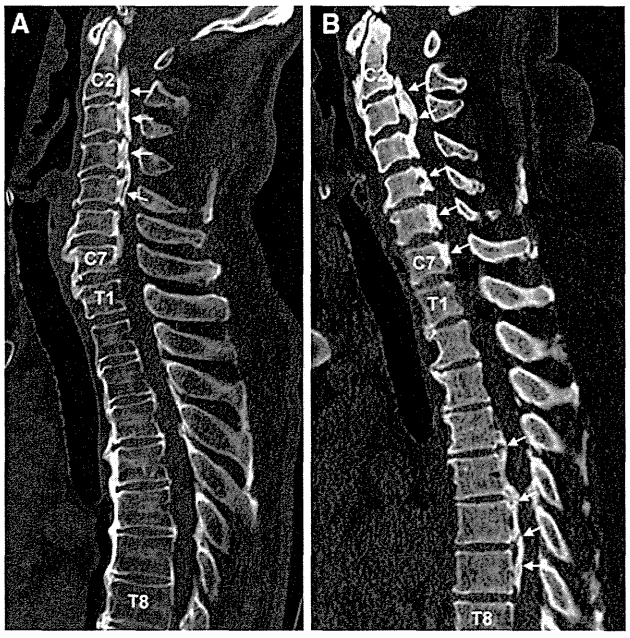

Fig. 1 Representative, mid-sagittal reconstruction images of 3-dimensional computed tomography (CT) for type C-OPLL (a type of OPLL limited to the cervical spine) and type TL-OPLL (a type of OPLL extended to the thoracic and/or lumbar spine) patients. **a** A 66-year-old male patient where OPLL is limited to the cervical spine (type C-OPLL). **b** A 54-year-old female patient where OPLL is extended to the thoracic spine (type TL-OPLL). *Arrows* indicate OPLL. *C2* 2nd cervical vertebra, *C7* 7th cervical vertebra, *T1* 1st thoracic vertebra, *T8* 8th thoracic vertebra

Table 2 Clinical characteristics of type C-OPLL (a type of OPLL limited to the cervical spine) and type TL-OPLL (a type of OPLL extended to the thoracic and/or lumbar spine) patients

	Female type C-OPLL versus type TL-OPLL		
	Type C ($n = 15$)	Type TL ($n = 42$)	p (Student's t)
Age (year)	58.6 ± 10	56.1 ± 8.6	N.S.
Height (cm)	153.1 ± 6.3	152.8 ± 6.9	N.S.
Weight (kg)	56.6 ± 10.1	59.8 ± 9.6	N.S.
BMI (kg/m^2)	24.2 ± 5	25.5 ± 4.1	N.S.
Serum leptin (ng/ml)	6.64 ± 4	10.7 ± 5*	<0.01
Leptin/BMI	0.261 ± 0.122	0.407 ± 0.168*	<0.01
Serum insulin (μU/ml)	10.1 ± 4.3	19.2 ± 22.2	N.S.
Serum FRA (μM)	511 ± 176	708 ± 418	N.S.
	Male type C-OPLL versus type TL-OPLL		
	Type C ($n = 48$)	Type TL ($n = 20$)	p (Student's t)
Age (year)	60.9 ± 8.6	61.9 ± 6.8	N.S.
Height (cm)	164.3 ± 5.6	162.5 ± 6.2	N.S.
Weight (kg)	64.7 ± 9	64.5 ± 9.8	N.S.
BMI (kg/m^2)	23.9 ± 2.6	24.3 ± 3.2	N.S.
Serum leptin (ng/ml)	3.62 ± 2.16	4.41 ± 2.33	N.S.
Leptin/BMI	0.148 ± 0.08	0.173 ± 0.075	N.S.
Serum insulin (μU/ml)	15 ± 16.7	20.1 ± 21.4	N.S.
Serum FRA (μM)	672 ± 293	739 ± 281	N.S.

N.S. not significant, *BMI* body mass index, *FRA* fructosamine

* Significantly different from type C-OPLL

significantly higher serum leptin concentrations in females than in male subjects, consistent with the findings of previous studies [14, 23]. In female subjects, serum leptin concentrations in the OPLL group were 1.5-fold higher than that in the non-OPLL group ($p < 0.01$). However, in male subjects there was no significant difference in serum leptin concentrations between the OPLL and non-OPLL groups.

In female subjects, the leptin/BMI ratio was significantly higher (1.3-fold) in the OPLL group than in the non-OPLL group ($p < 0.01$), whereas no significant difference was observed in the male subjects (Table 1).

Correlation of leptin/BMI ratios with biochemical markers of bone turnover, serum insulin and FRA concentrations, and the number of vertebrae with OPLL involvement in OPLL females

To determine the factors associated with the leptin/BMI ratio in OPLL females, we examined the correlation between leptin/BMI ratios and bone metabolic markers, circulating insulin and FRA concentrations, and the number of vertebrae with OPLL involvement (Fig. 2). There was only a relatively weak, non-significant positive correlation between the leptin/BMI ratio and both bone formation markers, BAP and PICP. In contrast, urine DPD levels, a bone resorption marker, showed a negative correlation with the leptin/BMI ratio ($r = -0.523$, $p < 0.05$). Serum insulin concentrations were correlated positively with the leptin/BMI ratio ($r = 0.344$, $p < 0.01$), whereas serum FRA levels showed no such significant relationship. It should be noted that there was a positive correlation between the number of vertebrae with OPLL involvement and the leptin/BMI ratio ($r = 0.271$, $p < 0.05$). We also examined all the above relationships in OPLL males and showed that there was no significant correlation between the leptin/BMI ratio and any other variable (data not shown).

Comparison of serum leptin, insulin, FRA concentrations, and leptin/BMI ratios between type C-OPLL and type TL-OPLL patients

The characteristics of the four subgroups of OPLL patients are presented in Table 2. In female subjects, there was no significant difference in age, height, weight, BMI, serum insulin and FRA concentrations between the groups except for serum leptin concentration which was 1.6-fold higher in type TL-OPLL than in type C-OPLL ($p < 0.01$). This difference was also found in serum leptin levels corrected by BMI, with significantly higher values in type TL-OPLL (1.6-fold, $p < 0.01$) than in type C-OPLL (Table 2). In male subjects, there were no significant differences in serum leptin concentrations and leptin/BMI ratios between the two subgroups (Table 2).