Cervical spondylotic amyotrophy

Sheng-Dan Jiang · Lei-Sheng Jiang ·
Li-Yang Dai

Received: 20 May 2010/Revised: 15 July 2010/Accepted: 25 July 2010/Published online: 8 August 2010
© Springer-Verlag 2010

Abstract Cervical spondylotic amyotrophy is characterized with weakness and wasting of upper limb muscles without sensory or lower limb involvement. Two different mechanisms have been proposed in the pathophysiology of cervical spondylotic amyotrophy. One is selective damage to the ventral root or the anterior horn, and the other is vascular insufficiency to the anterior horn cell. Cervical spondylotic amyotrophy is classified according to the most predominantly affected muscle groups as either proximal-type (scapular, deltoid, and biceps) or distal-type (triceps, forearm, and hand). Although cervical spondylotic amyotrophy always follows a self-limited course, it remains a great challenge for spine surgeons. Treatment of cervical spondylotic amyotrophy includes conservative and operative management. The methods of operative management for cervical spondylotic amyotrophy are still controversial. Anterior decompression and fusion or laminoplasty with or without foraminotomy is undertaken. Surgical outcomes of distal-type patients are inferior to those of proximal-type patients.

Keywords Cervical spondylotic amyotrophy · Pathophysiology · Management

Introduction

Cervical spondylosis often manifests with spastic tetraparesis with varying degrees of sensory dysfunction [6, 10, 11,

14, 26, 45]. Crandall et al. [10] indicated that somewhat less than 7% of patients with cervical spondylotic myelopathy present with minimal sensation loss, and classified this subtype of the disorder as cervical spondylotic amyotrophy. Cervical spondylotic amyotrophy is the clinical syndrome in cervical spondylosis characterized by severe muscular atrophy in the upper extremities, with no or insignificant sensory deficit and lower extremity symptoms [51]. In 1952, Brain et al. [7] first reported cases of cervical spondylosis with muscle atrophy of the upper extremities without sensory disturbance or pyramidal signs. The dissociated motor loss syndrome in cervical spondylosis was reported by Keegan [25], and the etiology of this syndrome was thought to be selective damage by bony spurs of the motor roots. In 1975, Sobue et al. [39] concluded that such condition was caused by segmental myelopathy and advocated nominating this condition as cervical spondylotic amyotrophy.

Clinical presentation

Cervical spondylotic amyotrophy is always associated with weakness and wasting of upper limb muscles without sensory or lower limb involvement. Difficulty in shoulder abduction, positive arm-drop sign, or positive wrist-drop sign is always found in patients with cervical spondylotic amyotrophy [30, 46]. Recently, Ahdab et al. [2] reported that a 65-year-old man with cervical spondylotic amyotrophy was referred for a dropped head syndrome because posterior neck and shoulder girdle muscles were atrophic.

Cervical spondylotic amyotrophy is usually reported as unilateral disorder, and occasionally, it presents as bilateral [15]. The age at onset of neurological symptom ranged from thirties to sixties, with men more frequently affected than women.

S.-D. Jiang · L.-S. Jiang · L.-Y. Dai (✉)
Department of Orthopedic Surgery, Xinhua Hospital, Shanghai
Jiaotong University School of Medicine, 1665 Kongjiang Road,
200092 Shanghai, China
e-mail: chinaspine@163.com

Pathophysiology

Two different mechanisms have been proposed for the pathophysiology of cervical spondylotic amyotrophy. Whether the pathogenesis of this syndrome is selective damage to the ventral root or to anterior horn is still controversial. On the basis of findings in an autopsy performed in one patient associated with cervical spondylotic amyotrophy, Keegan [25] demonstrated that selective ventral motor root lesions are the cause in the pathogenesis of cervical spondylotic amyotrophy. The autptic finding that Luschka joints significantly contribute to this anterior root impingement supports this mechanism [33].

Alternatively, the mechanism of vascular insufficiency to the anterior horn cell at the paramedian compression has been proposed. Yanagi et al. [51] have attributed cervical spondylotic amyotrophy to a circulatory insufficiency in the territories of anterior spinal arteries, as well as to selective damage to the anterior horn. The anterior horn, located in the terminal territory of the sulcal arteries, is known to be the most vulnerable to the effects of circulatory insufficiency [16]. Selective damage to the anterior horn has been observed in patients with spinal cord ischemia after aortic disease [18], and such damage to the anterior horn in patients with cervical spondylosis could be caused by circulatory insufficiency. Dynamics of the spinal cord associated with movement of the cervical spine may affect the intramedullary circulation by compressing or stretching the intra- and extramedullary vessels.

Fujiwara et al. [14] demonstrated that impingement against either the anterior horn or ventral nerve roots may cause cervical spondylotic amyotrophy. In their study of 32 patients, a higher number of cases had impingement against the anterior horn than the ventral nerve root, and 53% cases had impingement against both the anterior horn than the ventral nerve root. According to electrophysiologic findings, Shinomiya et al. [38] also proposed that the impingement against both the ventral nerve root and the anterior horn might cause cervical spondylotic amyotrophy.

Radiographic examination

Delayed CT myelography after intrathecal injection of metrizamide reveals enhancement in the area corresponding to the anterior horn, which represents cavitation or cystic necrosis [13]. It is logical to speculate that cavity formation or cyst necrosis in the anterior horn, probably secondary to infarction, leads to atrophy of the muscles.

Now, magnetic resonance imaging (MRI) is widely used to detect the lesion in the cervical cord. In all cases that

Kameyama et al. [22] reported, magnetic resonance images showed linear high-signal intensity lesions within the compressed spinal cord, extending to more than one segment on sagittal images and small symmetric intramedullary high-signal intensity areas, the so-called snake-eye appearance on axial images [4, 34, 47]. These lesions are not thought to represent potentially reversible edema but irreversible cystic lesion [34, 47], which have often been observed extending from the central gray matter to the anterior horns in autptic findings of cervical compression myelopathy [12, 23, 29].

Neuroradiologically, proximal-type patients have cord atrophy at C4/5 intervertebral level, and distal-type patients have cord atrophy at C5/6 and C6/7. The responsible lesion for cervical spondylotic amyotrophy is in the anterior horn at C5–C6 cord level for the proximal-type, and at C7–Th1 for the distal-type.

Electrophysiologic examination

Denervation potentials and decreased motor unit potentials were noted in the atrophic muscles on standard needle electromyography, but no abnormal findings was observed in the thoracic paraspinal muscles and lower limb muscles [24]. Electromyographic changes in patients with anterior radix or nerve root injury are characterized by fibrillation and positive sharp waves, whereas fasciculation and synchronization are often significant electromyographic findings in motor neuron injury of the anterior horn. However, fasciculation and synchronization are evident in patients with cervical spondylotic amyotrophy [46]. Thus, the anterior horn and motor axons could be damaged in cervical spondylotic amyotrophy. In addition, evoked spinal cord potentials (ESCPs) and cervical motion evoked potentials (MEPs) are useful for diagnosing cervical spondylotic amyotrophy.

In addition, ESCPs and MEPs are useful for diagnosing cervical spondylotic amyotrophy.

Intraoperative evoked muscle amplitude potentials (EMAPs), by stimulating the anterior dura mater and nerve roots through the anterior decompression site, can indicate the specifically responsible lesions easily because direct stimulation can be applied to pathogenetic sites and the EMAPs amplitude is high enough to evaluate these potentials correctly. Compared with the asymptomatic side, silent or delayed EMAPs on the symptomatic side were the proof of nerve root conduction block or disturbed activity of the anterior horn cells [38]. Kaneko et al. [24] demonstrated that attenuation of N13 potentials with preserved N11 potentials at multiple intervertebral levels were observed in patients with the distal-type cervical spondylotic amyotrophy.

Natural history

Cervical spondylotic amyotrophy is characterized by severe motor weakness and wasting in uni- or bilateral upper extremities that do not progress beyond a few myotomes. Sensory loss and pyramidal signs are typically absent or insignificant. Cervical spondylotic amyotrophy follows a self-limited course. After an initial progressive course, the symptoms usually stabilize for years.

Classification

Cervical spondylotic amyotrophy is classified as either proximal (scapular, deltoid, and biceps) or distal (triceps, forearm, and hand) according to the most predominantly affected muscle groups [44]. The proximal-type patients have muscular atrophy in the C5 and C6 myotomes [3, 19, 22, 25, 30, 38], whereas patients with the distal-type amyotrophy have muscular atrophy in C7, C8, and Th1, with muscular atrophy distributed to the forearm and intrinsic muscles. In one study of 16 proximal-type patients and 15 distal-type patients, the distal-type patients often presented cold paresis and/or postural finger tremor, and none of distal-type patients had extension of atrophy to the proximal muscles during a long course of their illness. However, two proximal-type patients had muscular atrophy extended to the distal end, and most proximal-type patients had neurogenic changes on electromyograph extended to the distal muscles.

There are some differences between these two types. Fujiwara et al. [14] demonstrated that distal-type cervical spondylotic amyotrophy was considered to be caused basically by the impingement against the anterior horn and not by impingement against only the ventral nerve root. And this type is characterized by a fewer number of cases, a longer preoperative period, greater number of stenotic canal levels, and more cases with a T₂ high intensity zone on MR images.

Diagnosis

Cervical spondylotic amyotrophy is characterized by severe motor weakness and wasting in uni- or bilateral upper extremities that do not progress beyond a few myotomes. Sensory loss and pyramidal signs are typically absent or insignificant. After an initial progressive course, the symptoms usually stabilize for years. The occurrence of cervical spondylotic amyotrophy is not correlated strictly to the severity of spondylotic changes [22, 31, 37, 38]. Cervical spine MRI may reveal abnormal T₂ hyperintense change in the cervical cord [23], but such change is not

constant [37]. When cervical cord MRI change is absent, the diagnosis of cervical spondylotic amyotrophy is based primarily on clinical presentation, disease course, electrophysiological findings, and the exclusion of other disorders that might account for the symptoms of patients.

Amyotrophic lateral sclerosis can closely resemble cervical spondylotic amyotrophy. Furthermore, some patients present with both cervical spondylosis and amyotrophic lateral sclerosis, thereby adding a diagnostic dilemma because both diseases preferentially affect middle-aged and elderly individuals [49]. It may be difficult to distinguish the clinical manifestations during the early stages of the diseases. Evidence of upper motor neuron degeneration and progressive spread of symptoms and signs are required for the diagnosis of amyotrophic lateral sclerosis. The presence of subtle but definite sensory signs or symptoms usually reveals the diagnosis, and bulbar muscle involvement obviously points to the diagnosis of amyotrophic lateral sclerosis. Electromyographic recordings of the affected atrophic muscles and muscles innervated by the upper cervical cord, such as the sternocleidomastoid, thoracic paravertebral, and lower limb muscles, should be conducted. Electromyographic changes are found only in the affected atrophic muscles in cervical spondylotic amyotrophy patients but are diffused in patients with amyotrophic lateral sclerosis, because cervical spondylotic amyotrophy does not evolve beyond a few myotomes.

Cervical spondylotic amyotrophy also should be distinguished from Hirayama's disease (Table 1). Tashiro et al. [43] described the clinical requirements for the diagnosis of Hirayama's disease. One of the diagnostic criteria is distal dominant muscle weakness and atrophy in the forearm and hand, which means the peak in the flexion position is generally at the C6 level. Maximal tension is distributed from the C7 to Th1 vertebral level, as it takes the shortest route through the posterior convex spinal canal, and muscle weakness is distributed from the C7 to Th1 myelomere. In Hirayama's disease, spinal MRI in cervical flexion shows forward displacement of the dural sac and compressive flattening of the lower cervical cord with widely opened epidural spaces, suggestive of the venous plexus with a flow void.

Treatment

Conservative therapy seems to arrest disease progression in some patients with proximal cervical spondylotic amyotrophy, but has not been documented to be effective in patients with distal cervical spondylotic amyotrophy. Shibuya et al. [37] added the administration of PGE₁ to the treatment of the patients with cervical spondylotic amyotrophy, and improvement of muscle strength after starting injections of

Table 1 Comparison of cervical spondylotic amyotrophy and Hirayama's disease

	Cervical spondylotic amyotrophy	Hirayama's disease
Other terminology	Dissociated motor loss in the upper extremity with cervical spondylosis	Juvenile amyotrophy of the distal upper extremity
Pathology	Cervical spondylosis	Flexion-induced cord compression
Age	Usually ranges from thirties to sixties	Young
Distribution of muscular atrophy	The proximal-type: scapular, deltoid and biceps muscles The distal-type: triceps, forearm and hand muscles	Extensor and flexor muscles of the fingers and wrist
Unilateral/bilateral	Usually unilateral	Unilateral in most patients, asymmetrically bilateral in some, and rarely symmetric
Sensory deficit	No or minimal sensory deficit	No sensory deficit
Muscle weakness	Mainly in the arm and some in the forearm and hand	In the forearm and hand
Deep tendon reflex	Usually normal or hypoactive in the upper limbs	Symmetrically normal in the upper and lower limbs
Pyramidal sign	None	None
MRI	Abnormal T ₂ hyperintense changes in the cervical cord	Dynamic MR imaging shows cervical cord compression

PGE₁ was observed in these patients. Although the improvement was measured by an electrophysiologic method, the mechanisms of PGE₁ are still unknown. Two effects of PGE₁ against the hypoxic injury of neural cells have been reported. One effect is the prevention of apoptotic cell death [1, 27, 28, 32, 35, 50]. Prostaglandin E₁ mediates the activation of adenylyl cyclase and increases the level of endogenous cyclic adenosine monophosphate [28, 35], and PGE₁-induced elevation of c-Fos and c-Myc mRNA levels reflects mitogenic activity [50]. Such effects may prevent apoptotic cell death during ischemic change [1, 27, 28, 32, 35, 50]. The other effect is the increase of blood flow to the central nervous system under ischemic injury. PGE₁ reduces the resistance of vessels by its dilating and antiplatelet effects [9, 17, 41]. It was demonstrated that PGE₁ increases the cerebral blood flow in patients with cerebral infarction [27, 32].

Another option is surgical management. Summary of literature on operative treatment and outcome is listed in Table 2. There was a close association between disease history and recovery of muscle power in patients with cervical spondylotic amyotrophy. With regard to human neuroanatomy and neural innervation of the paralyzed muscles, decompression of the spinal cord and/or the nerve roots should be undertaken. Uchida et al. [46] suggest that surgical treatment of cervical spondylotic amyotrophy requires urgent action. However, Ebara et al. [12] suggested that patients with distal cervical spondylotic amyotrophy undergo cervical traction at first and that they should only undergo surgery if there was a certain measure

of improvement in grip power, finger pinch, or finger function. Also, the methods of operative treatment for cervical spondylotic amyotrophy are still controversial. Anterior decompression and fusion [38] or laminoplasty with or without foraminotomy [30] has been reported. Some authors believe [8, 20, 21, 36] that anterior decompression with or without medial foraminotomy is important for eliminating the anterior and/or anterolateral lesion, whereas some [5, 14] advocate posterior laminoplasty with keyhole foraminotomy. In a study of seven patients with distal-type cervical spondylotic amyotrophy treated with central corpectomy, Srinivasa Rao et al. [40] reported that six patients had improved by a mean patient-perceived outcome score of 66.7% at a mean follow-up of 46.5 months. Similarly, in another study of 32 patients treated with laminoplasty with/without foraminotomy, Fujiwara et al. [14] reported excellent or good results in 78% of these patients. Foraminotomy without laminoplasty was considered a promising treatment means for patients with solitary impingement against the ventral nerve root. However, if patients with cervical spondylotic amyotrophy have spinal canal stenosis, decompression with laminoplasty is indicated. To date, there appears no significant difference in postoperative neurological improvement between the two alternative procedures. The anterior approach is believed to provide an optimal chance of neurological recovery through the complete elimination of the cord-compressing lesion, but can be rather technically demanding when the lesion is at the foraminal entrance and at two or three vertebral levels. On the other hand, posterior

Table 2 Summary of literature on operative treatment and outcome in patients with cervical spondylotic amyotrophy

Year	Number of patients	Number of patients of proximal and distal-type	Follow-up	Procedure	Outcome
Ebara et al. [12]	1988	7	Distal-type: 7	N/A	Laminoplasty: 6 Anterior decompression and fusion: 1 Grip strength improved in 6 patients
Matsunaga et al. [30]	1993	2	N/A	N/A	One patient recovered 5 months after surgery, and the other patient did not recover
Kaneko et al. [24]	2004	6	Distal-type: 6	Laminoplasty	Grip strength improved in 4 patients
Fujiwara et al. [14]	2006	32	Proximal-type: 24 Distal-type: 8	Posterior cervical laminoplasty with or without foraminotomy	In proximal-type patients, muscle power improved in 92% of cases but was improved in only 38% of the distal-type cases
Uchida et al. [46]	2009	51	Proximal-type: 37 Distal-type: 14	Anterior decompression and fusion	62% of patients with proximal muscle atrophy gained 1 or more grades of muscle power on manual muscle testing, whereas 64.3% with distal muscle atrophy failed to gain even 1 grade of improvement
Srinivasa Rao et al. [40]	2009	7	Distal-type: 7	Anterior decompression and fusion	6 improved; 1 worsened The mean improvement of the outcome score was 66.7%

N/A not available

decompression with keyhole foraminotomy is less technically demanding but has the disadvantage of leaving the anterior compressive lesion as is. The presence of a narrow spinal canal [5, 48] increases the likelihood of neurological symptom recurrence as well as adjacent-level instability after anterior fusion. In the absence of spinal canal narrowing, the anterior approach is indicated for a patient with lesions ventral to the cord at one or two intervertebral levels, whereas in the presence of a narrow spinal canal, posterior decompression is the choice for a lesion involving more than two intervertebral levels. Although the surgical procedure used for amyotrophy is still controversial, it does not exert a significant impact on clinical outcomes.

Fujiwara et al. [14] found that muscle power improved in 92% of proximal-type patients, whereas was improved in only 38% of distal-type patients after surgery in their series. It seems that the response to surgery in patients with distal-type cervical spondylotic amyotrophy was inferior to that in patients with proximal-type. One possible reason for this phenomenon is that distal-type patients basically have impingement against the anterior horn, because the spinal cord, including the anterior horn, has less ability than ventral nerve roots to regenerate. The other reasons may be the longer distance from the spinal cord to muscles, a long preoperative period, a greater number of cervical spine misalignment, and a narrow spinal canal. However, even in proximal-type patients, a long preoperative period and medial compression of the spinal cord on MRI were factors correlated with poor muscle power improvement.

Erb point-stimulated compound muscle action potentials (CMAPs) are useful for predicting surgical outcomes of cervical spondylotic amyotrophy [42]. Fujiwara et al. [14] reported that the patients with fair results after surgery had less than 10% preoperative Erb point stimulated CMAPs, whereas all patients with over 10% amplitude recovered. Therefore, recovery can be expected in the latter patients. However, caution should be taken because some patients with less than 10% also recovered.

Conclusions

Cervical spondylotic amyotrophy is not common, and should be distinguished from Hirayama's disease and motor neuron disease. Although cervical spondylotic amyotrophy always follows a self-limited course, it still remains a great challenge for spine surgeons. Treatment includes conservative and operative management. The methods of operative management for cervical spondylotic amyotrophy are still controversial. Anterior decompression and fusion or laminoplasty with/without foraminotomy is undertaken. And, surgical outcome of the distal-type patients is inferior to that of the proximal-type patients.

References

1. Abe K, Nishimura M, Kakiuchi M (1994) Spinal cord blood flow during prostaglandin E1 induced hypotension. *Prostaglandins Leukot Essent Fatty Acids* 51:173–176
2. Ahdab R, Creange A, Benaderette S, Lefaucheur JP (2009) Cervical spondylotic amyotrophy presenting as dropped head syndrome. *Clin Neurol Neurosurg* 111:874–876
3. Akiyama N, Kitamura H, Yoshimura Y, Tsuchiya T, Shiokawa A (1980) Dissociated motor loss in the upper extremities with cervical spondylosis, a report of autopsy case. *Nippon Seikeigeka Gakkai Zasshi* 54:303–310 (in Japanese)
4. Al-Mefty O, Harkey LH, Middleton TH, Smith RR, Fox JL (1988) Myelopathic cervical spondylotic lesions demonstrated by magnetic resonance imaging. *J Neurosurg* 68:217–222
5. Baba H, Chen Q, Uchida K, Imura S, Morikawa S, Tomita K (1996) Laminoplasty with foraminotomy for coexisting cervical myelopathy and unilateral radiculopathy: a preliminary report. *Spine* 21:196–202
6. Baba H, Maezawa Y, Uchida K, Furusawa N, Wada M, Imura S, Kawahara N, Tomita K (1998) Cervical myeloradiculopathy with entrapment neuropathy: a study based on the double-crush concept. *Spinal Cord* 36:399–404
7. Brain WR, Northfield D, Wilkinson M (1952) The neurological manifestations of cervical spondylosis. *Brain* 75:187–225
8. Brigham CD, Tsahakis PJ (1995) Anterior cervical foraminotomy and fusion. Surgical technique and results. *Spine* 20:766–770
9. Carlson LA, Ekelund LG, Oro L (1969) Circulatory and respiratory effects of different doses of prostaglandin E1 in man. *Acta Physiol Scand* 75:161–169
10. Crandall PH, Batzdorf U (1966) Cervical spondylotic myelopathy. *J Neurosurg* 25:57–66
11. Dorsen M, Ehni G (1979) Cervical spondylotic radiculopathy producing motor manifestations mimicking primary muscular atrophy. *Neurosurgery* 5:427–431
12. Ebara S, Yonenobu K, Fujiwara K, Yamashita K, Ono K (1988) Myelopathy hand characterized by muscle wasting. A different type of myelopathy hand in patients with cervical spondylosis. *Spine* 13:785–791
13. Fujiwara K (2001) Cervical spondylotic amyotrophy with intramedullary cavity formation. *Spine* 26:E220–E222
14. Fujiwara Y, Tanaka N, Fujimoto Y, Nakanishi K, Kamei N, Ochi M (2006) Surgical outcome of posterior decompression for cervical spondylosis with unilateral upper extremity amyotrophy. *Spine* 31:E728–E732
15. Gebere-Michael SG, Johnston JC, Metaferia GZ, Wuhib MZ, Fernandez HH (2010) Bilaterally symmetric cervical spondylotic amyotrophy: a novel presentation and review of the literature. *J Neurol Sci* 290:142–145
16. Gilles FH, Nag D (1971) Vulnerability of human spinal cord in transient cardiac arrest. *Neurology* 21:833–839
17. Hadhadzy P, Vizi EX, Magyar K, Knoll J (1976) Inhibition of adrenergic neurotransmission by prostaglandin E1 (PGE1) in the rabbit ear artery. *Neuropharmacology* 15:245–250
18. Herrick MK, Mills PE Jr (1971) Infarction of spinal cord. Two cases of selective gray matter involvement secondary to asymptomatic aortic disease. *Arch Neurol* 24:228–241
19. Ito T, Tsuji H, Tamak iT, Miyasaka H, Toyoda A (1980) The clinical consideration of the dissociated motor loss syndrome (Keegan) in diseases of the cervical spine. *Nippon Seikeigeka Gakkai Zasshi* 54:135–151 (in Japanese)
20. Jho HD (1996) Microsurgical anterior cervical foraminotomy for radiculopathy: a new approach to cervical disc herniation. *J Neurosurg* 84:155–160
21. Johnson JP, Filler AG, McBride DQ, Batzdorf U (2000) Anterior cervical foraminotomy for unilateral radicular disease. *Spine* 25:905–909
22. Kameyama T, Ando T, Yanagi T, Yasui K, Sobue G (1998) Cervical spondylotic amyotrophy. Magnetic resonance imaging demonstration of intrinsic cord pathology. *Spine* 23:448–452
23. Kameyama T, Hashizume Y, Ando T, Takahashi A, Yanagi T, Mizuno J (1995) Spinal cord morphology and pathology in ossification of the posterior longitudinal ligament. *Brain* 118:263–278
24. Kaneko K, Taguchi T, Toyoda K, Kato Y, Azuma Y, Kawai S (2004) Distal-type cervical spondylotic amyotrophy: assessment of pathophysiology from radiological findings on magnetic resonance imaging and epidurally recorded spinal cord responses. *Spine* 29:E185–E188
25. Keegan JJ (1965) The cause of dissociated motor loss in the upper extremity with cervical spondylosis. *J Neurosurg* 23:528–536
26. Kokubo Y, Uchida K, Kobayashi S, Yayama T, Sato R, Nakajima H, Takamura T, Mwaka E, Orwotho N, Bangirana A, Baba H (2008) Herniated and spondylotic intervertebral discs of the human cervical spine: histological and immunohistological findings in 500 en bloc surgical samples. Laboratory investigation. *J Neurosurg Spine* 9:285–295
27. Komaba Y, Kitamura S, Terashi A (1998) Effect of prostaglandin E1 on cerebral blood flow in patients with chronic cerebral infarction. *Intern Med* 37:841–846
28. Macphee CH, Drummond AH, Otto AM, Jimenez de Asua L (1984) Prostaglandin F2 alpha stimulates phosphatidylinositol turnover and increases the cellular content of 1, 2-diacylglycerol in confluent resting Swiss 3T3 cells. *J Cell Physiol* 119:35–40
29. Mair WG, Druckman R (1953) The pathology of spinal cord lesions and their relation to the clinical features in protrusion of cervical intervertebral discs; a report of four cases. *Brain* 76:70–91
30. Matsunaga S, Sakou T, Imamura T, Morimoto N (1993) Dissociated motor loss in the upper extremities. Clinical features and pathophysiology. *Spine* 18:1964–1967
31. Mori K, Yamamoto T, Nakao Y, Maeda M (2006) Cervical spondylotic amyotrophy treated by anterior decompression. Three case reports. *Neurol Med Chir* 46:366–370
32. Olesen J (1976) Effect of intracarotid prostaglandin E1 on regional cerebral blood flow in man. *Stroke* 7:566–569
33. Ota H, Ono K (1975) Dissociated motor loss in the upper extremity with cervical spondylosis. *Rinsho Seikei Geka* 10:1124–1131 (in Japanese)
34. Ramanauskas WL, Wilner HI, Metes JJ, Lazo A, Kelly JK (1989) MR imaging of compressive myelomalacia. *J Comput Assist Tomogr* 13:399–404
35. Rozengurt E, Collins MK, Keehan M (1983) Mitogenic effect of prostaglandin E1 in Swiss 3T3 cells: role of cyclic AMP. *J Cell Physiol* 116:379–384
36. Saringer W, Nobauer I, Reddy M, Tschabitscher M, Horacek A (2002) Microsurgical anterior cervical foraminotomy (uncoforaminotomy) for unilateral radiculopathy: clinical results of a new technique. *Acta Neurochir* 144:685–694
37. Shibuya R, Yonenobu K, Yamamoto K, Kuratsu S, Kanazawa M, Onoue K, Yoshikawa H (2005) Acute arm paresis with cervical spondylosis: three case reports. *Surg Neurol* 63:220–228
38. Shinomiya K, Komori H, Matsuoka T, Mutoh N, Furuya K (1994) Neuroradiologic and electrophysiologic assessment of cervical spondylotic amyotrophy. *Spine* 19:21–25
39. Sobue I, Kato H, Yanagi T (1975) Clinical characteristics and classification of cervical spondylotic myelopathy. *Rinsho Seikeigaku* 10:999–1006 (in Japanese)

40. Srinivasa Rao NV, Rajshekhar V (2009) Distal-type cervical spondylotic amyotrophy: incidence and outcome after central corpectomy. *J Neurosurg Spine* 10:374–379
41. Szczeklik J, Dubiel JS, Mysik M, Pyzik Z, Krol R, Horzela T (1978) Effects of prostaglandin E1 on pulmonary circulation in patients with pulmonary hypertension. *Br Heart J* 40:1397–1401
42. Tani T, Kishimoto H, Tsuboya H, Kimura J (2002) Electrophysiologic assessment of shoulder girdle weakness in patients with cervical spondylosis: prognostic value of supraclavicular stimulation. *J Clin Neuromuscul Dis* 4:11–18
43. Tashiro K, Kikuchi S, Itoyama Y, Tokumaru Y, Sobue G, Mukai E, Akiguchi I, Nakashima K, Kira J, Hirayama K (2006) Nationwide survey of juvenile muscular atrophy of distal upper extremity (Hirayama disease) in Japan. *Amyotroph Lateral Scler* 7:38–45
44. Tsuboi Y, Tokumaru Y, Hirayama K (1995) Clinical difference between “proximal” and “distal” type of cervical spondylotic amyotrophy. *Rinsho Shinkeigaku* 35:147–152 (in Japanese)
45. Uchida K, Nakajima H, Sato R, Kokubo Y, Yayama T, Kobayashi S, Baba H (2005) Multivariate analysis of the neurological outcome of surgery for cervical compressive myelopathy. *J Orthop Sci* 10:564–573
46. Uchida K, Nakajima H, Yayama T, Sato R, Kobayashi S, Kokubo Y, Mwaka ES, Baba H (2009) Anterior and posterior decompressive surgery for progressive amyotrophy associated with cervical spondylosis: a retrospective study of 51 patients. *J Neurosurg Spine* 11:330–337
47. Wada E, Ohmura M, Yonenobu K (1995) Intramedullary changes of the spinal cord in cervical spondylotic myelopathy. *Spine* 20:2226–2232
48. Wolf BS, Khilnani M, Malis L (1956) The sagittal diameter of the bony cervical spinal canal and its significance in cervical spondylosis. *J Mt Sinai Hosp NY* 23:283–292
49. Yamada M, Furukawa Y, Hirohata M (2003) Amyotrophic lateral sclerosis: frequent complications by cervical spondylosis. *J Orthop Sci* 8:878–881
50. Yamashita T, Tsuda T, Hamamori Y, Takai Y (1986) Possible involvement of cyclic AMP and calcium ion in prostaglandin E1-induced elevation of c-myc mRNA levels in Swiss 3T3 fibroblasts. *J Biol Chem* 261:16878–16882
51. Yanagi T, Kato H, Sobue I (1976) Cervical spondylotic amyotrophy simulating motor neuron disease. *Rinsho Shinkeigaku* 16:520–528 (in Japanese)