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ORIGINAL COMMUNICATION

Brachial multisegmental amyotrophy caused by cervical anterior horn cell disorder associated with a spinal CSF leak: a report of five cases

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Abstract

Objective Common symptoms in patients with a spinal CSF leak include orthostatic headaches, neck stiffness, and hearing difficulties. The main outcome of this report was to introduce and characterize brachial multisegmental amyotrophy, a rare, but treatable symptom associated with a spinal CSF leak.

Methods Between 2013 and 2017, five patients who developed progressive amyotrophy were referred to our hospital. A retrospective and prospective analysis of clinical, electrophysiological, and neuroimaging findings is presented. Data were analyzed between August 2013 and April 2019.

Results Amyotrophy was observed in the C5–C8 myotomes and was more prominent in the proximal muscles than in the distal muscles. Amyotrophy was unilateral in three patients and asymmetric bilateral in two. Electromyography revealed active and chronic denervation in the C5–C8 myotomes, particularly C5–6, of all patients. Although the clinical manifestations of these cases were similar to amyotrophic lateral sclerosis, unusual neuroimaging findings were observed: spinal T2-weighted MRI revealed high-signal-intensity lesions in the bilateral anterior horns at the C2–C4 spinal levels in all five cases; ventral epidural fluid collection was also observed. Thin-cut MRI or digital subtraction myelography showed ventral dural defects associated with CSF leaks at high thoracic levels in four patients; four underwent surgical dural repair, which attenuated or stabilized neurological symptoms, while upper limb weakness worsened in the other patient who did not undergo surgery.

Conclusions A spinal dural defect may be the essential cause of brachial multisegmental amyotrophy. Surgical dural repair may alter the progressive course of this rare condition.

Keywords Cerebrospinal fluid leak · Dural defect · Motor neuron disease · Amyotrophic lateral sclerosis; neurosurgery

Objective

Cerebrospinal fluid (CSF) leaks are a pathological condition in which CSF leaks from the subarachnoid space into the extradural space [1]. Orthostatic headaches, neck stiffness, vomiting, hearing difficulties, and photophobia are the main symptoms of intra-cranial hypotension due to CSF leaks [2]. Motor neuron disease similar to amyotrophic lateral sclerosis (ALS), multisegmental amyotrophy, has rarely been reported in patients with CSF leaks [3–8]; therefore, limited information is currently available on the diagnosis and treatment of this condition due to its rarity.

Ryo Morishima and Keisuke Takai have contributed equally to this work.

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Methods

Data on consecutive patients who presented with brachial multisegmental amyotrophy and CSF leaks at our hospital between 2013 and 2017 were analyzed. All patients gave their informed consent prior to their inclusion in the study.

Results

Five patients (Table 1) had slowly progressive amyotrophy in the C5–C8 myotomes. Amyotrophy was more prominent in the proximal muscles than in the distal muscles in four patients and in the distal muscles in one patient. In two patients, amyotrophy developed in one limb and progressed to the other limb 3 or 16 years after its onset. Electromyography (EMG) revealed active and chronic denervation of varying severities in the C5–C8 myotomes, particularly C5–6, of all patients. Opening CSF pressures were within normal ranges, and no patient developed symptoms of intracranial hypotension. Although CSF was clear, red blood cells (RBCs) were detected in three patients. Brain MRI showed superficial hemosiderosis in three patients, with cerebellar ataxia being observed in two. In all patients, spinal T2-weighted MRI (T2WI) revealed high-signal-intensity lesions in the bilateral anterior horns at the C2–C4 spinal levels with ventral epidural fluid collection (VEFC) at the C2–T12 spinal levels (Fig. 1). A dural defect on the ventral side of the upper thoracic level was identified in four patients on neuroimaging. Close observation was selected for the first two patients, because the causal relationship between amyotrophy and the spinal CSF leak was unclear at that time. The surgical repair of dural defects was performed on the three other patients, including one who had been misdiagnosed with ALS at another institution. Ventral epidural fluid collection and RBCs in CSF disappeared after surgery. Clinical symptoms improved or stabilized in the three patients; however, upper limb weakness deteriorated in the follow-up period in the two patients who did not undergo surgery. Of these two patients, one died from cerebral hemorrhage, and we performed surgical dural repair on the other, which stabilized symptoms.

Table 1 Clinical and radiological findings in five patients with multisegmental amyotrophy associated with a spinal cerebrospinal leak

Age/sex	Amyotrophy	Ataxia/hearing loss	Symptom duration (year)	CSF pressure (cmH_2O)	RBCs in CSF (cells/μl)	CNS siderosis on brain MRI	T2 high signal on cervical MRI	Ventral CSF collection	Dural defect	Dural repair	Outcome
66/M	R > L C5–8	Yes/no	11	NA	NA	Yes	C3–C4	C2–T6	ND	No	Deterio[a]
48/M	L C5–6	No/no	1	18	0	No	C2–C3	C2–T11	C7/T1	Yes	Stable[b]
62/F	R C5–6	No/no	7	12	150–325	Yes	C3–C4	C4–T6	T2/3	Yes	Stable
55/M	L C5–8	Yes/yes	10	18	275–375	Yes	C3	C7–T7	T1/2	Yes	Stable
67/M	R < L C5–8	No/no	20	9	75–675	No	C2–C4	C2–T12	T2/3	Yes	Improved[c]

CNS central nervous system, *CSF* cerebrospinal fluid, *Deterio* deterioration, *L* left, *MRI* magnetic resonance imaging, *NA* not applicable, *ND* not detected, *R* right, *RBC* red blood cell

[a]Upper limb weakness deteriorated in the 4-year follow-up period. This patient died from cerebral hemorrhage

[b]Before surgery, left deltoid muscle weakness deteriorated in the 3-year follow-up period

[c]After surgery, right deltoid muscle weakness improved, although bibrachial amyotrophy did not change

Case presentation

Case 2

A 48-year-old man presented with a 1-year history of weakness of the left arm and a tingling sensation on the left side of his body and leg. He had a previous history of

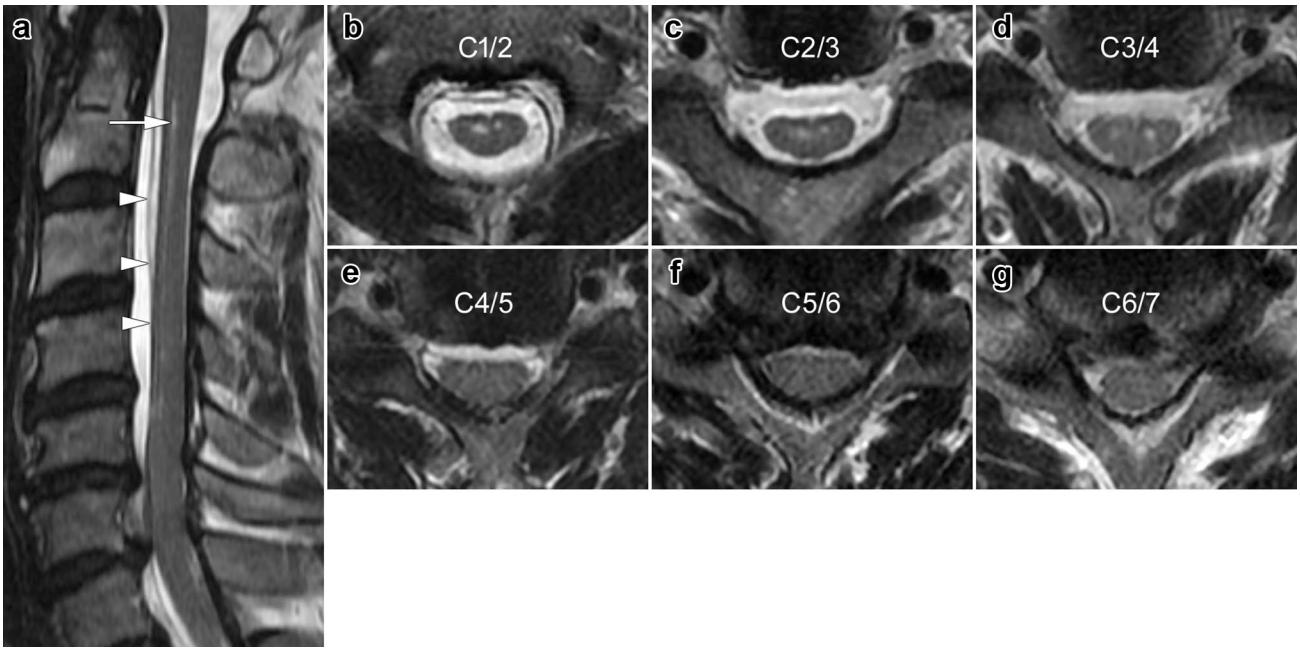

Fig. 1 (Case 5) Sagittal (**a**) and axial (**b**–**g**) T2-weighted MRI of the cervical spine showing bilateral high-signal-intensity lesions located at the anterior horns at the C2–C4 levels (arrow) and ventral epidural fluid collection (arrowheads). Note that a T2 high-signal-intensity lesion was not found at the C5–7 levels

head-and-neck trauma due to a skiing accident 15 years before. A neurological examination revealed amyotrophy in the left C5–6 myotomes, particularly in the deltoid muscle [Medical Research Council (MRC) grade 4]. EMG showed active and chronic denervation in the left C5–6 myotomes. The opening pressure was 18 cmH_2O and no RBCs were detected in CSF. Spinal MRI showed high-signal-intensity lesions on T2WI in the bilateral anterior horns and posterior funiculus at the C2–C3 spinal levels and VEFC at the C2–T11 spinal levels. Close observation was selected, because the causal relationship between multisegmental amyotrophy and the spinal CSF leak was unclear. However, his deltoid muscle weakness suddenly worsened 3 years later (MRC 3). On thin-cut spinal FIESTA MRI, a dural defect was suspected at the C7/T1 level. Surgical repair of the dural defect was performed through a posterior transdural approach [9]. The dural defect (5 × 3 mm) was identified ventral to the spinal cord. VEFC disappeared after surgery, which stabilized symptoms.

Case 3

A 62-year-old woman presented with a 7-year history of weakness and atrophy of the right arm. She had been misdiagnosed with ALS at another institution and was complicated by interstitial pneumonia after the administration of riluzole. The patient also developed femoral head necrosis after the administration of corticosteroids to treat interstitial pneumonia. Hip joint replacement surgery was performed. A neurological examination revealed amyotrophy in the right C5–6 myotomes, particularly in the deltoid muscle (MRC 3). EMG showed active and chronic denervation in the C5–7 myotomes and trapezius muscle. Neurogenic changes were not observed in thoracic or lumbar segmental muscles. The opening pressure was 12 cmH_2O and RBCs were detected in CSF. Brain MRI showed slight hemosiderin deposition on the cerebellum; however, she did not have any symptoms of superficial hemosiderosis. Spinal MRI showed high-signal-intensity lesions on T2WI in the bilateral (right > left) anterior horns at the C3–4 spinal levels (Fig. 2a–c) and VEFC at the C4–T6 spinal levels (Fig. 2d). On digital subtraction myelography, a dural defect was suspected at the T2/3 level (Fig. 2e). This patient underwent similar direct surgery via a posterior approach (Fig. 2f, g). VEFC and RBCs in CSF disappeared after surgery. The progression of symptoms did not occur in the 20-month follow-up period.

Discussion

We herein described five cases of CSF leaks that presented with brachial multisegmental amyotrophy, which included four surgically treated cases. Common MRI findings were high-signal-intensity lesions on T2WI in the bilateral cervical anterior horns and VEFC. EMG findings were consistent with lower motor neuron dysfunction in the C5–8 segmental

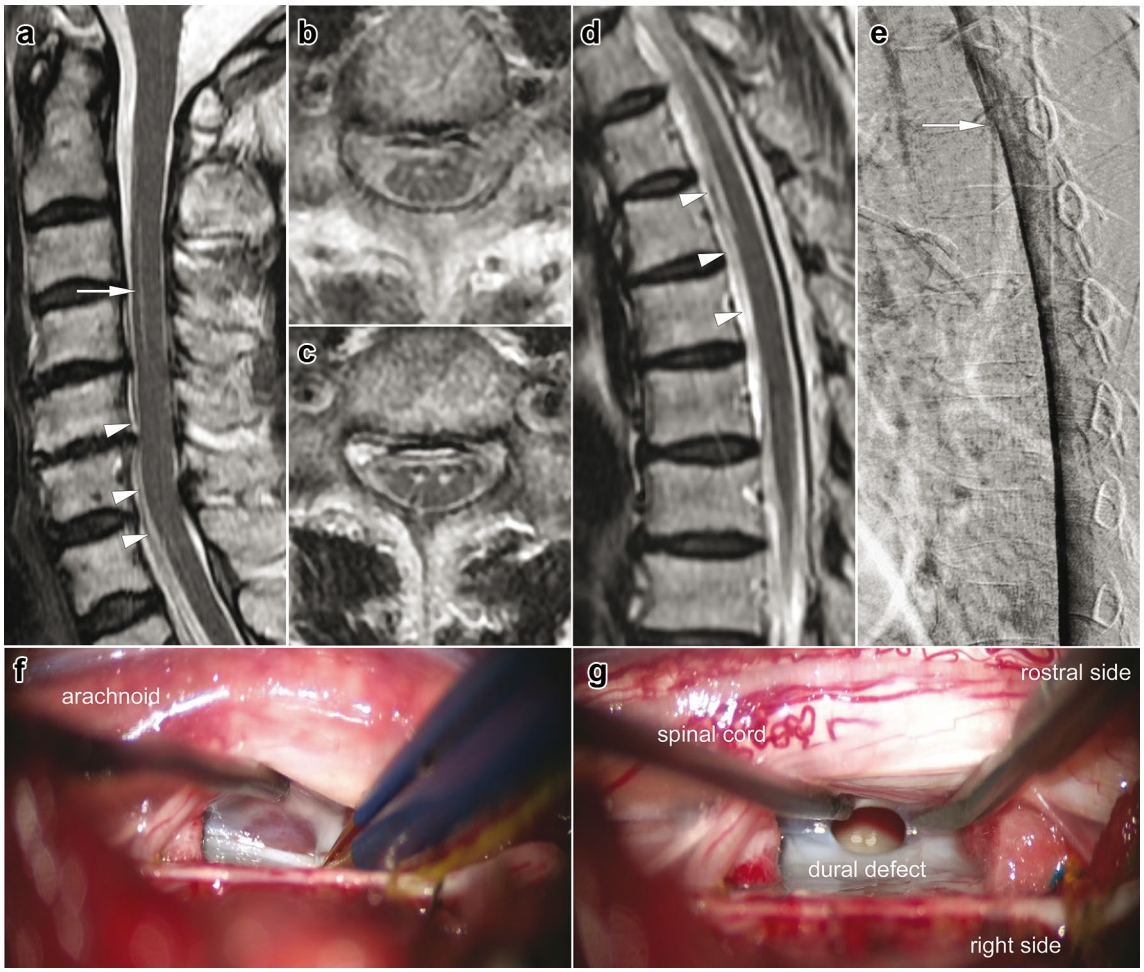

Fig. 2 (Case 3) Sagittal (**a**) and axial (**b**, **c**) T2-weighted MRI of the cervical spine showing bilateral high-signal-intensity lesions located at the anterior horns at the C3–C4 levels (arrow). Sagittal MRI of the cervical (**a**) and thoracic (**d**) spine showing ventral epidural fluid collection (arrowheads). Digital subtraction myelography (**e**) showing a dural defect at the T2/3 spinal level (arrow). Intraoperative image (**f**, **g**) showing a dural defect (4 × 2 mm) ventral to the spinal cord

myotomes, particularly C5–6, of all five patients. Lower motor neuron dysfunction may be explained by anterior horn lesions, because their localization was compatible with the C5–6 segmental myotomes [8].

To the best of our knowledge, only case reports of upper limb weakness with VEFC have been published to date (Table 2) [3–8]. Among eight cases, four had cervical anterior horn lesions [4, 6–8]. Two cases had superficial hemosiderosis [3, 6]. Six cases had idiopathic VEFC and the other two had VEFC due to nerve root avulsion injury or spine injury [3, 4]. In all cases, upper limb weakness progressively deteriorated; however, six cases underwent neurosurgery [3–6], which improved (four cases) [4, 5] or stabilized (two cases) [3, 6] upper limb weakness.

Three theories have been proposed for lower motor neuron dysfunction in patients with VEFC. The first theory is that superficial hemosiderosis itself may cause spinal cord dysfunction [3, 6]; the second theory is that this is a different condition to Hirayama disease, in which encapsulated VEFC may cause compression of the spinal cord, leading to mechanical anterior horn cell damage [5]; and the third theory is that a posterior shift in the spinal cord may cause the tethering of anterior motor nerve roots, which may cause anterior horn cell loss [5]. We consider the present results to support the third theory for three reasons. Two out of five patients did not have superficial hemosiderosis. From a surgical perspective, we do not consider this to be a different condition to Hirayama disease, in which the spinal cord is compressed by a tight dural canal in neck flexion [10], because VEFC in our five patients was so small that it was insufficient to cause severe spinal cord compression. Furthermore, although patients with Hirayama disease commonly have asymmetric spinal cord atrophy resulting from physical compression [11], spinal cord atrophy was not detected in any of our patients; we suggest that an intermittent posterior shift in the spinal cord by VEFC caused the

Table 2 Reported cases of arm weakness associated with a spinal cerebrospinal leak

Authors, year	Age/sex	Etiology	Weakness	Ataxia, hearing loss	Symptom duration (year)	CNS siderosis on brain MRI	T2 high signal on cervical MRI	Ventral CSF collection	Dural defect	Dural repair	Outcome
Driver-Dunckley et al., 2010	54/M	Thoracic spine fracture	R-arm	Yes	18	Yes	No	C3–T12	T3	Yes	Stable
Kotani et al., 2010	18/M	L-root avulsion	R-arm	No	10	No	C2–C5	C3–L3	C6,7	Yes	Improved
Deluca et al., 2011	48/M	Idiopathic	Bil-arms	No	5	Yes	No	C2–L4	T12/L1	Yes	Improved
	40/M	Idiopathic	Bil-arms	No	2	No	No	C3–L1	T11/12	Yes	Improved
	32/M	Idiopathic	R-arm	No	10	No	No	C2–T12	C4	Yes	Improved
Kumar et al., 2012	58/M	Idiopathic	Bil-arms	Yes	1.5	Yes	C3–C4	C2–L5	T2/3	Yes	Stable
Zakaria et al., 2013	68/M	Idiopathic	Bil-arms	No	2	No	C2–C5	C2–C5	ND	No	Stable
Foster et al., 2014	48/M	Idiopathic	Bil-arms	No	17	No	C3–C5	C2–T9	ND	No[a]	Stable

Bil bilateral, *CNS* central nervous system, *CSF* cerebrospinal fluid, *L* left, *MRI* magnetic resonance imaging, *ND* not detected, *R* right

[a]Surgical exploration failed to confirm a dural defect

tethering of anterior motor nerve roots. In a spinal position, VEFC was small; however, in a prone or lateral position, VEFC may enlarge, because the dural defect was located ventral to the spinal cord (Fig. 2). C5 anterior motor nerve roots are more likely to be affected by tethering of the cervical cord. For example, in cervical decompression surgery, the rate of C5 palsy was markedly higher than that observed with other nerves [12]. The tethering of anterior nerve roots may lead to axonotmesis, which may result in anterior horn cell loss.

Conclusions

We herein reported five patients with brachial multisegmental amyotrophy with cervical anterior horn dysfunction associated with a spinal CSF leak. The clinical manifestations of these patients were similar to ALS; however, the differential diagnosis of our patients from those with ALS was achieved based on cervical MRI. A spinal dural defect may be the essential cause of brachial multisegmental amyotrophy. Surgical dural repair may alter the progressive course of this rare condition.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval This study was approved by the Institutional Review Board at Tokyo Metropolitan Neurological Hospital. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Committee and with the 1964 Declaration of Helsinki and its later amendments. All patients gave their informed consent prior to their inclusion in the study.

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