Congenital cervical spinal muscular atrophy: a non-familial, non progressive condition of the upper limbs

G Hageman, V Th Ramaekers, B G J Hilhorst, A R Rozeboom

Abstract
Two patients with congenital cervical spinal muscular atrophy had symmetrical severe muscle weakness and wasting confined to the upper limbs, areflexia and congenital contractures. The shoulders were internally rotated, elbows extended and wrists flexed. There were no sensory or bulbar symptoms, scoliosis, long tract signs or lower limb involvement. This condition should be regarded as a neurogenic type of arthrogryposis, limited to the upper limbs.

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The most common cause of congenital contractures and muscle weakness present at birth is anterior horn cell degeneration. This condition is classified as arthrogryposis multiplex congenita, neurogenic type in the Classification of Neuromuscular Diseases, in the section Spinal Muscular Atrophies and other disorders of motor neurons.1 Price in 1933 was the first to describe a reduction in the number of alpha motor neurons in the spinal cord of a child with congenital contractures and neurogenic muscular atrophy.2 More recent neuropathological studies have shown a degeneration of anterior horn cells, rather than dysplasia.3,4 Claren and Hall5 compared the spinal cords of 10 infants with anterior horn cell degeneration, one with contractures due to oligohydramnios and 8 cases of Werndig-Hoffmann disease, with those of 11 age matched normal controls. In this study alpha motor neurons were absent in both the patients with anterior horn cell degeneration and those with Werndig-Hoffmann disease, whereas small motor neurons were increased in the former, but decreased in the latter.

The clinical picture is characteristic: severe muscle weakness and congenital contractures, hypotonia and areflexia, absent skin creases, dimpling of the skin, abnormal dermatoglyphics and normal intelligence, non-progressive and non-familial.6

In a prospective clinical study of 75 cases with multiple congenital contractures a diagnosis of anterior horn cell degeneration was made in 17 cases.7 Of these 17 cases all four limbs were involved in 11 and only the lower limbs in 5 cases. In one case, only the upper limbs were affected, suggesting that anterior horn cell degeneration limited to the upper extremities, with a symmetrical flaccid paresis involving proximal and distal muscle groups is very rare. In 1981 Darwish, Sarnat et al described 3 similar cases,8 for which they used the term "congenital cervical spinal atrophy". Despite extensive search of the literature, we could not find other cases of congenital cervical spinal muscular atrophy. We present two additional cases of non familial, non progressive congenital cervical spinal muscular atrophy, with the characteristic clinical picture as previously described by Darwish, Sarnat, et al and Hageman et al.9,8

Case reports
CASE 1
The patient was the first born child of healthy non-consanguineous parents. She presented at birth with "congenital arthrogryposis multiplex", restricted to the joints of both upper limbs. The family history was negative for neurological or neuromuscular diseases. Pregnancy and delivery of the patient had been uneventful. Severe bilateral shoulder girdle, arm and hand weakness had been present from the time of birth. Physiotherapy was started soon after birth. General paediatric examination at 12 months revealed no abnormalities.

On neurological examination (fig 1) severe bilateral hypotonia and weakness was manifest in her shoulder girdle, arms and hands. Both arms remained internally rotated and adducted with extended elbows, the wrists in a flexed and ulnar deviated position and fingers in an extended position. Despite a puffy appearance of both arms and the dorsum of both hands due to a large subcutaneous fat mass, palpation detected serious wasting and atrophy of all muscle groups extending from the shoulder girdle to the hand muscles. Cutaneous dimples were noted over the dorsal region of both wrists, in the vicinity of the elbow joints and over the left shoulder. Spontaneous activity was seriously impaired and limited to slight shoulder adduction, elbow extension and limited arm flexion and supination of the forearm due to preserved brachioradialis muscle function. Hand function remained severely impaired due to both the contractures of wrists and finger joints and severe weakness of wrist extension and finger flexion. All tendon reflexes (biceps, triceps and brachioradialis) were absent. All sensory qualities including pain and temperature sensation remained intact. Both palms of the hands showed abnormal dermatoglyphic patterns with absent distal digital flexion...
Figure 1  Hypotonia and weakness of the upper limbs with extended elbows, flexed wrists with ulnar deviation. Note the cutaneous dimpling at the wrists.

Figure 2  Severe muscle weakness and wasting confined to the upper limbs with congenital contractures in a characteristic position (Publication of photography with permission).

creases, distal translocation of the axial tri-radii, hypoplastic ridges and abnormal vertical alignment of papillary ridges. Testing of muscle strength, tone and reflexes in all other muscle groups of the neck, trunk and lower extremities were normal. The cranial nerves, bulbar function and coordination were found to be normal and intact. Special investigations included normal skull and spinal x-rays as well as normal and proportionate skeletal architecture of the shoulders and arms. Hand x-rays revealed ulnar deviation of the metacarpal bones II-V. Ultrasonography of the shoulder girdle and arms confirmed severe atrophy and wasting of all muscle groups with the presence of echodense signals within the atrophic muscles which was considered to be consistent with fat replacement.

In addition there was a large space occupied by an abundant subcutaneous fat mass. MRI of the brain and upper spinal region at the age of two weeks showed a normal width of the cervical spinal canal with a normal diameter and structure of the medulla oblongata and spinal cord. Repeated biochemical investigations disclosed normal serum levels for electrolytes, liver transaminases, alkaline phosphatase, CK and aldolase. Serological investigations excluded infections by herpes simplex, herpes zoster, cytomegalovirus, rubella, hepatitis A and B, Ebstein-Barr virus, Toxoplasma and listeria.

Needle EMG of the triceps muscle did not detect any activity. At the age of 12-5 months a triceps muscle biopsy showed severe neurogenic muscle atrophy with grouped atrophic fibres and signs of compensatory collateral reinnervation and muscle fibre hypertrophy. Radial nerve biopsy consisted of 7 nerve fasciculi and showed numerous atrophic axons, but no de- or remyelination. Electronmicroscopy did not show any specific ultrastructural changes.

CASE 2
This was a 31 year old man, born with severe muscle weakness and congenital contractures of the upper limbs. His parents were healthy and non-consanguineous with no family history of neuromuscular disorders. His two sisters were healthy. Fetal movements were experienced as normal during the whole pregnancy. Delivery was in head position. Shortly after birth conservative treatment was started with casts. Psychomotor development and growth were normal.

To increase flexion of one of both fixed extended elbows, orthopaedic surgery was performed on the right elbow at the age of 5 years, probably anterior transfer of the triceps muscle. At the age of 31 years physical examination showed normal intellectual function, speech, cranial and cerebellar functions.

He had severe bilaterally symmetrical wasting and weakness of all muscles of the upper limbs (fig 2) with (congenital) contractures of the shoulders, elbows and wrists. There was a
severe rigidity of the joints with internal rotation of the shoulders and marked limitation of abduction, fixed extended elbows with some flexion possibility on the right side after surgery and flexed wrists. Tendon reflexes were decreased or absent in the upper limbs and normal in the lower limbs. Plantar responses were flexor. No fasciculations were seen. All sensory modalities were normal. The trunk muscles and lower limb muscles were of normal size and power. There was no kyphoscoliosis or contractures of the lower limbs. Dimpling of the skin over the affected joints was absent. The hands showed absent digital flexion creases in most fingers and hypoplastic palmar creases.

Conventional radiographs of the cervical spine were normal. Muscle CT scanning showed severe atrophy of the shoulder girdle and the upper limb muscles with fat surrounding the muscles. Slices through trunk, pelvic region and lower limb muscles were normal.

Data of electromyography and magnetic stimulation of the left motor cortex, cervical and the lumbar spine are presented in the table. Cervical spine—MRI showed herniation of the intervertebral discs C2-C4 and C5-C7 with impingement of the spinal cord but with a normal signal intensity of the cord on the T2-weighted images. The transverse and sagittal T1-images showed a slight atrophy of the thoracic cord and the transverse diameter of the cervical cord was at the lower limit of normal.6

Discussion

Our cases are remarkably similar to the cases described by Darwish et al.8 severe symmetric lower motor neuron deficit in the upper extremities at the time of birth, no history of injury to the cervical spinal cord or the brachial plexus during delivery and severe muscle wasting suggesting chronic denervation in utero. The absence of sensory deficits and the normal motor nerve conduction velocities in case 2 suggest involvement at the anterior horn cell level. There is no progression of weakness and the family history is negative. Scoliosis, long tract signs, cerebellar or cranial nerve involvement are absent.

In our opinion, congenital cervical spinal muscular atrophy should be regarded as arthrogryposis, neurogenic type (anterior horn cell degeneration) with a rare distribution, that is, limited to the upper limbs.

More often anterior horn cell degeneration has been described as only affecting the lower limbs, both sporadically9 and running in families by a dominant inheritance pattern.10,11

The distribution of muscle weakness and congenital contractures in anterior horn cell degeneration has been studied by Brown et al,2 who were able to relate the affected muscles to involvement of specific cell columns in the anterior horns.12 The degree of congenital contractures depends on the time of onset of muscle weakness during pregnancy: the earlier and the more severe limitation of joint movements, the more severe will be the contractures at birth. The presence of dimpling in case 1 and abnormal dermatoglyphics in both cases may be clinical symptoms representing a defect in morphogenesis at an early stage.6

In our cases diagnosis was made mainly on clinical grounds, aided by electromyography and muscular CT-scan/ultrasound. Our EMG findings were consistent with previous results.4,13 There may be a marked or absolute reduction of motor unit activity as in case 1, nerve conduction velocities are normal and fibrillation potentials and positive waves are rarely detected.

Magnetic stimulation in case 2 showed minimal conduction slowing at cortical and cervical stimulation to the biceps brachii and abductor digiti minimi muscle, with low amplitudes in these muscles, compared with the lower limb muscles and normal values. MRI may show narrowing of the cervical spinal cord in cases of segmental spinal muscular atrophy.14 There was a normal diameter of the cervical cord in case 1 and a marginal diameter in case 2. The degenerative cervical disc abnormalities in case 2 may have been coincidental, since asymptomatic disc herniations are common findings on MRI.15

The clinical picture, congenital onset and non-progressive course differentiate this form of segmental muscular atrophy from the acquired and slowly progressive juvenile forms, which are usually sporadic,16 but have been described in identical twins.17 The etiology of prenatal conditions with loss of anterior horn cells is unknown. Although infections causing the initial lesion are assumed, only one case of neurogenic contractures has been described in humans asso-

Table Data of electromyography and magnetic stimulation.

<table>
<thead>
<tr>
<th>Electromyography Case 1</th>
<th>Latency in ms to</th>
</tr>
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<tbody>
<tr>
<td>Triceps muscle:</td>
<td>Biceps brachii</td>
</tr>
<tr>
<td>no voluntary motor unit potentials</td>
<td>Abductor pollicis brevis</td>
</tr>
<tr>
<td></td>
<td>Vastus lateralis</td>
</tr>
<tr>
<td></td>
<td>Tibialis anterior muscles:</td>
</tr>
<tr>
<td></td>
<td>normal motor unit</td>
</tr>
<tr>
<td></td>
<td>action potentials</td>
</tr>
<tr>
<td></td>
<td>no denervation</td>
</tr>
<tr>
<td></td>
<td>Median NCV 57 m/s</td>
</tr>
<tr>
<td></td>
<td>Distal sensory latency 2.0 m/s</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Magnetic stimulation Case 2</th>
<th>Stimulation site</th>
<th>BB (11-14)</th>
<th>ADM (8-53)</th>
<th>VL (22-26)</th>
<th>EDB (35-44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical amplitude (mV)</td>
<td>15.0</td>
<td>23.0</td>
<td>26.0</td>
<td>43.2</td>
<td></td>
</tr>
<tr>
<td>Cervical C5 amplitude</td>
<td>7.5</td>
<td>0.2</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>C7 amplitude</td>
<td>1.0</td>
<td>15.4 (12-15.0)</td>
<td>0.5</td>
<td>8.7 (8.5-12)</td>
<td></td>
</tr>
<tr>
<td>Lumbar L4 amplitude</td>
<td>5.0</td>
<td>27.2 (24-27)</td>
<td>4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCT</td>
<td>7.6</td>
<td>(7-8.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BB = Biceps Brachii muscle. ADM = Abductor digiti minimi muscle. VL = Vastus lateralis muscle. EDB = Extensor digitorum brevis muscle. CT = Central conduction time (latency difference between cortical and cervical stimulation).
associated with maternal exposure to rubella in the first trimester.4

Based on the cases described by Darwish et al 4 and our cases, congenital cervical spinal muscular atrophy appears non-familial.

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2 Price DS. A case of amyoplasia congenita, with pathological report. Arch Dis Child 1933;8:343-54.
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