Parkinsonism and Neck Extensor Myopathy

A New Syndrome or Coincidental Findings?

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Background: Dropped head in parkinsonism has been attributed to dystonia or unbalanced muscle rigidity. To our knowledge, isolated neck extensor myopathy with parkinsonism has been described in only one patient.

Objectives: To assess the occurrence of neck extension weakness resulting in dropped head in patients with parkinsonism and to explore whether the head drop might be the consequence of neck extensor myopathy.

Patients and Methods: All patients who were evaluated because of parkinsonism in the Department of Neurology in our hospital between January 1, 1997, and December 31, 1999, and were found to have both parkinsonism and neck extension weakness resulting in head drop were studied. The patients underwent clinical examination, blood tests including the levels of creatine kinase and myoglobin and neurophysiological evaluation with needle electromyography and autonomic tests. Open biopsy on a neck muscle was performed in the patients who could cooperate.

Results: Of 459 patients evaluated because of parkinsonism, 7 were found to have neck extensor weakness resulting in head drop. Needle electromyography revealed myopathic changes in all 7 patients. Muscle biopsy, which was performed in 5 patients, disclosed myopathic changes in all 5 patients. Electron microscopy revealed mitochondrial abnormalities in 2 of these 7 patients. Three of the patients had concomitant neck rigidity that could contribute to the neck position. All 7 patients had autonomic dysfunction and 6 responded poorly to levodopa therapy, making a diagnosis of multiple system atrophy probable.

Conclusion: Parkinsonism may be associated with isolated neck extensor myopathy resulting in dropped head, and this condition should be suggestive of multiple system atrophy.

Arch Neurol. 2001;58:232-237

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REPORT OF CASES

CASE 1

A 62-year-old woman was seen with a 2-year history of slowly progressive walking difficulties, poor balance, orthostatic hypotension, and urinary incontinence and...
PATIENTS AND METHODS

All patients who on examination in the Department of Neurology in our hospital between January 1, 1997, and December 31, 1999, were found to have both parkinsonism and neck extension weakness resulting in head drop were studied. Parkinsonism was defined as the presence of at least 2 of the following findings: hypokinesia, rigidity, and resting tremor. Probable MSA was defined, according to the consensus statement on the diagnosis of MSA, as poorly levodopa-treated responsive parkinsonism plus autonomic failure. Head drop was defined as the patient’s inability to hold the head up against gravity while sitting or standing. The strength of the neck muscles was tested manually with the patient in the sitting position and graded according to the Medical Research Council scale, where grade 0 indicates no contraction and grade 5 indicates normal power. With the patient in the sitting position, rigidity in the neck was also tested and graded as mild, moderate, or pronounced. In addition to clinical examination, the patients underwent blood tests including the levels of creatine kinase and myoglobin, neurophysiological evaluation with needle electro + myography (EMG), and autonomic tests (R-R–interval variation testing parasympathetic function, galvanic skin response, and digital vasocostriction for sympathetic function). Open biopsy on a neck muscle was performed in the patients who could cooperate. The biopsy specimens were cut in cryostat and transverse sections were stained with hematoxylin-eosin, van Gieson, and Gomori 1-step trichrome. Histochemical stainings were also performed for demonstration of adenosine triphosphatase at pH 9.4 and 4.6, nicotinamide adenine dinucleotide, and cytochrome oxidase. Other samples from the biopsy were fixed in glutaraldehyde, postfixed in osmium tetroxide, and embeded in epoxy resin (Epon) for electron microscopy.

A 1-year history of weakness and pain in the neck. Levodopa therapy, 500 mg/d, had very limited effect on improving walking difficulties. Neurological examination disclosed pronounced weakness of the neck extensors (grade 1) resulting in maximal head drop. The neck extensors were tense on palpation. The sternocleidomastoid muscles were atrophic. There was mild rigidity in the neck and in the limbs. The patient walked slowly, taking short steps, and had no arm swing. Retropulsion was noted when the pull test was performed. Diadochokinesis was impaired on both sides. There was no tremor. Blood pressure was 170/95 mm Hg when the patient was lying down and 110/80 mm Hg when the patient was standing. Except for these findings, the physical examination revealed no other abnormalities. Serum myoglobin was 71 µg/L (reference range, <50 µg/L); all other laboratory findings including the creatine kinase level were normal. Magnetic resonance imaging of the neck did not show any abnormality of the medulla or of the cervical nerve roots. Needle EMG revealed myopathic changes in paraspinal muscles at the cervical and upper thoracic levels (C6, T2) and in the left sternocleidomastoid muscle. Autonomic test results disclosed dysfunction of both the sympathetic and parasympathetic nervous system. A biopsy specimen from the semispinalis capitis muscle (Figure 1A) revealed marked fiber-size variability, degeneration and regeneration of muscle fibers, and an increased amount of extracellular matrix. There were no signs of inflammation. A few ragged-red fibers were observed in the Gomori staining. Electron microscopy revealed mitochondrial abnormalities (Figure 2A-B). A biopsy specimen from the left deltoideus muscle did not show any pathological changes.

CASE 2

A 66-year-old woman was seen because of a 1-year history of walking difficulties and stiffness in the body. On physical examination she walked slowly, taking short steps, and had decreased arm swing. There was rigidity in the right arm, but no tremor. A diagnosis of Parkinson disease was made and the patient was treated with levodopa, up to 500 mg/d. Her gait initially was moderately improved. On reexamination 1 year later she reported an inability to raise her head over the previous 3 months. She had pronounced weakness (grade 1) in neck extension resulting in maximal head drop (Figure 3). Her voice was monotonous and weak. She walked slowly, taking short steps, and had decreased arm swing. There was moderate rigidity in the neck and mild rigidity in the arms, but no tremor. Blood pressure was 120/65 mm Hg when the patient was lying down and the systolic blood pressure was 80 to 90 mm Hg when the patient was standing. Except for these findings, physical examination disclosed no other abnormalities. Myoglobin level was 82 µg/L (reference range, <50 µg/L), but all other blood test results were normal. Autonomic test results disclosed dysfunction of both the sympathetic and the parasympathetic nervous system. Needle EMG disclosed marked myopathic changes in a paraspinal muscle at the C7 level (Figure 4) and in the splenius muscle. A muscle biopsy specimen from the splenius muscle (Figure 1B) revealed a pronounced increase in interstitial connective tissue, uniform fiber atrophy, and areas with internal nuclei and “ring fibers.” Electron microscopy disclosed areas with mitochondrial aggregates. One year after undergoing biopsy, the rigidity of the neck had increased to such an extent that her head was completely fixated in a maximal flexed position.

RESULTS

Of 459 patients with parkinsonism evaluated in the Department of Neurology, University Hospital, Uppsala, between January 1, 1997, and December 31, 1999, 7 patients were unable to hold their head upright. These 7 patients were all found to have neck extensor myopathy. In 3 of the subjects there was also rigidity of the neck.
to such an extent that it could contribute to the head drop. All 7 patients had autonomic dysfunction and 6 responded poorly to levodopa therapy, making a diagnosis of MSA probable. Patients 1 and 2 were described earlier and the characteristics of all 7 patients are summarized in Table 1 and Table 2. Muscle biopsy specimens could not be obtained on patients 6 and 7 as these patients developed confusion and could not cooperate.

Figure 1. A, Patient 1. Cryostat section from the muscle biopsy specimen showing myogenic features with 1 necrotic fiber in the center (asterisk). There is also variation in fiber diameters and an increased extracellular matrix between the fibers (hematoxylin-eosin, original magnification ×150). B, Patient 2. Muscle biopsy specimen showing loss of muscle fibers, a marked increase of extracellular matrix between the fibers, and large variations in fiber diameters (hematoxylin-eosin, original magnification ×75).

Figure 2. A, Patient 1. Electron microscopy of the muscle biopsy specimen showing a collection of abnormal mitochondria with variation of their size and internal changes with abnormal positions of circular profiles (original magnification ×3000). B, Another region of the biopsy specimen showing abnormal mitochondria and crystalline inclusions (original magnification ×30 000).

Figure 3. Patient 2. Severe neck extensor weakness is present.

The dropped head syndrome resulting from neck extensor myopathy seems to be a heterogeneous condition with different causes. In most reported cases an unspecific, re-
stricted, noninflammatory myopathy has been found, but there are also reports about inclusion body myositis, focal myositis, congenital myopathy, nemaline myopathy, and hyperparathyroidism presenting with severe neck weakness. The origin of the myopathy in our patients is unknown. It has been suggested that mechanical stretching produces the injury in isolated neck extensor myopathy. Kyphotic postural changes and loss of tissue elastic associated with aging may place increasing workloads on cervical spinal muscles that leave some individuals susceptible to injury. Patients with parkinsonism, especially those with MSA, may be more vulnerable because of their posture. If this hypothesis would be correct, it is, however, difficult to explain why the neck weakness may precede the parkinsonism by years, as in our patients 4 and 5. All 7 patients described herein had autonomic dysfunction and 6 responded poorly to levodopa therapy, making a diagnosis of MSA probable. It cannot be excluded that higher levodopa doses might have induced a better response, but because of orthostatic hypotension and psychiatric side effects, it was impossible to increase the doses further. “Disproportionate antecollis” has been reported to be much more frequent in MSA than in Parkinson disease. It is possible that a neck extensor myopathy may be overlooked in a patient with pronounced rigidity in the neck. Yoshiyama et al reported that the muscle strength in the neck was almost normal in all of their patients who had parkinsonism and the dropped head sign, but conventional needle EMG was only performed in 2 of their 7 patients. Our patients 2, 5, 6, and 7 illustrate that pronounced rigidity and myopathy in the neck can occur in the same patient. In patient 2, the neck rigidity increased over time to such an extent that at the latest physical examination...
It was impossible to assess the patient’s muscle strength. It is essential to differentiate neck muscle weakness from hyperactive neck flexors. In our patient there were, however, no signs of hyperactivity of the neck flexors whether on palpation or on the needle EMG. As the biopsy findings confirmed myopathy in all 5 cases in which biopsies were performed, we do not think that we have overdiagnosed myopathy on needle EMG. For most limb muscles, as well as facial muscles, reference values for motor unit potential size have been collected. However, for paraspinal and neck muscles, reference studies are difficult for practical and ethical reasons. Therefore, needle EMG findings from these muscles are not evaluated as myopathic unless they are convincing enough. Around 20 motor unit potentials have been collected from each examined muscle to participate in analysis of amplitude, duration, and the number of phases. At maximal voluntary activation of a muscle a dense interference pattern was obtained in congruence with myopathy. No denervation activity was seen in any of our patients, indicating that the myopathies found had had a longer course.

A mitochondrial disease may be a possibility, when 2 organ systems are involved as in our patients. Mitochondrial changes were also observed in the neck muscles from patients 1 and 2. However, it is doubtful if the findings of ragged-red fibers and mitochondrial abnormalities in the semispinalis capitis muscle of patient 1 is due to a true mitochondrial myopathy, as no such findings were observed in the deltoid muscle biopsy specimen from the same patient. It has also been reported that paraspinal cervical muscles develop pathologic abnormalities with increasing age and that both ragged-red fibers and accumulation of mitochondria are frequent findings in these cases. All of our patients were older than 60 years and it seems that age is a contributing factor to the development of neck extensor myopathy in patients with parkinsonism. In predisposed persons, age is, on the whole, a risk factor for neurodegenerative diseases.

During this 3-year period we found in total 10 patients with isolated neck extensor myopathy among 4782 patients investigated by quantitative needle EMG. Seven of these patients, whom we have described herein, also had parkinsonism. We do not think that the combination of these conditions is coincidental, but that it represents a clinical entity. It is impossible from this study to determine the true prevalence of this disorder and we can only make a crude estimation. We can establish that 1.5% (7 of 459 patients) of the patients with parkinsonism examined in the Department of Neurology, University Hospital, Uppsala, during this study period had neck extensor myopathy. Five of the patients came from our primary reception area, which has a population of 300000 and 2 of the patients were referred from other parts of the country. As the symptoms are so striking and un-

### Table 1. Clinical Characteristics of 7 Patients

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Neck Extensor Weakness (Grade)*</th>
<th>Neck Rigidity Grade</th>
<th>First Symptom</th>
<th>Response to Levodopa Therapy (Dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/62</td>
<td>Pronounced (1)</td>
<td>Mild</td>
<td>Parkinsonism</td>
<td>Poor (500 mg/d)</td>
</tr>
<tr>
<td>2/F/66</td>
<td>Pronounced (1)</td>
<td>Moderate</td>
<td>Parkinsonism</td>
<td>Poor (500 mg/d)</td>
</tr>
<tr>
<td>3/M/82</td>
<td>Pronounced (1)</td>
<td>None</td>
<td>Parkinsonism</td>
<td>None (300 mg/d)</td>
</tr>
<tr>
<td>4/M/91</td>
<td>Mild (4)</td>
<td>None</td>
<td>Head drop</td>
<td>Good (900 mg/d)</td>
</tr>
<tr>
<td>5/M/74</td>
<td>Moderate (3-4)</td>
<td>Pronounced</td>
<td>Head drop</td>
<td>None (400 mg/d)</td>
</tr>
<tr>
<td>6/M/70</td>
<td>Pronounced (1)</td>
<td>Pronounced</td>
<td>Parkinsonism</td>
<td>Poor (900 mg/d)</td>
</tr>
<tr>
<td>7/F/74</td>
<td>Pronounced (1)</td>
<td>Pronounced</td>
<td>Parkinsonism</td>
<td>Poor (600 mg/d)</td>
</tr>
</tbody>
</table>

* Grades refer to muscle strength testing described in the “ Patients and Methods ” section.

### Table 2. Neurophysiological and Muscle Biopsy Findings

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Autonomic Test Results*</th>
<th>Electromyographic Findings</th>
<th>Muscle From Which Biopsy Specimen Was Obtained</th>
<th>Biopsy Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Decreased RRIV, GSR, DVC</td>
<td>Myopathic changes C3-Th3</td>
<td>Semispinalis</td>
<td>Myopathic changes including “ragged-red fibers” and mitochondrial abnormalities on EM*</td>
</tr>
<tr>
<td>2</td>
<td>Decreased RRIV, GSR, DVC</td>
<td>Myopathic changes in splenius</td>
<td>Splenius</td>
<td>Myopathic changes and mitochondrial abnormalities on EM*</td>
</tr>
<tr>
<td>3</td>
<td>Decreased GSR, DVC</td>
<td>Myopathic changes C6</td>
<td>Trapezius</td>
<td>Myopathic changes</td>
</tr>
<tr>
<td>4</td>
<td>Decreased RRIV, GSR</td>
<td>Myopathic changes in semispinalis, trapezius</td>
<td>Trapezius</td>
<td>Myopathic changes</td>
</tr>
<tr>
<td>5</td>
<td>Decreased GSR</td>
<td>Myopathic changes in splenius, scalenus semispinalis, and trapezius</td>
<td>Trapezius</td>
<td>Myopathic changes</td>
</tr>
<tr>
<td>6</td>
<td>Decreased RRIV, GSR, DVC</td>
<td>Myopathic changes in splenius, scalenus, semispinalis, trapezius, paraspinal (Th1)</td>
<td>Not performed</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>Decreased RRIV, GSR, DVC</td>
<td>Myopathic changes in splenius</td>
<td>Not performed</td>
<td>None</td>
</tr>
</tbody>
</table>

* RRIV indicates R-R–interval variation; GSR, galvanic skin response; DVC, digital vasoconstriction; and EM, electron microscopy.
usual, it is probable that every patient with this disorder in our primary reception area has been referred to our department. If this is true, the prevalence should be 1 to 2 per 100,000 in the population.

We conclude that parkinsonism may be associated with isolated neck extensor myopathy resulting in dropped head and that this condition should be suggestive of MSA.

Accepted for publication May 27, 2000.

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REFERENCES