Neuromuscular Disorders in Severe Acute Respiratory Syndrome

Li-Kai Tsai, MD; Sung-Tsang Hsieh, MD, PhD; Chi-Chao Chao, MD; Yee-Chun Chen, MD, PhD; Yea-Huey Lin, MS; Shan-Chwen Chang, MD, PhD; Yang-Chyuan Chang, MD

**Objective:** To delineate and clarify neuromuscular disorders in patients with probable severe acute respiratory syndrome (SARS).

**Design:** Case series with follow-up ranging from 3 weeks to 2 months.

**Setting:** National Taiwan University Hospital, Taipei.

**Patients:** We investigated 4 patients with SARS who had concomitant neuromuscular problems. A diagnosis of SARS was based on the demonstration of serum coronavirus antibodies. Clinical presentations, laboratory results, electrophysiologic findings, and follow-up conditions were determined.

**Results:** Patients developed neuromuscular problems approximately 3 weeks after the onset of SARS. Two women experienced motor-predominant peripheral nerve disorders. A man developed myopathy and a third woman experienced neuropathy and myopathy. Cerebrospinal fluid obtained from 2 patients with neuropathy disclosed normal protein content and the absence of pleocytosis and SARS coronavirus antibodies. Both patients with myopathy had elevated serum creatine kinase levels. A rapid clinical and electrophysiologic improvement was evident during follow-up examinations, with a good prognosis.

**Conclusions:** The neuromuscular problems in patients with SARS are considered to be critical-illness polyneuropathy or myopathy, possibly coexistent. Further pathological and microbiological studies are necessary to determine the relationship between SARS coronavirus and neuromuscular problems.

Arch Neurol. 2004;61:1669-1673

IN THE WORLDWIDE OUTBREAK OF severe acute respiratory syndrome (SARS) from 2002 to 2003, 664 patients likely contracted the illness in Taiwan alone.1 Patients with SARS usually present with fever, nonproductive cough, dyspnea, generalized malaise, and diarrhea.2-7 Neurologic manifestations have rarely been described, and the relationship, if any, between the causative coronavirus and neuromuscular problems is still unknown.2

For editorial comment see page 1647

Such a relationship is entirely conceivable. A viral infection may cause neuromuscular disorders in different ways, including direct attacks in the form of viral neuritis or myositis, inflammatory reaction through immune mimicry, or as a part of systemic inflammatory response syndrome.6,7

In this report, we describe 4 patients with probable SARS who developed peripheral nerve and/or muscle problems after the onset of the illness. The clinical presentations, electrophysiologic findings, and follow-up conditions of their neuromuscular disorders were delineated and clarified.

**METHODS**

**PATIENTS**

Between March 3 and June 15, 2003, a total of 76 patients whose disease met the diagnostic criteria for probable SARS as defined by the World Health Organization8 were under treatment at the National Taiwan University Hospital, Taipei. Among them, 4 patients were referred to neurologists to evaluate weakness. The group consisted of 1 man and 3 women. Their mean age was 46 years.

**CME course available at www.archneurol.com**

The patients’ medical records were reviewed with special attention to their clinical presentations, laboratory findings, radiologic results, and clinical courses. Table 1 shows the clinical data and SARS-related therapy in
these 4 patients. Multiple organ failure was defined according to published criteria.9 The patients were positive for serum coronavirus antibodies with or without the corresponding reverse transcription polymerase chain reaction identification of the coronavirus from serum or throat swabs.

The administered medications included ribavirin, high-dose methylprednisolone, and intravenous immunoglobulin, in accordance with the standard treatment protocol.10 There was no history of any major medical problem such as diabetes mellitus or uremia, nor any symptoms suggestive of neuromuscular disorders before the development of SARS. Symptoms indicative of neuromuscular abnormality developed in each patient approximately 3 weeks after the onset of SARS. The clinical features of the first patient who developed neuromuscular problems (patient 1 in the present series) have been described elsewhere.5

NEUROLOGIC AND LABORATORY INVESTIGATIONS

Each patient was examined by at least 2 neurologists. All 4 patients were conscious, lucid, and cooperative during the examinations. We also focused on the serum creatine kinase (CK) levels of these patients during their full course of SARS (normal CK levels are <190 and 190 U/L for men and women, respectively). Cerebrospinal fluid (CSF) was obtained by lumbar puncture from patients 2 and 3 for measurements of pressure, cell count, total protein level, glucose level, and coronavirus antibody. The presence of bacteria was determined by application of gram stain and via bacterial culture. The course of each patient was followed up clinically and electrophysiologically for 3 weeks to 2 months.

Routine nerve conduction studies (NCSs) were performed with an electromyograph (Viking IV; Nicolet Biomedical, Madison, Wis). Motor NCSs, including F wave, were carried out on bilateral median, ulnar, peroneal, and tibial nerves. Sensory NCSs were carried out on the median, ulnar, and sural nerves. All patients underwent needle electromyography (EMG) studies.

RESULTS

Neuromuscular manifestations and electrophysiologic findings are shown in Table 1 and Table 2, respectively.

Table 1. Clinical Data, Therapy, and Neurologic Manifestations in Patients With Probable SARS

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>1/F/51</th>
<th>2/F/48</th>
<th>3/F/42</th>
<th>4/M/31</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS features</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial symptoms</td>
<td>Fever, dyspnea, diarrhea</td>
<td>Fever, dyspnea, myalgia</td>
<td>Fever, dyspnea</td>
<td>Fever, cough, soft stool</td>
</tr>
<tr>
<td>Consolidation on chest x-ray film</td>
<td>+ (Throat)</td>
<td>+ (Serum)</td>
<td>+</td>
<td>+ (Throat)</td>
</tr>
<tr>
<td>Coronavirus RT-PCR</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Serum coronavirus Ab</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Organ failure and management</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple organ failure*</td>
<td>+ (R/H)</td>
<td>+ (R/C/H)</td>
<td>+ (R/C)</td>
<td>–</td>
</tr>
<tr>
<td>Intubation</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Methylprednisolone†</td>
<td>1000</td>
<td>3060</td>
<td>2520</td>
<td>1400</td>
</tr>
<tr>
<td>Dose, mg</td>
<td>10</td>
<td>18</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Duration, d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisatracurium besylate†</td>
<td>NA</td>
<td>900</td>
<td>756</td>
<td>NA</td>
</tr>
<tr>
<td>Dose, mg</td>
<td>NA</td>
<td>19</td>
<td>7</td>
<td>NA</td>
</tr>
<tr>
<td>Duration, d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics before onset of neurologic symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ribavirin, ciprofloxacin lactate, vancomycin hydrochloride, minocycline hydrochloride, imipenem, meropenem, moxifloxacin</td>
<td>Ribavirin, ciprofloxacin, vancomycin, ceferoline, cefpodoxime, floraxone</td>
<td>Ribavirin, vancomycin, cefepime, cefotaxime sodium, clarithromycin</td>
<td>Ribavirin, levofloxacin, clindamycin, oxacillin sodium</td>
<td></td>
</tr>
<tr>
<td>Neurologic presentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days after onset of SARS</td>
<td>21</td>
<td>24</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>Neurologic symptom</td>
<td>Weakness of 4 limbs; numbness of legs</td>
<td>Weakness of 4 limbs; numbness of bilateral fingers</td>
<td>Weakness of 4 limbs; numbness of left foot</td>
<td>Weakness of proximal lower limbs</td>
</tr>
<tr>
<td>Neuromuscular findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor</td>
<td>Distal-predominant weakness of 4 limbs</td>
<td>Distal-predominant weakness of 4 limbs</td>
<td>Distal-predominant weakness of 4 limbs</td>
<td>Weakness of bilateral hip flexor muscles</td>
</tr>
<tr>
<td>Deep tendon reflex</td>
<td>Mild hyperreflexia</td>
<td>Mild hyperreflexia</td>
<td>Proximal hyperreflexia</td>
<td>Normal</td>
</tr>
<tr>
<td>Sensory</td>
<td>Hypesthesia in legs</td>
<td>Hypesthesia in legs</td>
<td>Hypesthesia in legs (left&gt;right)</td>
<td>Normal</td>
</tr>
<tr>
<td>Laboratory study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak serum creatine kinase, U/L</td>
<td>174</td>
<td>76</td>
<td>9050</td>
<td>366</td>
</tr>
<tr>
<td>CSF findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein, mg/dL</td>
<td>ND</td>
<td>46</td>
<td>15</td>
<td>ND</td>
</tr>
<tr>
<td>Cells</td>
<td>ND</td>
<td>0</td>
<td>0</td>
<td>ND</td>
</tr>
<tr>
<td>Coronavirus Ab</td>
<td>ND</td>
<td>–</td>
<td>–</td>
<td>ND</td>
</tr>
</tbody>
</table>

Abbreviations: Ab, antibody; C, cardiovascular system; CSF, cerebrospinal fluid; H, hematologic system; NA, not applicable; ND, not done; R, respiratory system; RT-PCR, reverse transcription–polymerase chain reaction; SARS, severe acute respiratory syndrome; +, present; –, absent.

*Organ failure with involvement of at least 2 systems is considered multiple organ failure.
†Cumulative dose and treatment duration before onset of clinical neuromuscular symptoms.
PATIENT 1

Complete clinical information of this patient has been reported elsewhere. Only the main clinical and laboratory findings are included in Tables 1 and 2.

PATIENT 2

A 48-year-old woman developed a fever and myalgia on May 11, 2003 (day 1). On day 12, she was intubated in response to respiratory distress. After extubation on day 24, she experienced weakness in 4 limbs and numbness in her fingers bilaterally. A neurologic examination on day 39 showed distal-predominant weakness of 4 limbs, minimally more severe on the left side. Muscle power as graded with the Medical Research Council scale was 4 to 5 in the proximal parts of the limbs and 3 to 4 in the distal parts of the limbs. Deep tendon reflexes (DTRs) were mildly decreased, with bilateral flexor plantar responses. There was hypesthesia to temperature and vibration below the knees. Other neurologic examination results were unremarkable.

Nerve conduction studies conducted on day 43 showed decreased amplitudes of compound muscle action potential (CMAP) in bilateral peroneal nerves. Other NCS findings were within normal limits. A needle EMG study in the right tibialis anterior muscle detected mildly decreased recruitment with abundant spontaneous activities (positive waves) and large polyphasic waves. In view of the clinical features and electrophysiologic findings, axonopathic sensorimotor polyneuropathy was diagnosed.

The patient underwent a lumbar puncture on day 44. The opening pressure was 17.5 cm H2O. The CSF was clear in appearance with zero cell count, a total protein level of 46 mg/dL, and a glucose concentration of 68 mg/dL (3.77 mmol/L). Negative results were obtained for coronavirus antibody determination and bacteria. A follow-up neurologic examination 7 weeks after the first neurologic evaluation (day 92) showed nearly full muscle power in the proximal parts of the limbs and power

Table 2. Electrophysiologic Results in Patients With Probable SARS

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 31*</td>
<td>Day 96</td>
<td>Day 43</td>
<td>Day 70</td>
</tr>
<tr>
<td></td>
<td>Day 45</td>
<td>Day 94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor nerve conduction study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp (distal), mV</td>
<td>&gt;5.0</td>
<td>6.2/6.1†</td>
<td>7.8/NR</td>
<td>6.7/6.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp (proximal), mV</td>
<td>6.4/6.0</td>
<td>7.2/NR</td>
<td>4.6/5.5</td>
<td>6.4/5.9</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>56/57</td>
<td>55/NR</td>
<td>57/58</td>
</tr>
<tr>
<td>NCV, m/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp (distal), mV</td>
<td>&gt;5.0</td>
<td>7.7/8.8</td>
<td>9.1/NR</td>
<td>6.2/6.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp (proximal), mV</td>
<td>6.8/8.1</td>
<td>8.5/NR</td>
<td>5.1/5.6</td>
<td>6.8/7.6</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>58/62</td>
<td>64/NR</td>
<td>64/68</td>
</tr>
<tr>
<td>NCV, m/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peroneal nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp (distal), mV</td>
<td>&gt;2.0</td>
<td>1.6/1.5</td>
<td>3.2/2.9</td>
<td>0.8/0.8</td>
</tr>
<tr>
<td>Amp (proximal), mV</td>
<td>1.6/1.5</td>
<td>3.2/2.6</td>
<td>1.0/1.0</td>
<td>1.2/1.4</td>
</tr>
<tr>
<td></td>
<td>&gt;40</td>
<td>43/45</td>
<td>49/49</td>
<td>52/49</td>
</tr>
<tr>
<td>NCV, m/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibial nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp (distal), mV</td>
<td>&gt;6.0</td>
<td>9.9/6.2</td>
<td>11.5/7.8</td>
<td>9.6/7.3</td>
</tr>
<tr>
<td>Amp (proximal), mV</td>
<td>8.5/5.7</td>
<td>9.5/6.8</td>
<td>7.8/6.1</td>
<td>12.6/10.0</td>
</tr>
<tr>
<td>NCV, m/s</td>
<td>&gt;40</td>
<td>40/42</td>
<td>46/46</td>
<td>50/48</td>
</tr>
<tr>
<td>Sensory nerve conduction study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp, µV</td>
<td>&gt;10</td>
<td>49/62</td>
<td>47/NR</td>
<td>51.4/47.5</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>60/64</td>
<td>57/NR</td>
<td>64/70</td>
</tr>
<tr>
<td>NCV, m/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp, µV</td>
<td>&gt;10</td>
<td>44/35</td>
<td>41/NR</td>
<td>31.0/39.3</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>62/60</td>
<td>67/NR</td>
<td>58/64</td>
</tr>
<tr>
<td>NCV, m/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sural nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amp, µV</td>
<td>&gt;5</td>
<td>7/7</td>
<td>8/11</td>
<td>13.2/14.1</td>
</tr>
<tr>
<td></td>
<td>&gt;40</td>
<td>39/44</td>
<td>47/52</td>
<td>54/56</td>
</tr>
<tr>
<td>Electromyography study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous activities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effort</td>
<td>NA</td>
<td>Fib, PW</td>
<td>NR</td>
<td>PW</td>
</tr>
<tr>
<td>Recruitment</td>
<td>NA</td>
<td>Decrease</td>
<td>NR</td>
<td>Decrease</td>
</tr>
<tr>
<td>Polyphasia</td>
<td>NA</td>
<td>Increase</td>
<td>NR</td>
<td>Increase</td>
</tr>
<tr>
<td>Morphology</td>
<td>NA</td>
<td>Large</td>
<td>NR</td>
<td>Large</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Amp, amplitude; Fib, fibrillation; NA, not applicable; NCV, nerve conduction velocity; NR, not reported; PW, positive wave; SARS, severe acute respiratory syndrome.

*Days after onset of SARS.
†Electrophysiologic results on the right/left sides.
of grade 4 to 5 in the distal parts of the limbs. Follow-up NCSs showed a generalized increase of the CMAP amplitudes.

**PATIENT 3**

A 42-year-old woman developed a fever on May 10, 2003 (day 1), and received intubation on day 14 for respiratory failure. She displayed weakness in 4 limbs on day 25. Serial serum examinations showed marked elevation of the CK level from 161 U/L (day 23) to a peak of 9050 U/L (day 26). The serum myoglobin level determined on day 28 was 2136 µg/L (122.0 nmol/L), which was markedly elevated from the normal value of less than 70 µg/L (4.0 nmol/L). In addition, numbness of the left foot was noted after extubation on day 31. On examination on day 45, the patient displayed weakness in 4 limbs, more severe on the left side. The Medical Research Council–rated muscle power was 4 to 5 in the proximal parts of the upper limbs, 3 to 4 in the distal parts of the upper limbs, 2 to 3 in the proximal parts of the lower limbs, and 1 to 2 in the distal parts of the lower limbs. The DTRs were hypoactive in the proximal parts of the limbs but normal in the distal parts. Sensory examination showed hypesthesia to temperature, pinprick, and vibration below the left knee and the right midshin. The results of other neurologic examinations were unremarkable.

Nerve conduction studies conducted on day 48 showed decreased amplitudes of CMAP in bilateral peroneal nerves. The CMAP on the left tibial nerve was absent. Amplitudes of sensory action potential in plantar nerves were 6.4 µV on the right side and 3.0 µV on the left side. F waves were absent in the left leg and poorly elicited on the right peroneal nerve. Other NCS results were within reference ranges. Needle EMG in the left vastus lateralis, tibialis anterior, and gastrocnemius muscles showed early recruitment with spontaneous activities of fibrillations and positive waves. There was an increase in polyphasia. In view of the clinical presentations, we diagnosed myopathy with superimposed asymmetric sensorimotor polyneuropathy of axonopathic type.

The patient underwent a lumbar puncture on day 49. The opening pressure was 11.5 cm H2O. The CSF was clear in appearance with zero cell count, a total protein level of 15 mg/dL, and a glucose concentration of 73 mg/dL (4.05 mmol/L). Negative results were obtained for coronavirus antibody determination, gram stain, and bacterial culture.

Three weeks after the initial neurologic evaluation (day 70), the muscle power had improved, with, for example, a recovery to grade 3 to 4 in the distal part of the legs. There were no significant changes in hypoactive DTRs or sensory deficits. A follow-up NCS demonstrated the return of CMAP amplitudes and F-waves in the left leg. The CMAP amplitudes in median nerves decreased in the follow-up NCS. However, this electrophysiologic deterioration did not parallel the great improvement in the patient’s muscle power. The patient reported continuous improvement in muscle power in 4 limbs, but no improvement in the sensory problems, in a telephone interview conducted on day 87.

**PATIENT 4**

A 31-year-old man developed a fever and cough on May 11, 2003 (day 1). He did not undergo intubation. On day 22, he developed weakness and muscle aches in the proximal parts of both legs. He did not complain of any sensory symptoms. The serum CK level on day 21 was 366 U/L. Examination on day 45 showed mild weakness (grade 4-5) of the hip flexor muscles bilaterally. Other neurologic examination results were unremarkable.

Needle EMG (day 45) in the right ilioptosus and vastus medialis muscles showed normal recruitment with active spontaneous activities (fibrillations and positive waves) and abundant brief small polyphasic waves. The NCS findings were normal. Myopathy was diagnosed. A follow-up neurologic examination 7 weeks after the initial neurologic evaluation (day 94) showed full muscle power. Follow-up NCSs did not disclose any electrophysiologic changes.

The present report documents neuromuscular disorders in 4 patients with probable SARS. Patients 1 and 2 experienced sensorimotor peripheral nerve disorders. Patient 3 developed both myopathy and neuropathy. Patient 4 had only mild myopathy.

These neuromuscular disorders were not temporally coincident with the onset of SARS. Rather, symptoms appeared some 3 weeks later. Patients 1, 2, and 3 developed sensorimotor peripheral nerve disorders 21 to 25 days after the onset of SARS. Patients 2 and 3 exhibited weakness in all 4 limbs with slight asymmetry. The DTRs were mildly decreased. All 4 patients had sensory deficits that manifested as distal limb paresthesia and hypesthesia.

Asymmetry in sensory problems was noted in patient 3. The NCSs disclosed reduced CMAP amplitudes, which proved to be temporary. There was no slowing of nerve conduction velocity, prolonged distal motor latency, conduction block, or temporal dispersion. The EMG showed acute denervation with increased polyphasia. These findings are consistent with motor-predominant axonal polyneuropathy or polyradiculoneuropathy.

Patients 1, 2, and 3 received intensive care for multiple organ failure. In such a situation, combined with the clinical and electrophysiologic findings, a diagnosis of critical-illness polyneuropathy (CIP) is likely. Factors mediating systemic inflammatory response syndrome are also recognized as possibly being responsible for causing CIP.7 Systemic inflammatory response syndrome may occur in response to severe infection or trauma of any type.11 Therefore, the peripheral nerve disorder in our patients can be considered to be CIP caused by SARS-related systemic inflammatory response syndrome.

Axonal Guillain-Barré syndrome or acute motor sensory axonal neuropathy should also be taken into consideration.12 However, the observed normal protein levels in the CSF, relative preservation of DTRs as compared with the severity of muscle weakness, and rapid clinical as well as electrophysiologic improvement in these 4 pa-
tients do not favor a diagnosis of axonal Guillain-Barré syndrome.\textsuperscript{12,13}

Some viruses, such as cytomegalovirus and varicella zoster virus, may cause peripheral neuropathy through direct attacks on the nerves.\textsuperscript{6} Whether such a mechanism exists in SARS-related neuropathy is unknown. Presently, a viral link to the observed neuropathy is not favored, in the absence of detectable antibodies to the SARS coronavirus in the CSF of patients 2 and 3. Further investigations including pathological and microbiological studies are necessary to delineate this issue.

Patients 3 and 4 developed acute myopathy 25 and 22 days after the onset of SARS, respectively. Both patients had clinical, biochemical, and EMG evidence of myopathy. However, differences were evident between these 2 patients. Patient 3 developed severe weakness of all 4 limbs, while patient 4 developed only mild weakness in his bilateral hip flexor muscles. Patient 3 also developed concomitant peripheral neuropathy, which was not seen in patient 4. Patient 3 had rhabdomyolysis, while patient 4 had only mildly elevated serum CK levels. We observed more frank rhabdomyolysis in 2 other patients who had probable SARS in our hospital. Their conditions were accompanied by markedly elevated serum CK levels, which peaked at 339750 and 7659 U/L.\textsuperscript{14} Unfortunately, these patients died of multiple organ failure before detailed neurologic investigation could be performed. Therefore, myopathic manifestations of SARS seem to vary from mild weakness in the proximal parts of the legs to frank rhabdomyolysis.

High-dose intravenous corticosteroid therapy, which was applied in patients 3 and 4, may yield acute steroid myopathy (clinical-illness myopathy [CIM]).\textsuperscript{15} Clinical and electrophysiologic features in the 2 patients were compatible with CIM.\textsuperscript{16,17} Coexistence of CIM and CIP, as in patient 3 in our series, has also been reported.\textsuperscript{11,16,18} To prevent CIM, it has been suggested that corticosteroid therapy be avoided.\textsuperscript{17} Current standard treatment with high-dose methylprednisolone for SARS might thus be in need of reassessment.

The coronavirus group is a diverse group of large enveloped RNA viruses that can cause respiratory and enteric diseases in humans and other animals.\textsuperscript{19} Among the coronavirus-induced animal diseases, infection with feline infectious peritonitis virus, mouse hepatitis virus, and hemagglutinating encephalomyelitis virus can be complicated by encephalitis.\textsuperscript{15,19} Direct attack on the peripheral nerves or muscles by the SARS virus may therefore be possible. Further investigations into the relationship between SARS and neuromuscular problems are necessary.

In conclusion, we have presented data from 4 patients with probable SARS who developed axonal polyneuropathy, myopathy, or both. The neuromuscular disorders developed approximately 3 weeks after the onset of SARS, and the prognosis was good. The most likely diagnoses are CIP and/or CIM.

Accepted for Publication: February 24, 2004.
Correspondence: Yang-Chyuan Chang, MD, Department of Neurology, National Taiwan University Hospital, No. 7 Chung-Shan South Rd, Taipei 100, Taiwan, ROC (ychang@ha.mc.ntu.edu.tw).

Author Contributions: Study concept and design: Tsai, Hsieh, S.-C. Chang, and Y.-C. Chang. Acquisition of data: Tsai, Chao, Chen, Lin, and Y.-C. Chang. Analysis and interpretation of data: Tsai, Hsieh, Chao, and Y.-C. Chang. Drafting of the manuscript: Tsai. Critical revision of the manuscript for important intellectual content: Hsieh, Chao, Chen, Lin, S.-C. Chang, and Y.-C. Chang. Administrative, technical, and material support: Chen, Lin, and S.-C. Chang. Study supervision: Y.-C. Chang.

REFERENCES