Preliminary Report

Sternothyroid Muscle Biopsy* A Diagnostic Technique in Respiratory Failure of Neuromuscular Origin

Gloria Galloway, M.D.;† Fred G. Fedok, M.D.;‡ David A. Wiegand, M.D.;‡ and Javad Towfighi, M.D.§

Patients with neuromuscular disease may develop respiratory failure requiring mechanical ventilation. We describe a sternothyroid muscle biopsy technique as a diagnostic aid in such patients undergoing tracheostomy for prolonged ventilatory support. The biopsy procedure is quick and without added discomfort or morbidity for the patient. Our preliminary observations in three patients suggest that the sternothyroid muscle biopsy may be a useful diagnostic tool in this selected group of patients. (Chest 1991; 100:540-43)

MATERIALS AND METHODS

Sternothyroid muscles from three patients with neuromuscular disease (see case histories) and two controls were used for histologic studies. Informed consent was obtained for the biopsies preoperatively. One of the controls was a 16-year-old male patient with osteosarcoma of the rib who died of bronchopneumonia. The sternothyroid muscle was removed a few hours after death. The other control was a 71-year-old male patient with squamous cell carcinoma localized to the right pyriform sinuses and larynx admitted to the hospital for laryngectomy and bilateral modified radical neck dissection.

Histologic Method

Muscle samples were quickly frozen and the sections were stained with a battery of stains, including hematoxylin-eosin (H&E), Gomori's trichrome, periodic acid-Schiff, oil red O, adenosine triphosphates (ATPases) (pH = 9.6 and pH = 4.3), and reduced nicotinamide adenine dinucleotide-tetrazolium reductase (NADH-TR). Part of the muscle was fixed in 10 percent buffered formalin and processed for paraffin sectioning and H and E staining.

Sternothyroid Muscle Biopsy Technique

The sternothyroid muscle biopsy is performed during tracheostomy, which may be done under either local or general anesthesia. The patients are prepared and draped in the routine fashion for tracheostomy. Intravenous perioperative antibiotics are routinely given for tracheostomy at our institution. Either a horizontal or vertical skin incision is made. Tracheostomy proceeds in routine manner until the trachea is exposed. The strap muscles are then identified. The sternothyroid muscle is recognized as the most medial and superficial of the infrahyoid strap muscles (Fig 1). Using biopsy clamps, the muscle is isolated and secured in isometric position. Care is taken to avoid crushing the muscle or stretching it. The biopsy specimen (10 x 15 mm) is cut sharply from the surrounding muscle and removed. The muscle specimen is immediately transported to the pathology laboratory in the biopsy clamps. The tracheostomy then proceeds as usual. The muscle biopsy adds about 5 min to the tracheostomy procedure.

Clinical Summary of Cases

Patient 1: A 66-year-old woman was transferred from an outside hospital with a six- to eight-month history of increasing shortness of breath and fatigue. She also had a one-month history of dysphagia for liquids. She denied limb weakness, muscle twitching, difficulty with vision, or bowel or bladder dysfunction. There was no history of paresthesias, recent trauma, muscle pains, or family history of neuromuscular diseases.

Her physical examination on admission to The Hershey Medical Center of The Pennsylvania State University revealed an intubated woman with poor inspiratory effort. She was oxygenating well with 30 percent supplemental oxygen. Abnormalities on neurologic examination included weakness of left quadriceps and bilateral plantar flexors. Fasciculations and atrophy were not noted. Deep tendon reflexes were present symmetrically. No sensory abnormalities were found.

*From the Milton S. Hershey Medical Center, The Pennsylvania State University, Hershey, Pa.
†Resident, Department of Medicine (Neurology).
‡Assistant Professor, Department of Surgery (Otolaryngology).
§Professor, Department of Pathology (Anatomic Pathology).
Reprint requests: Dr. Towfighi, Department of Pathology, Milton S. Hershey Medical Center, Hershey 17033

ATPase = adenosine triphosphatase; NADH-TR = reduced nicotinamide adenine dinucleotide-tetrazolium reductase

Sternothyroid Muscle Biopsy (Galloway et al)
Her laboratory findings included normal findings from a serologic workup for rheumatoid disease, lupus, bacterial and fungal infection, and Lyme disease. Cervical and cranial magnetic resonance imaging (MRI) scan were normal. A chest roentgenogram revealed right lower lobe subsegmental atelectasis and bilateral pleural effusions. Cerebrospinal fluid (CSF) revealed a mildly increased number of cells (four neutrophils and five lymphocytes per cubic millimeter), normal total protein and glucose, normal immunoglobulin profile, negative culture and cytology. Serum creatine kinase (CK) and antistriated muscle antibody were normal, and results of tests for myasthenia gravis (acetylcholine receptor antibody and double blind neostigmine test) were normal.

She was weaned from the ventilator and maintained adequate oxygenation. A diagnosis of motor neuron disease was entertained. Accordingly, a right deltoid muscle biopsy specimen was obtained. Diaphragmatic fluoroscopy revealed bilaterally reduced excursion, suggesting phrenic nerve involvement. A videofluoroscopic examination revealed diminished movements of both vocal cords, suggesting additional involvement of the recurrent laryngeal nerves.

Subsequently, the patient’s oxygen saturations deteriorated. She became acidoic and required reintubation. Subsequent T-piece trials failed due to hypercarbia. The patient underwent tracheotomy and sternohyoid muscle biopsy. The patient’s condition became stabilized. However, she required the ventilator nightly due to fatigue and anxiety even on discharge to home.

Patient 2: The patient was a 56-year-old man admitted from an outside hospital because of severe hypoxia and hypercarbia necessitating intubation. He had a history of shortness of breath, hypersomnolence, paroxysmal nocturnal dyspnea, orthopnea, and lower extremity weakness and edema despite increasing diuretic therapy. There was no history of droopy eyelids, dysphagia, dysphonia, or easy fatigability. There was a history of hypertension, morbid obesity, degenerative joint disease, and bilateral lower extremity ulcers. Family history was negative for neuromuscular diseases.

At our institution, examination revealed the patient to be alert and slightly febrile. He had diffuse rhonchi, a loudly split S2, pitting edema of his lower extremities, and bilateral healing calf ulcers. His neurologic examination showed no bulbar weakness, extracocular eye movements were intact, and there was no ptosis present. His grip strength was bilaterally decreased. He was able to lift both legs against gravity but not against resistance. There were no fasciculations and the only deep tendon reflexes elicited were biceps graded at 2/4. Plantar responses were bilaterally flexor. No abnormalities were noted on sensory and cerebellar examinations.

Serologic workup for thyroid disease and lupus were negative and serum aldolase and CK were normal. He was found to have an iron deficiency anemia secondary to repeated gastrointestinal bleeding. His chest roentgenogram showed patchy alveolar infiltrates and cardiac enlargement. Tracheal aspirate and blood cultures were negative. A nerve conduction study of the median and ulnar nerves of the right upper extremity was considered to be normal. A repetitive nerve stimulation test was negative for the diagnosis of myasthenia gravis. The patient remained hypoxic and slightly hypercarbic despite 50 percent supplemental oxygen. He underwent tracheotomy and biopsy of the sternohyoid muscle.

Patient 3: The patient was a 62-year-old woman who was well until three months prior to hospital admission when she developed progressive muscle weakness and low-grade fever. There was no history of paresthesias, difficulty with swallowing or vision. No family history of neuromuscular diseases was noted.

On examination, she was found to have a low-grade fever and to be lethargic but oriented to person and place. Results of her cardiac examination were normal. Neurologic examination revealed bradykinesia, diffuse muscle weakness, cogwheeling, and normal deep tendon reflexes. Her plantar responses were flexor. Her voice was hypophonic. Her extraocular eye movements were intact. There were no sensory abnormalities.

Workup for thyroid disease, multiple myeloma, and other serum immunoglobulinopathies was negative. Cervical MRI showed only mild C5, C6 spondylosis. Chest roentgenogram showed a left pleural effusion, bifidular atelectasis, and perivascular markings compatible with interstitial pulmonary edema. Serum CK and CSF studies were normal. The patient had an elevated erythrocyte sedimentation rate of 95. Her hospital course was complicated by urinary tract infection, nephrogenic diabetes insipidus, and deep venous thrombosis.

A sural nerve biopsy 1½ months prior to death, showed that 3 percent of fibers had axonal degeneration, segmental demyelination was present in 11 percent of fibers in teased fiber preparation, and minimal axonal loss was seen in resin sections. These findings were consistent with a predominantly demyelinating neuropathy that was also confirmed by nerve conduction study and electromyography of both upper and lower extremities. A deltoid muscle biopsy was done one month after the sural nerve biopsy.

The patient subsequently had a cardiac arrest. This was thought to be due to ventricular ectopy. She was intubated and cardioverted. She remained hypotonic and unresponsive to painful stimuli.

The patient subsequently underwent tracheotomy and sternohyoid muscle biopsy. She had a second cardiac arrest and died five weeks after hospital admission. Autopsy revealed aspiration pneumonia, disseminated herpes simplex virus infection, and extensive hypotensive encephalopathy. There was evidence of denervation in the muscle but segmental demyelination was minimal suggesting that remyelination had occurred.

RESULTS

Control sternohyoid muscles, in H and E stain, showed muscle fascicles with normal endomysial and perimysial connective tissue and minimal variation in the muscle fiber diameter. The muscle fiber nuclei were located in the periphery (Fig 2, left). In histochemical stains, there was normal checkerboard dis-
FIGURE 2. Normal sternohyoid muscle from a 71-year-old man. Left, Mild variation of muscle fiber diameter is present (H&E stain, ×170). Right, Fast twitch fibers (dark) and slow twitch fibers (light) are distributed in random (ATPase stain, pH = 9.4 × 170).

FIGURE 3. Sternohyoid muscle in patient 2 showing denervation changes. Left, Group atrophy and angulated fibers (arrows) (H&E × 130). Right, Fiber type grouping (ATPase, pH = 9.4 × 80).

Distribution pattern of the type one and two fibers with slight predominance of the latter (Fig 2, right). Type two fibers also had a slightly larger diameter than type one. All the study patients had evidence of denervation changes in the sternohyoid muscle. The changes are
briefly described for each case. Sternohyoid muscle in case 1 showed prominent denervation changes. These changes consisted of group atrophy, angulated fibers, and type grouping. A right deltoid biopsy performed a month earlier had shown denervation changes that were less severe. Case 2 also had marked denervation changes, including prominent group atrophy, type grouping, and angulated fibers (Fig 3). Denervation changes in case 3 were milder and consisted of scattered round to angulated fibers and small type grouping. A deltoid muscle biopsy done several days before showed a type two fiber atrophy and a small number of angulated fibers. The latter was weakly suggestive of denervation changes.

DISCUSSION

Muscle biopsy is a well-established tool in the diagnosis of neuromuscular diseases.\textsuperscript{1,2} It is often used to confirm the neurogenic or myopathic nature of the disorder. Less commonly, etiologic diagnosis such as polymyositis/dermatomyositis, vasculitis or special forms of metabolic and congenital myopathies can be made in muscle biopsy.\textsuperscript{3} It is also well known that a variety of neuromuscular diseases, including motor neuron disorders such as amyotrophic lateral sclerosis, inflammatory myopathies such as polymyositis, inflammatory demyelinating neuropathies such as Guillain-Barré syndrome, myasthenia gravis, and muscular dystrophies may involve respiratory muscles resulting in ventilatory failure.\textsuperscript{4} Patients with these diseases often require prolonged ventilatory assistance necessitating tracheostomy. In these cases, we believe simultaneous sternohyoid muscle biopsy may provide useful information in the diagnosis of their neuromuscular disease.

The denervation changes were readily demonstrated in the sternohyoid muscle biopsy specimens of the patients in this study. Moreover, the pathologic alterations in cases 2 and 3 were more prominent in the sternohyoid muscle than in the conventionally biopsied deltoid muscle. Based on the sternohyoid biopsy findings and the clinical information, the first two patients were diagnosed as having a motor neuron disorder. The third patient was considered to have a predominantly demyelinating neuropathy based on sural nerve and sternohyoid muscle biopsy specimens and electrophysiologic findings.

Our observations on the patients presented herein suggest the following: (1) sternohyoid muscle biopsy can be rapidly performed without added morbidity or discomfort to the patient, and (2) the sternohyoid muscle biopsy specimen may provide useful information in the diagnosis of underlying denervating disorders in patients with respiratory failure. Further studies, however, are needed to confirm the usefulness of this diagnostic procedure in neurogenic as well as other neuromuscular disorders.

ACKNOWLEDGMENTS: The authors thank Cathy Housman, H.T.L., for technical assistance and Carole Johnson for secretarial help.

REFERENCES

1 Carpenter S, Karpati G. Pathology of skeletal muscle. New York: Churchill Livingstone Inc; 1984
2 Dubowitz V. Muscle biopsy: a practical approach, 2nd ed. London: Bailliere Tindall; 1965