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Evaluation of simultaneous muscle and nerve biopsies for the diagnosis of neuromuscular diseases☆

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ABSTRACT

Skeletal muscle and peripheral nerve are occasionally simultaneously biopsied with the goal of increasing diagnostic yield in patients with an uncertain clinical diagnosis or in cases where the pathology is known to be focal or multifocal (eg, vasculitis or amyloidosis). The purpose of the present study is to evaluate the diagnostic utility of performing simultaneous muscle and nerve biopsies. A surgical pathology database was searched from 1993 to 2011 to identify patients who had concomitant skeletal muscle and peripheral nerve biopsies. Demographic and pathologic findings were recorded for all cases. Two hundred eighty-seven patients were included for study. There were 161 (56%) males and 126 (44%) females with a mean age at the time of biopsy of 51 years. The most commonly sampled sites were gastrocnemius muscle (n = 186, 65%) and sural nerve (n = 264, 92%). Most cases (n = 166, 58%) were found to have a definitive diagnosis in either muscle or nerve. Of the cases with definitive diagnoses, 44 (27%) were based off the muscle only, 100 (60%) off the nerve only, and 22 (13%) had a definitive diagnosis in both the muscle and nerve. The most common diagnoses made on muscle biopsy alone were denervation atrophy (n = 34) and inflammatory myopathy (n = 7). The most common diagnosis made on nerve biopsy alone was a moderate or greater degree of axonal loss (n = 82). Vasculitis was found in muscle in 2 cases, in the nerve in 14 cases, and both muscle and nerve in 4 cases. Amyloidosis was exclusive to muscle in no cases, was seen in nerve only in 1 case, and was found in both muscle and nerve in 4 cases. Performing simultaneous muscle and nerve biopsies can improve diagnostic yield (from 8% to 58% in the current study).

1. Introduction

The diagnosis of neuromuscular disorders can be challenging and relies on a thorough history, physical examination, imaging, and electromyographic and nerve conduction studies. Biopsies of the muscle and nerve may be required in a subset of patients to diagnose or confirm clinical suspicions or identify potentially treatable conditions; however, these procedures are invasive and can be complicated by paresthesias/dysesthesias, persistent pain, and infection [1].

Simultaneous skeletal muscle and peripheral nerve biopsies are occasionally performed to improve diagnostic yield, when the clinical impression is obscure or when the disease is known to be focal or multifocal, such as with vasculitis and amyloidosis [2-6]. Conflicting data exist, specifically for vasculitis, regarding the necessity for simultaneously procuring a muscle biopsy sample at the time of nerve biopsy [7]. The purpose of the present study is to determine the diagnostic utility of performing simultaneous muscle and nerve biopsies for the evaluation of patients with suspected neuromuscular disorders.

2. Materials and methods

After approval by the institutional board review, the surgical pathology database was searched to identify patients who had concomitant skeletal muscle and peripheral nerve biopsies during the period of July 1993 to December 2011. For each of the cases, demographic and pathologic findings were recorded including the patient's age and sex, site of the muscle and nerve biopsies, histologic diagnoses for both muscle and nerve biopsies, and electron microscopic findings when performed. Nerve tease preparations were not a part of routine workup. Biopsy diagnoses of each case were made by a neuropathologist.

The histologic findings were evaluated on whether a definitive diagnosis or a nondefinitive diagnosis was rendered. For cases where a definitive diagnosis was present, the source (either being from the muscle, nerve, or both) was documented. Cases where there was a nerve biopsy diagnosis of at least "moderate axon loss" were included as a definitive diagnosis from the nerve only, whereas cases of "mild

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axon loss" were designated as a nondefinitive diagnosis for the purposes of this study. All cases previously defined as being a definitive diagnosis of "axon loss" were further subdivided into the categories of axonopathy, demyelinative neuropathy, mixed neuropathy, or not otherwise specified based on electron microscopy results.

When pathologic examination resulted in a nondefinitive diagnosis, the cases were further subclassified as being either "normal," "type II muscle fiber atrophy," "type I muscle fiber atrophy," "mild axon loss," or "nonspecific." Types I and II muscle fiber atrophy and mild axon loss were categorized as nondefinitive because these findings may often be seen with disuse and aging. Routinely performed adenosine triphosphatase stains distinguished types I and II atrophy from "denervation atrophy." If either biopsy diagnosis included descriptive but not definitive terminology, such as "mild variation in muscle fiber size" or "muscle fiber degeneration," the case was categorized as nonspecific.

3. Results

Two hundred eighty-seven patients were identified who underwent simultaneous muscle and nerve biopsy and formed the study group. There were 161 (56%) males and 126 (44%) females. The mean age at the time of biopsy was 51 years (median, 56 years).

Most cases (n = 166, 58%) were found to have a definitive diagnosis in either the muscle or nerve biopsy; the remaining 121 (42%) cases were classified as nondefinitive. Of the cases where there was a definitive diagnosis, 44 (27%) of the diagnoses were based off the muscle only and 100 (60%) off the nerve only. In 22 (13%) cases, a definitive diagnosis was made in both the muscle and the nerve biopsies; in 10 (45%) of these cases, the same diagnosis was made in both the muscle and nerve (Figure).

The most commonly sampled muscles included the gastrocnemius and the quadriceps, and the most commonly sampled nerve was the sural nerve. The gastrocnemius was biopsied in 186 cases and yielded a muscle-only definitive diagnosis in 28 (15%) cases; the quadriceps was biopsied in 66 cases and yielded a muscle-only definitive diagnosis in 10 (15%) cases. The sural nerve was biopsied in 264 cases and yielded a nerve-only definitive diagnosis in 96 (36%) cases (Table 1).

For the cases where there was a definitive diagnosis in the muscle biopsy only, 34 cases demonstrated denervation atrophy and 7 had inflammatory myopathy. Most cases where a definitive diagnosis was only found in the nerve comprised various forms of axon loss. Overall, there were 82 nerve biopsies that demonstrated axon loss that could be further subdivided as the following: 38 cases of axonopathy; 10 cases of demyelination; 8 cases of mixed pathology; and 26 cases, which were not otherwise specified (Table 2).

Table 1
Sites for muscle and nerve biopsies and associated diagnostic yield

Skeletal muscle biopsies

Site	Total cases	Percent	Cases with definitive diagnosis in muscle only	Percent yield for site
Gastrocnemius	186	64.8	28	15.1
Quadriceps	66	23.0	10	15.2
Tibialis	20	7.0	0	0.0
Deltoid	6	2.1	2	33.3
Not otherwise specified	9	3.1	4	44.4
Total	287	100.0	44	

Peripheral nerve biopsies

Site	Total cases	Percent	Cases with definitive diagnosis in nerve only	Percent yield for site
Sural	264	92.0	96	36.4
Femoral cutaneous	9	3.1	0	0.0
Peroneal	1	0.3	0	0.0
Not otherwise specified	13	4.5	4	30.8
Total	287	100.0	100	

Cases where the same diagnosis was found in both muscle and nerve biopsies included predominantly vasculitis and amyloidosis, with 4 cases of each. The remaining cases where unique definitive diagnoses were found in the muscle and nerve biopsies consisted of various pathologies found in muscle combined with different types of axon loss in the nerve. There were 8 cases of inflammatory myopathy, 3 cases of vasculitis, and 1 case of myopathic changes found in the muscle, all in association with axon loss found in the nerve (Table 3).

Of the total 287 cases in this study, only 8% (n = 22) had a definitive diagnosis of vasculitis, amyloidosis, or other disease present in both the muscle and the nerve biopsies. In 54% (n = 156) of cases, the muscle biopsy or nerve biopsy independently provided a definitive diagnosis. Overall, nerve biopsies had a higher diagnostic yield (43%, n = 122) compared with muscle biopsies (23%, n = 66). For cases where there was a nondefinitive diagnosis in the nerve (n = 165), the addition of muscle biopsy provided a definitive diagnosis in

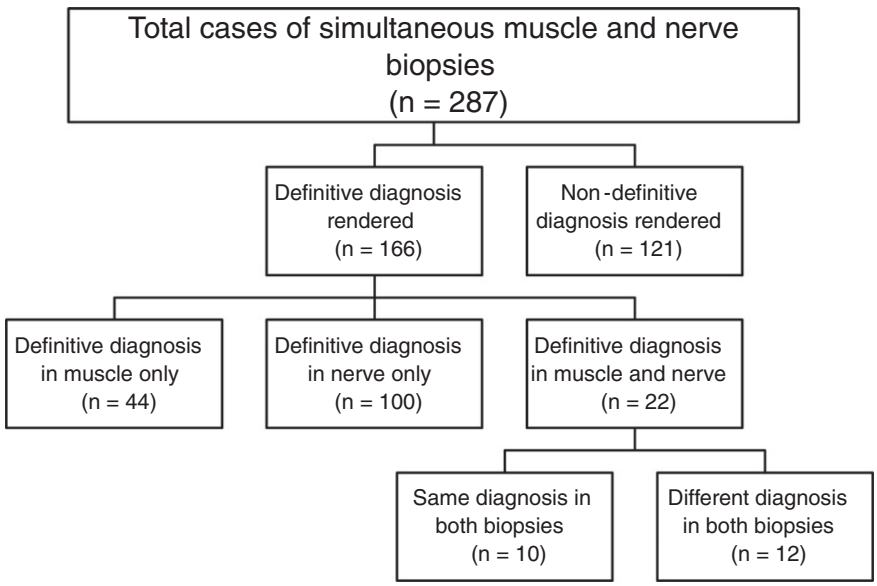

Fig. Categorization of muscle and nerve biopsy cases.