Skeletal Muscle and Peripheral Nerve Histopathology in COVID-19

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Study Question
What is the spectrum of skeletal muscle and nerve pathology of patients who died following SARS-CoV-2 infection, and is there evidence for direct viral invasion of these tissues?

What Is Known and What This Paper Adds
Patients with COVID-19 may develop symptoms and signs of a myopathy or neuropathy, including myalgias, elevated creatine kinase (CK) levels, and neuropathy, but few studies have examined the histopathologic features of persons who die of COVID-19. This study provides class IV evidence that muscle and nerve biopsies document a variety of pathologic changes in patients dying with COVID-19. This study demonstrated inflammatory/immune-mediated damage likely related to release of cytokines in muscle and nerve, but there was no evidence of direct SARS-CoV-2 invasion of these tissues.

Methods
For this cross-sectional study, the investigators used light microscopy along with immunohistochemistry (IHC) staining to examine psoas muscle and femoral nerve samples from autopsy of 35 persons who died following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and 10 SARS-CoV-2–negative controls who died during the COVID-19 pandemic. The investigators conducted chart reviews to obtain clinical and laboratory data. The primary outcomes were the histopathologic features observed in the persons who died of COVID-19 and to assess for direct invasion of muscle and nerve tissue by SARS-CoV-2 IHC.

Results and Study Limitations
Four decedents in the COVID-19 group had neuromuscular symptoms, and 74% had elevated peak CK levels. The commonly observed muscle tissue abnormalities included type 2 muscle fiber atrophy (n = 32), necrotizing myopathy (n = 9), and myositis (n = 7), while 9 patients had neutritis. Major histocompatibility complex–1 (MHC-1) expression occurred in all decedents with necrotizing myopathy and myositis and 8 additional decedents. Abnormal myxovirus resistance protein A (MxA) expression was present on capillaries in muscle in 9 patients and in nerve in 7. SARS-CoV-2 IHC was negative in muscle and nerve in all patients. Of the 10 control decedents, all had type 2 muscle atrophy, 1 had necrotic muscle fibers, 3 had MHC-1 expression in non-necrotic/non-regenerating fibers, and 2 had abnormal MxA expression on capillaries. This study provides Class IV evidence that muscle and nerve biopsies document a variety of pathologic changes suggestive of inflammatory/immune-mediated damage in patients dying with COVID-19, but there was no evidence of direct SARS-CoV-2 invasion of these tissues. A limitation was that most of the patients presented to the hospital severely ill that precluded a detailed neuromuscular history and examination prior to death. As such, the investigators did not perform targeted histopathologic examinations of clinically symptomatic muscle and nerve tissues. Other limitations include the unavailability of frozen tissues and potentially limited generalizability to patients who survive COVID-19.

Study Funding and Competing Interests
This study received no funding. Dr. Amato reports serving as a neurology consultant for Johnson & Johnson and serving on medical advisory boards for Alexion, Sarepta, CSL Behring, Strongbridge Pharma, Argenta, Ra Pharmaceuticals, and Orphazyme. Go to Neurology.org/N for full disclosures.

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