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LETTER TO THE EDITOR

Muscle Biopsy Findings in a Case of SARS-CoV-2-Associated Muscle Injury

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To the Editor:

SARS-CoV-2 viral particles have been demonstrated by electron microscopy in tissue, such as lung and kidney, organs known to be affected significantly during infection. A retrospective study in China first revealed neurologic manifestations of COVID-19 patients who presented conscious impairment, acute cerebrovascular disease, and skeletal muscle injury (1). Subsequent study has confirmed the presence of SARS-CoV-2 in the cerebrospinal fluid of COVID-19 patients with meningitis/encephalitis (2). A most recent brain autopsy report revealed a range of neuropathological lesions, with features resembling a primary vascular origin and secondary myelin loss, although no direct evidence of viral particles detected in the brain was shown (3). Skeletal muscle injury presents as muscle pain and elevated serum creatine kinase level in COVID-19 patients (4). It is not clear whether muscle injury is caused by direct SARS-CoV-2 viral infection or through parainfectious mechanisms. Herein, we describe the first histopathologic changes and electron microscopy findings in the skeletal muscle of a patient who died with SARS-CoV-2.

A woman in her 60s with a history of prediabetes, hypertension, and hyperlipidemia initially presented with flu-type symptoms and was diagnosed as SARS-CoV-2-positive by nasopharyngeal swab. She returned one week later with worsening shortness of breath, was intubated, and subsequently became hypotensive and bradycardic with severe metabolic and respiratory acidosis. She was transitioned to comfort care and died one day later. An autopsy including removal and evaluation of chest organs and in situ sampling of all other organs was performed. The BMI was 34.5. The lungs were heavy (780 g right, 1000 g left) and showed patchy irregular consolidation centrally, radiating to the periphery. There was a single thromboembolus in the right lower lobe. Hematoxylin and eosin (H&E)-stained slides of the lungs showed the typical SARS-CoV-2 spectrum of exudative phase diffuse alveolar damage as well as a brisk acute bronchopneumonia (1). There were numerous fibrin microthrombi in the lungs as well as areas of possible venous endothelitis. Histologic examination of skeletal muscle revealed fibrin microthrombi, perimysial microhemorrhages, and adjacent muscle fiber vacuolar degeneration and necrosis (Fig. 1A, B). There was minimal associated inflammatory infiltrate. No angulated atrophic fibers, basophilic regenerating fibers or increased central nuclei were seen. In the absence of a reliable antibody against SARS-CoV-2 and to better demonstrate the presence of viral particles, electron microscopy was performed on 3% glutaraldehyde fixed tissue. Degenerated cells with cytoplasmic condensation and degenerated mitochondria were noted (Fig. 1C inset, D). Most striking in the degenerated cells were cytoplasmic clusters of virus-like structures consistent with previously reported SARS-CoV-2 (Fig. 1C–E) (5). Overall, the pattern was most consistent with endothelial injury and vascular damage, and less likely direct myocyte infection.

The SARS-CoV-2 clinical syndrome frequently includes symptoms of severe myalgias and fatigue that can persist into the convalescent period. In the current case, histology of the muscle shows damage to tissues with scarce inflammatory cells and directly demonstrates the viral particles, similar to those observed in the lung, highly suggestive of a result of primary vascular origin. This is supported by a high-level expression of the ACE2, the host cell surface receptor for SARS-CoV-2, in vasculature in contrast to only very low ACE2 expression in skeletal myocytes (6). Viral elements were in close contact with vesicles and membranous structures resembling modified endoplasmic reticulum and Golgi apparatus as described in previous reports of the organellar architecture of the replication complex of RNA viruses including the MERS and SARS viruses (5, 7). Of interest, myopathies, including necrotizing myopathies that produce similar pathology, have been attributed to other systemic viruses. Chiefly amongst these are influenza viruses, but also human immunodeficiency virus, enteroviruses, parainfluenza virus, adenovirus, respiratory syncytial virus, and SARS (8). Influenza virus has also been demonstrated in muscle via specific immunofluorescence and electron microscopy (9). Autopsy evaluation of all tissues, not just the lungs, may elucidate more information about viral infection and mechanisms of damage and treatment response.

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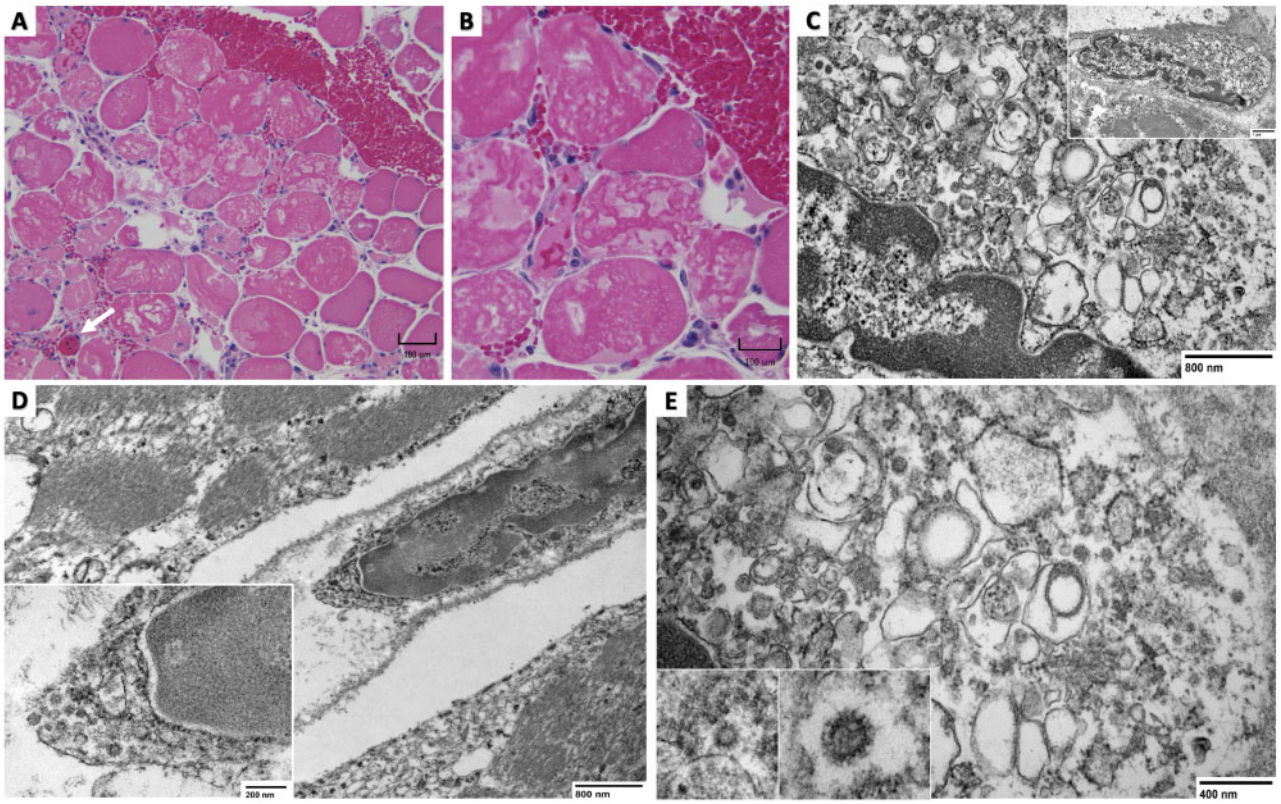

FIGURE 1. (A) Perimysial hemorrhages, vacuolated fibers and one adjacent fibrin microthrombus (arrow) (H&E, ×200). **(B)** Degenerated/atrophic myocyte (H&E, ×400). **(C)** A degenerated cell (inset: direct magnification, ×15 000) with several virus-like particles in cytoplasm (direct magnification, ×25 000). **(D)** Degenerated cell (direct magnification, ×20 000) with a cluster of virus-like particles in the cytoplasm (inset: direct magnification, ×60 000). **(E)** Virus-like particles in close contact with membranes of organelles (direct magnification, ×40 000); cytoplasmic virus-like particles with hairy/spike-like features surrounding the spherical structure (insets: average diameter of 61.47 nm [22 measurements; minimum 49.9–maximum 78.9 nm]).

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COMPETING INTERESTS

The authors have no duality or conflicts of interest to declare.

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