Case Report

Peripheral Polyneuropathy Associated with COVID-19 in Two Patients: A Musculoskeletal Ultrasound Case Report

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Abstract

As coronavirus disease 2019 (COVID-19) spreads, we are encountering multiple different symptoms and related complications. Although the vast majority of literature is focused on its pulmonary manifestations, recent reports have mentioned neurologic manifestations but typically those related to the central nervous system and diagnosed utilizing magnetic resonance imaging. We present two cases of COVID-19–associated peripheral polyneuropathy diagnosed utilizing musculoskeletal ultrasound (US), which to our knowledge is the first such case report. US is an instrumental portable modality that can be used for COVID-19 patients in isolation. As this virus continues to spread, understanding and recognizing these COVID-19 related complications and their sonographic findings are crucial.

Keywords: Axonal sensorimotor neuropathy, COVID-19, musculoskeletal ultrasound, peripheral neuropathy

Introduction

The coronavirus disease 2019 (COVID-19) pandemic now has over 45 million confirmed cases worldwide and has taken the lives of nearly 1.2 million people worldwide and these numbers continue to rise daily.[1] Patients with this disease, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, typically present with cough, fever, and shortness of breath.[2]

However, as we learn more about this novel infection, we encounter a multitude of extrapulmonary manifestations at presentation and COVID-19–related complications during the course of infection.[2-4] Recent publications have reported neurological symptoms and complications associated with COVID-19, although the vast majority are related to the central nervous system.[2-4]

The use of musculoskeletal (MSK) ultrasound (US) has significantly increased over the past decades because of its many advantages, when compared to magnetic resonance imaging.[5-8] Given its high spatial resolution of intrinsic nerve architecture and the ability to compare with the contralateral side and real-time Doppler capabilities, MSK US is especially useful in the diagnosis of peripheral neuropathies and has even been endorsed as the first-line imaging modality for peripheral neuropathies in many institutions.[5,6] In addition, in hospitalized patients in isolation, given its portable nature, US is an invaluable tool and could help with earlier identification of COVID-19–related complications.[6-8]

We report two companion cases of COVID-19–associated peripheral polyneuropathy, both of which developed during the course of the disease and caused long-lasting symptoms. We present this unique case report and the sonographic findings of peripheral neuropathy to make clinicians aware of this complication and the use of MSK US in its diagnosis.

All examinations and procedures in this manuscript were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent and protocol review were exempt as per our institutional review board policies for this type of study and since these examinations

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were clinically indicated. Both US examinations were performed by a trained dedicated MSK sonographer (13 years of MSK US experience), who possesses the registered MSK sonographer (RMSKS) designation through the American Registry for Diagnostic Medical Sonography (Rockville, MD, USA). Scanning was performed utilizing 9–15 MHz linear transducers (GE LOGIQ E9 unit; General Electric Company, Milwaukee, WI, USA). Both examinations were interpreted by fellowship-trained MSK radiologists, highly skilled in MSK US performance and interpretation (15 years and 3 years of clinical experience, respectively).

Case Reports

COVID-19 patient A

A 66-year-old man with type II diabetes and obesity (body mass index of 37 kg/m^2) presented to the emergency department with a 3-day history of fever, shortness of breath, and cough. The patient was found to be COVID-19 positive via SARS-CoV-2 reverse transcription-polymerase chain reaction and admitted to the hospital in isolation. After failing initial conservative measures, the patient was transferred to the intensive care unit, intubated, and placed on mechanical ventilation for 24 days. He was treated with antibiotics and tocilizumab. Following extubation, the patient complained of body weakness, mainly proximally, and a right foot drop. He was then sent to inpatient rehabilitation where he spent 3 weeks and slightly improved. The patient was hospitalized for a total of 71 days. However, following discharge, the patient had multiple readmissions for bilateral deep vein thromboses, acute tubular necrosis, tension pneumothorax, sepsis, and atrial flutter.

Approximately 4 months following the initial discharge, the patient presented to the neurology clinic with a persistent right foot drop. He wore a brace that he used while walking and also required assistance with a walker or cane. He reported experiencing diffuse numbness and tingling in both his arms and legs. He also felt that his left hand grip was weaker than the right side. In addition, he reported hypersensitivity from the left elbow to the fingers, at the left toes, from the right knee to the toes, and at the right fingertips. This included a constant burning sensation in the bottom of the feet and sensitivity to touch on the dorsum of the feet, more pronounced on the left.

On physical examination, he was unable to dorsiflex or evert the right foot. He had significant weakness throughout the left upper extremity and was unable to make a fist with the left hand. He also had weakness in regard to the bilateral legs and the core. He had hyperesthesia to light touch diffusely from the left elbow to all the fingertips, diffusely from the right knee to the toes, and from the left toes to the ankle. Subsequently, he was referred for a diagnostic MSK US of the left arm and right leg to evaluate for peripheral polyneuropathy.

US imaging demonstrated the left ulnar nerve to be enlarged and markedly hypoechoic at the left elbow; above, at, and below the level of the cubital tunnel, with loss of the normal fascicular architecture and measuring up to 17 mm^2 [Figure 1].

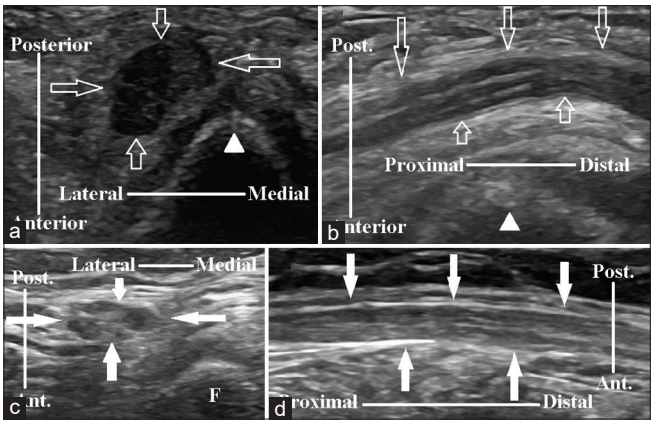

Figure 1: A 66-year-old COVID-19–positive man with polyneuropathy. (a) Short-axis and (b) long-axis sonographic images at the level of the left cubital tunnel, near the medial epicondyle, (arrowheads) demonstrate a diffusely enlarged and markedly hypoechoic left ulnar nerve (open arrows) with complete ill-definition of the normal fascicular architecture, (c) short-axis and (d) long-axis sonographic images near the level of the right fibular head (F) show a diffusely enlarged hypoechoic right common peroneal nerve (solid arrows) with significant fascicular dilatation

The common peroneal nerve at the level of the right knee and fibular head also demonstrated fascicular dilatation and enlargement [Figure 1]. Sonographic findings were reported as left ulnar and right common peroneal polyneuropathy.

US findings were confirmed by a subsequent electromyogram (EMG) of the bilateral upper and lower extremities, which showed axonal sensorimotor polyneuropathy, including severe right peroneal neuropathy across the fibular head, moderate-to-severe left radial neuropathy across the spiral groove, and ulnar neuropathy of the left upper extremity. The patient was then scheduled for further therapy and continued use of a brace.

COVID-19 patient B

A 54-year-old man with type II diabetes and morbid obesity (body mass index of 44 kg/m^2) was also hospitalized in isolation for COVID-19 (positive via SARS-CoV-2 reverse transcription-polymerase chain reaction) after presenting with a fever and shortness of breath. The patient was immediately intubated and placed on mechanical ventilation for 7 days. He was treated with antibiotics and corticosteroids. Following extubation, the patient reported significant weakness and numbness in the left foot and was unable to walk. He also complained of generalized body weakness, mainly involving both legs. The patient was hospitalized for a total of 19 days.

Two months following discharge, the patient presented to the neurology clinic with significant weakness in both legs and a persistent left foot drop. He also reported 2 months of numbness in the left leg, extending from the lateral aspect of the left lower leg to the dorsolateral left foot and great toe.

On physical examination, he demonstrated significant weakness in both legs, with an inability to dorsiflex the left foot. He also had reduced sensation to pinprick over the

dorsolateral aspect of the left foot. His left Achilles reflex was absent. A diagnostic MSK US of the left leg to evaluate for peripheral neuropathy was ordered.

Sonographic findings included an enlarged hypoechoic left common peroneal nerve with fascicular dilatation extending into the superficial peroneal nerve distally, consistent with left peroneal neuropathy [Figure 2].

A subsequent EMG of the bilateral lower extremities was confirmatory, demonstrating an asymmetric, axonal sensorimotor polyneuropathy, worse on the left, including an absent peroneal motor response at the left ankle. Active denervation and reduced recruitment were noted in the distal left lower extremity muscles. The patient was then referred for physical therapy and prescribed a brace.

Discussion

As this pandemic continues to spread and time elapses, newer clinical presentations of COVID-19 are becoming apparent.[2-4] Although the vast majority of COVID-19 patients present with the more common symptoms, recent studies have reported neurological symptoms, although the majority related to the central nervous system.[2-4] We present two unique cases of COVID-19–associated peripheral polyneuropathy, diagnosed initially utilizing MSK US, in an effort to make those caring for these patients aware of this unique complication and the use of US in its diagnosis.

MSK sonography has become very popular given its many advantages and is especially ideal as the first-line imaging modality for the evaluation of the peripheral nerves. Benefits over magnetic resonance imaging include ease of portability, dynamic imaging capabilities, higher soft-tissue resolution, cost-effectiveness, and the ability to scan the entire extremity and even the contralateral extremity quickly. The unique portability of US is especially instrumental with hospitalized COVID-19 patients who are in isolation and unable to be transported, and subsequently, US could assist in the earlier detection of this complication.[5-8]

When compared to magnetic resonance imaging, US has been shown to have a greater sensitivity (93% vs. 67%) and an equal specificity (86%) for the evaluation of peripheral nerve diseases.[6] Furthermore, with the recently introduced ultra-high–frequency transducers (20–70 MHz), which are able to display extremely fine anatomic detail including extraordinary nerve fascicular detail, the superiority of US for peripheral neuropathies will likely become more evident.[5,6] In addition, with the use of Doppler US, including newer microvascular imaging techniques, it can identify subtle intraneural hypervascularity. This has been shown to correspond with early neuropathies, occur before nerve enlargement/swelling, and strongly correlate with the severity of some neuropathies on EMG studies.[5]

The normal peripheral nerve on US, when evaluated in the long axis, demonstrates multiple paralleling hypoechoic linear areas separated by hyperechoic bands [Figures 3a and 4a]. These hypoechoic areas histologically are the distinct nerve fascicles and the hyperechoic bands between the fascicles are the epineurium. In the short axis, these same fascicles surrounded by the epineurium have been likened to the appearance of a honeycomb [Figures 3b and 4b].[5,6]

The most common sonographic finding of a peripheral neuropathy is nerve swelling/enlargement, resulting in an increased cross-sectional area in the short axis [Figures 1 and 2]. Additional sonographic findings of neuropathy include fascicular dilatation, a diffusely hypoechoic edematous appearance with obscuration, and indistinctness of the normal fascicular architecture or hyperechoic thickening of the epineurium [Figures 1 and 2].[5,6] Furthermore, during dynamic imaging, the transducer pressure over an abnormal nerve can often times elicit symptoms, functioning as a sonographic diagnostic "Tinel's sign."[5]

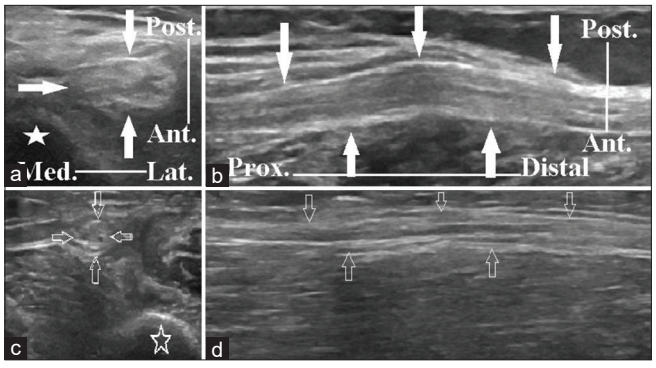

Figure 2: A 54-year-old COVID-19–positive man with left peroneal polyneuropathy. (a) Short-axis and (b) long-axis sonographic images adjacent to the left fibular head (star) demonstrate an enlarged left common peroneal nerve (arrows) with obscuration of the fascicular architecture and hyperechoic thickening of epineurium. Fascicular dilatation was also seen extending into the distal aspect of the enlarged left superficial peroneal nerve (open arrows) on both the (c) short-axis and (d) long-axis images, near the level of the mid distal fibula (open star)

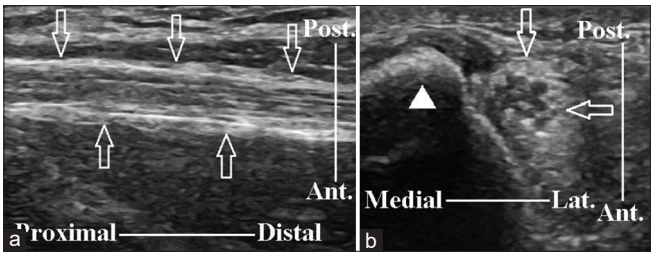

Figure 3: Normal sonographic appearance of the right ulnar nerve in a 39-year-old man. (a) Long-axis sonographic image of the right ulnar (open arrows) obtained at the right elbow, just distal to the cubital tunnel, demonstrates multiple paralleling hypoechoic linear fascicles separated by the hyperechoic linear bands of epineurium. (b) Short-axis sonographic image of the right ulnar (open arrows) obtained at the level of the cubital tunnel, adjacent to the medial epicondyle (arrowhead), showing the normal distinct fascicular architecture in a "honeycomb" appearance, made up of the definable hypoechoic nerve fascicles surrounded by the hyperechoic epineurium

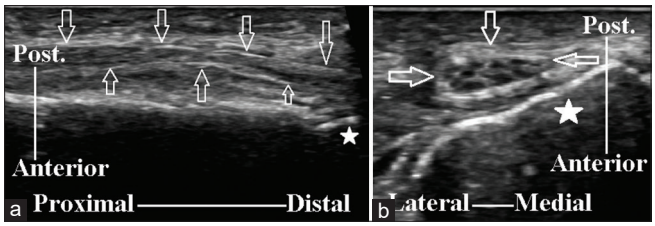

Figure 4: Normal sonographic appearance of the right common peroneal nerve in an 85-year-old-woman. (a) Long-axis and (b) short-axis sonographic images demonstrate the normal fascicular appearance of the common peroneal nerve (open arrows) at the level of the fibular head (star)

Recent publications have reported neurological symptoms and complications associated with COVID-19. However, the majority of these are related to the central nervous system; these include loss of taste and smell, headaches, dizziness, infarcts, and encephalopathies.[2-4] A few cases of COVID-19–related postviral peripheral polyneuropathies including axonal sensorimotor neuropathy and Guillain-Barré syndrome have been reported.[3,9] Our cases report is unique in that it not only demonstrates two patients both presenting in a similar fashion with COVID-19–related peripheral polyneuropathy, but both diagnosed initially utilizing MSK US and with similar sonographic and EMG findings.

Postinfectious-related neurological symptoms and complications are not unique to COVID-19 (SARS-CoV-2) but have also been reported in patients with other previously identified SARS-CoV strains and the Middle East respiratory syndrome-CoV as well as other viruses including the Zika and Epstein–Barr viruses.[3,9] These symptoms and complications are thought to be the result of direct viral infection of cells outside of the respiratory tract and a subsequent cascade of systemic inflammation including cytokine release.[2,3] Furthermore, extended times on mechanical ventilation can induce pro-inflammatory conditions in these patients, contributing to the systemic complications.[2]

Peripheral neuropathy more commonly affects diabetic patients, which is thought to be related to metabolic alterations to the peripheral nerves, resulting in structural changes.[10] Diabetic patients are also known to be at an increased risk for COVID-19 and have been reported to have worse outcomes, increased intensive care unit admissions, and an increased mortality risk from COVID-19.[11] Although both of our patients had type II diabetes, neither patient complained of nor demonstrated any of these symptoms before presenting with COVID-19.

We present a unique case report of COVID-19–related peripheral polyneuropathy in two patients both diagnosed initially utilizing MSK US. The sonographic findings in both of these patients highlight the importance and benefits of the use of US for the diagnosis of peripheral neuropathies. US is especially instrumental in hospitalized COVID-19 patients who are in isolation, and its use may facilitate earlier detection of this complication. As the COVID-19 pandemic continues to spread worldwide, both clinicians and radiologists must be aware of these complications and their sonographic findings as they play a crucial role in the early diagnosis and management of peripheral polyneuropathy.

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Declaration of patient consent

The authors certify that they have obtained appropriate patient consent forms. In the forms, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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