Atypical cutaneous and musculoskeletal manifestation of SARS-CoV-2: ‘COVID-19 toes’ and spasticity in a 48-year-old woman

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SUMMARY
Establishing accurate symptomatology associated with novel diseases such as COVID-19 is a crucial component of early identification and screening. This case report identifies an adult patient with a history of clotting dysfunction presenting with rare cutaneous manifestations of COVID-19, known as ‘COVID-19 toes’, previously described predominantly in children. Additionally, this patient presented with possible COVID-associated muscle spasticity of the lower limbs, as well as a prolonged and atypical timeline of COVID-19 infection. The rare occurrence of ‘COVID-19 toes’ in this adult patient suggests that her medical history could have predisposed her to this symptom. This supports the coagulopathic hypothesis of this manifestation of COVID-19 and provides possible screening questions for patients with a similar history who might be exposed to the virus. Additionally, nervous system complaints associated with this disease are rare and understudied, so this novel symptom may also provide insight into this aspect of SARS-CoV-2.

BACKGROUND
With most of the world affected by the COVID-19 pandemic, much attention has been turned to studying the features of its source: SARS-CoV-2. Although primarily the cause of a respiratory illness, this strain of the single-stranded RNA virus has been shown to affect nearly every organ system without reliable predictability.1–4 The wide variety of associated symptoms makes categorisation of this illness difficult. One of the more curious features of COVID-19 includes the cutaneous manifestations known colloquially as ‘COVID-19 toes’. These chilblain-like lesions appear primarily on the feet and are generally described as painful violaceous papules on the dorsal surface of the toes, although there can be some variation in colour and location.5 The true mechanism for this pathology has yet to be fully explained. Colmenero et al studied these lesions in paediatric patients, finding both viral particles and histological evidence of vascular damage. They postulated that the mechanism could be direct endothelial damage inflicted by the virus.6 Vinayagam and Sattu also linked this endothelial dysfunction to the increased number of thrombotic events in COVID-19 patients due to increased thrombin generation that halts fibrinolysis, leading to hypercoagulopathy.7 The current literature reports that this symptom of COVID-19 occurs predominantly in children and young adults later in their disease course.8 We present a case of ‘COVID-19 toes’ in a 48-year-old woman with underlying coagulopathic syndrome.

CASE PRESENTATION
This patient presented to the clinic in late April 2020 with a painful, swollen lesions on the feet bilaterally. Associated symptoms included generalised fatigue and muscle spasticity of the lower limbs that started around the same time as the foot lesions. Additionally, she had anosmia, shortness of breath and chest pain but no fever or chills at that time. However, she did have an episode of high fever (103.4 °F (39.7°C) per home thermometer), cough, shortness of breath, fatigue and body aches that lasted for 4 days about 8 weeks prior (early March 2020). These symptoms started approximately 48 hours after a COVID-19 exposure, but the patient was not tested at that time due to lack of availability. However, she met the criteria for a presumptive diagnosis of COVID-19 per the CDC guidelines established at the time. Vital signs included a blood pressure of 139/83 mm Hg, heart rate of 94 bpm, respiratory rate of 26 bpm with increased work of breathing, pulse oximetry of 92% and temperature of 102.9 °F (39.4°C). Medical history included hypertension, atrial fibrillation and antiphospholipid syndrome (APS) with recurrent transient ischaemic attacks. She had been taking metoprolol and aspirin for her cardiovascular problems for the past 15 years. A nasopharyngeal culture for COVID-19 at a drive through testing centre was positive on the day of...
her April visit so she was instructed to quarantine for 14 days and increase her daily aspirin from 81 to 325 mg.

She described the lesions as blisters that emerged individually, starting on the left foot and eventually affecting the right foot. They were acutely painful and began to enlarge, erupt and became confluent over the course of a week (figure 1A–H). During this time, she experienced re-emergence of respiratory symptoms including shortness of breath on minimal exertion with severe dry cough and chest pain. As the lesions progressed, the muscle spasticity in her lower limbs increased to approximately 10 episodes per day of intense, squeezing pain in the calves that lasted 30 s to 2 min. Both the spasticity and pain in the toes would worsen when sitting for any length of time and were refractory to gabapentin. Resolution of the blisters took approximately 30 days; however, some discoloration and minimal pain persists as of the date of this report (figure 2A–D). The discoloration still worsens during periods of sitting; figure 3 shows the results of sitting for approximately 20 min. The fatigue and shortness of breath have also persisted and are currently being managed with an albuterol inhaler and fluticasone as needed. The patient was recently prescribed ropinirole, which has improved the lower limb spasticity. She has been advised to continue her aspirin at the higher dose, as her medical history along with COVID-19 exposure compounds her risk for clotting.

INVESTIGATIONS
As mentioned previously, the availability of COVID-19 testing for the public was quite limited at the time this patient first presented with symptoms. Having test results from that time period would have been helpful in determining whether or not she did indeed contract COVID-19 twice. However, this patient was presumed positive by her primary care physician, as she met the criteria for a clinical diagnosis (confirmed exposure, fever >100.4° F (38° C), respiratory symptoms, etc) of the disease. Her vital signs, as reported above, also supported this diagnosis. She did not have a chest X-ray performed during the first infection but did at her subsequent presentation. This showed diffuse, bilateral infiltrates in all lobes and scarring with no evidence of infarction. A pulmonary contusion of the right lower lobe was noted; however, its aetiology was unclear. No CT pulmonary angiography was performed during either presentation, as the suspicion for pulmonary embolism was low per Well’s criteria. Additionally, her D-dimer was not elevated.

The patient initially applied over the counter topical triple antibiotic ointment to the emerging foot lesions but there was no symptom relief, making a cutaneous infection unlikely. She also denied any recent changes in footwear or other exposure that could have explained them.

TREATMENT
Because this patient contracted COVID-19 at a time before a consistent treatment protocol was established, she received only supportive care for the initial management of her respiratory symptoms. The persistence of her shortness of breath prompted the use of an albuterol inhaler. Due to her hypercoagulable state and the reported clotting risk associated with this infection, she was instructed to increase her daily aspirin from 81 to 325 mg and avoid long periods of stasis. Treatment of the cutaneous and musculoskeletal symptoms was more complicated; gabapentin and codeine 30 mg with acetaminophen 300 mg (T3) did not help with the pain, though the T3 was slightly effective for the spasticity. After these medications failed, the patient was started on ropinirole, which provided almost complete relief of the muscle symptoms.

OUTCOME AND FOLLOW-UP
To date, this patient continues to experience dyspnoea on exertion, for which she still uses the inhaler. There have been no overt signs of clotting other than some leg swelling during long travel and the persistent toe discoloration. The patient is unable to sit for more than 20 min without experiencing the blue-black mottling of both feet. She is now experiencing Raynaud’s phenomenon-type numbness, pain and paresthesia of just the affected toes related to cold exposure. Her muscle spasticity is well managed with the ropinirole and she continues to have regular scheduled visits with her primary care physician.
DISCUSSION

Though many hypotheses have been proposed regarding the aetiology of ‘COVID-19 toes’, a consensus has yet to be reached. Some studies postulate that they are a result of vasculitis, others say coagulopathic changes are responsible, along with several alternative theories. 5–8 Landa et al discussed the fact that these lesions often show up late in the disease course, often when viral load is low or even undetectable. They used this fact to hypothesise the cause of damage could either be from an antigen-antibody immunological process or from microthrombi secondary to the hypercoagulable state. 9 This patient’s unique history of APS could have predisposed her to this COVID-19-related thrombotic microangiopathy or at least compounded her clotting risk, leading to her prolonged disease course. The severe worsening of foot discoloration after sitting certainly lends credence to a thrombotic or venous stasis-related cause. Given her previous thrombotic events, it is reasonable to say that this case supports the coagulopathic theory of ‘COVID-19 toes’ aetiology.

The emergence and persistence of lower limb muscle spasticity presents an intriguing puzzle. Generally, muscle spasticity is related to nerve dysfunction. 10 However, this patient’s symptoms were refractory to gabapentin and only improved after administration of ropinirole. This suggests more of a dopaminergic imbalance of the central nervous system (CNS), similar to restless legs syndrome, despite the pattern and quality of the episodes being more descriptive of spasticity. There have been some reports of CNS involvement of COVID-19, but these are few and far between and generally involve strokes and other thrombotic complaints. 11 Again, a vascular disruption to dopamine-producing regions of the brain would further support a coagulopathic explanation for this patient’s symptoms. Perhaps these symptoms represent another neurological manifestation of COVID-19 that should be explored when taking a history on a patient with possible COVID-19 exposure.

Additionally, there is the possibility that this patient was infected with COVID-19 twice—once during the prior illness following exposure, and again when the cutaneous manifestations began. The assumption was made that the first illness was when the patient was initially infected and that the subsequent symptoms 8 weeks later were simply late effects of that primary infection. Given the lack of testing available at the time of first illness, there is no way to verify this. However, because of the extended timeline and concurrent emergence of respiratory symptoms alongside the cutaneous lesions, it is possible that reinfection could have occurred. To date, there is extremely limited data regarding reinfection and—while this is only one case—it could represent a possible scenario where the initial infection followed a more ‘standard’ course, where reinfection introduced the more atypical features accompanying the disease. Clearly much more research is necessary in this area. The utility of this report lies in the expansion of patient questioning regarding timelines and atypical features, as well as the addition of possible symptomatology associated with this novel virus.

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Patient’s perspective

‘Prior to having Covid 19, I considered myself to be in good health with very few lifestyle restrictions. I worked as a floral designer and farmer, putting in long hours of climbing, standing, lugging etc. and was comfortable with daily physical labour. As soon as I contracted Covid-19 my daily routine was drastically impacted. The leg/foot pain and spasms that I continue to experience months later mean that I must plan my tasks around best times and limited physical activity.’

Learning points

► This case represents a rare occurrence of cutaneous manifestations of SARS-CoV-2 in an adult with pre-existing coagulopathic anomalies, as well as the first reported instance of possible musculoskeletal effects.
► Not only is it unique in that ‘COVID-19 toes’ occurred in an adult, there were also associated central nervous system or musculoskeletal symptoms in the form of lower limb spasticity.
► Given the patient’s history, the emergence of her foot lesions lends credibility to the coagulopathic theory of ‘COVID-19 toes’ aetiology.
► Additionally, the muscle spasticity could represent a novel manifestation of COVID-19’s effect on the nervous system. We hope that this report offers some insight into the more atypical features of COVID-19.
