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LETTER TO THE EDITOR

Addressing the Question of Dermatologic Manifestations of SARS-CoV-2 Infection in the Lower Extremities

A Closer Look at the Available Data and its Implications

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Introduction

The first case of SARS-CoV-2 infection, also known as the Coronavirus Disease of 2019 (COVID-19) was reported in December of 2019 by doctors in Wuhan, China.(1) Since then, physicians have reported a peculiar sequelae for the novel coronavirus involving various manifestations and courses of the disease as well as a predilection for morbidity and mortality based on certain pre-existing conditions and age groups. Recently, there has been growing interest in anecdotal findings of skin manifestations by several healthcare providers who are postulating a possible correlation to COVID-19.

What We Already Know

One of the largest studies published to date regarding clinical characteristics of COVID-19 patients reviewed the cases of 1,099 confirmed positive COVID-19 patients in China. This

study found that the median incubation period for the disease was 4 days, and that the most common symptoms included fever (43.8% of patients were febrile on admission, and 88.7% of patients became febrile throughout the duration of their hospital stay), cough (67.8%), and fatigue (38.1%). The study also noted that 2 patients (0.2%) had rashes, a very small portion of the sample size, with no further details outlined regarding these lesions.(2)

Examining the Data

Most of the buzz on this topic in the United States can be traced back to a video posted by Dr. Maria Del Mar Ruiz Herrera, a podiatrist from Spain. The slides were originally posted in Spanish and later translated by a US-based podiatrist. They entail a few slides with several collages of hands and feet and a few pointers regarding what to do if similar presentations are encountered in practice. The slide also notes that these are chilblains-like lesions or having a vasculitic consistency. No other relevant clinical information is provided in this slide-show, including whether the patients have any other constitutional symptoms or ever tested for COVID-19.(3)

The video was posted on April 9th, the same day that the General Council of Colleges of Podiatrists released a statement announcing that it was launching a registry. In the statement, the council also reported that there have been cases of purple-colored lesions on the toes, which they compare to chickenpox, measles, or chilblains. Some of the same images used in Dr. Herrera's slide show are also included in the statement, without any additional relevant clinical information regarding the patients. The council also notes that there is little scientific evidence to discuss yet, but mentions a case report recently

published by the International Federation of Podiatrists (IFP) on the organization's website.(4)

The article published by IFP is titled "Acute Acro-ischemia in the Child at the Time of COVID-19." It describes a 13-year-old boy in Italy who presented with pedal purpura that was complicated by blistering and necrosis that ultimately improved. The patient presented febrile 2 days later with a temperature of 38.5 degrees Celsius and experiencing muscle pain, itching and burning to the skin lesions, as well as complaining of a headache. Upon further investigation, it was revealed that the patient's mother and sister had both experienced COVID-19—like symptoms including a fever, cough and dyspnea 6 days prior to the skin lesions presenting. The study notes that the physician was unable to confirm the patient's COVID-19 status.(5)

The same authors published another report in the *European Journal of Pediatric Dermatology* (EJPD) titled "A New Vasculitis at the Time of COVID-19." This case series exhibits several examples of what are described as "Multifocal, often asymmetric" lesions of a vasculitic nature. The report states that this presents mostly in healthy children and adolescent patients, with no other symptoms besides the skin manifestations. The study also notes that the patients do not have any reported history of similar lesions, and that 10% of cases involve a sibling with similar skin manifestations. The authors found that the parents do not share these presentations even as they report contact with COVID-19 patients or have tested positive themselves. While the lesions were found on the hands and feet, the lesions on the feet were more severe and complicated by a sequelae consisting of "infiltration, formation of blisters, bruising and superficial necrosis." The lesions on the feet were found on the digits, heels, and plantar aspect. The patients were reported to heal

within 12-20 days. The case series represents a descriptive report rather than an analytical one, as important data points are left out such as the sample size and gender distribution. Other data points such as the number of adult family members who were positive or had Covid-19-like symptoms were not provided either.(6)

On March 26, 2020, Italian dermatologist Dr. Recalcati published what appears to be the largest study to date examining “Cutaneous Manifestations of COVID-19: a first perspective” in the *Journal of European Academy of Dermatology and Venerology*. In the study, 88 patients were assessed at Lombardy’s Lecco Hospital and none had taken any new medications in the previous 15 days. Eighteen patients (20.4%) were found to have cutaneous manifestations. Of the 18, 8 had developed the lesions at the onset of the disease and the remainder developed them during the course of their hospital stay. These presentations consist of an “erythematous rash (14 patients), widespread urticaria (3 patients) and chickenpox-like vesicles (1 patient).” However, this study notes that the main involved region is the trunk and no mention of the feet or lower extremities is made. The lesions are described as being minimally itchy or not itchy at all, and the author states that they heal within a few days. Additionally, the author notes that the presence or lack of cutaneous manifestations did not appear to impact severity of the disease.(7)

In France, a press release on April 6 by the National Syndicate of Dermatologists-Venereologists (SNDV) stated that a WhatsApp group of over 400 dermatologists were sharing information on prevalent skin lesions at this time whether or not they are associated with classical COVID-19 symptomatology.(8)

On the same day that The SNDV issued its press release, Manalo et al published a case series on two patients with transient livedo reticularis (LR) in the *Journal of the American Academy of Dermatology*. Both patients were confirmed to be positive for COVID-19. The first patient, a 67-year-old male, developed a livedoid patch on his right anterior thigh 7 days after onset of symptoms. The patient also developed gross hematuria at this time. Both the lesion and hematuria resolved within a day later. The second patient, a 47-year-old female, developed a similar asymptomatic rash to the right leg that was noticed when the patient went from being outdoors to indoors. This rash reportedly resolved in 20 minutes and did not recur. The authors note that LR may be caused by disseminated intravascular coagulation (DIC), which has been increasingly reported in critical cases involving COVID-19 patients. The authors suggest that these presentations, including the hematuria, may be explained by a low-grade DIC.(9)

The Manalo et al article is not the only report to mention DIC in the setting of dermatologic manifestations in COVID-19 patients. An article in the *Chinese Journal of Hematology* presented a retrospective analysis of 7 critically ill COVID-19 patients who were admitted to the hospital. All 7 lived in Wuhan, developed fevers and respiratory symptoms, and had various stages of limb ischemia. Three of the 7 patients had co-existing conditions such as diabetes, hypertension, and coronary heart disease. Their limb ischemia presented ranging from plantar acral discoloration to dry gangrene. The average time from onset to limb ischemia was 19 days. These lesions correlated with progressive worsening of the disease and occurred a few days before to a few days after mechanical ventilation. Across all 7 patients, an increased D-dimer level to more than 20 times the upper limit of normal was recorded. Reports have shown that an increase in D-dimer was statistically

significant between ICU and non-ICU patients. Fibrin and fibrinogen degradation product (FDP), a test to diagnose DIC was also greatly increased.(10)

Discussion

In light of the copious anecdotal reports that have circulated among podiatrists and dermatologists mainly in Europe and the United States, many healthcare professions are sharing their takes on social media with understandable intrigue and curiosity. It is important however to be very cautious in the wording and distribution of such commentary as it may easily be misconstrued by other practitioners and the general public, especially during a time of wide-spread anxiety relating to the pandemic.(11)

In the last few weeks, several pieces have been published in the mainstream media (MSM) using the images shared by Dr. Herrera and the General Council of Colleges of Podiatrists in Spain. These pieces paint a picture of a consensus that simply is not there yet in the medical community. A piece published on April 17th by Fox News spuriously titled “Researchers discover new coronavirus symptoms: feet lesions,” shares a selective portion of the council’s statement without mentioning perhaps the most important line regarding there being little evidence to discuss yet.(12, 4) The council took the appropriate step of creating a registry to crowdsource more data from practitioners.(4)

There are several other examples of MSM using categorical language to report on what are largely unsubstantiated claims. If you spend enough time combing through the social media posts, press releases, and few inconclusive studies published to date on this

matter, you will gain an appreciation for the proverbial game of telephone that has ensued in the past several days.

For example, in a video by celebrity dermatologist, Dr. Sandra Lee (also known as Dr. Pimple Popper), she states that dermatologists across the nation have noticed certain skin conditions that may be associated with COVID-19. As she speaks, the chyron beneath her notes: “It appears that approximately 20% of known COVID-19 patients have skin findings.” She continues explaining that the most common of these findings is a livedoid-patterned rash and displays examples of these lesions, all presenting in the lower extremities.⁽¹³⁾ It is unclear whether the images used to illustrate these lesions are from a particular study, however it is likely that the 20% statistic she is quoting is referring to Dr. Recalcati’s report which was recently published in the *Journal of European Academy of Dermatology and Venerology*, as there are no other published studies quoting that statistic.⁽⁷⁾

As described earlier, Dr. Recalcati reported that 18 out of 88 COVID-19 patients (20.4%) were found to have cutaneous manifestations. These manifestations were most commonly found on the trunk, and not on the lower extremities. In fact, Dr. Recalcati’s study does not make mention of the extremities, which were the sole focus of Dr. Lee’s video.⁽⁷⁾ Dr. Lee then segues to what she describes as the second most common finding: perniosis or chilblains, most commonly occurring on the toes. To the average viewer, it may appear that the first and second most common findings as described by Dr. Lee relate to the statistic of 20% noted at the beginning of the video; however, this is not the case.⁽¹³⁾ The source of these subsequent claims involving the fingers and toes at least in part trace back

to the slide-show by Dr. Herrera highlighted earlier in our report, evidenced by the usage of the same collage from Dr. Herrera's slide-show in Dr. Lee's video.(13, 3) It is important to note again that these photos have no associated clinical information on the subjects or any correlated data points and are not the subject of a published study as of the time of writing this manuscript.(3)

Social media has increasingly been used as a source of information for the average consumer. A study published in 2017 stated that over 40% of the healthcare consumer population relies on social media for health-related information, with that value increased to 90% in the 18-24 age group.(14) This reality compounded with the current pandemic calls on all healthcare providers to emphasize a conscientious approach to delivering health-related information to the general public. While Dr. Lee makes it a point to note that these lesions do not necessarily imply a patient has COVID-19, the claims made in her video, which has up to this point been viewed over 520,000 times, are a concoction of selectively cropped studies and reports presented out of context.(13)

As unequivocal claims of skin manifestations in the lower extremities related to SARS-CoV-2 infection continue to spread with little supportive evidence available, we are faced with the question of the potential ramifications moving forward. A few days ago, a New York-based podiatrist posted a collection of photos of a patient with what he describes are "Symptoms similar to vasculitis" on social media. The post uses definitive terms to state that "We now know there are skin changes that occur on the feet that have been tied to COVID-19." He continues to give a descriptive assessment of these lesions and states that while "this does not mean that the patient has COVID-19... They can now get tested." The

podiatrist concludes his post by encouraging others to share it, and as of right now the post has been shared 228 times.(15)

An increasing number of practitioners are calling for performing COVID-19 tests on otherwise asymptomatic patients presenting with skin manifestations in the lower extremities. This poses a dilemma on two-fronts. Firstly, the data available to support a correlation-causation relationship is insufficient at this time. Secondly, tests are currently being rationed all across the country due to shortages.(16) The Centers for Disease Control and Prevention (CDC) has also published “Criteria to Guide Evaluation and Laboratory Testing for Covid-19.” The criteria notes 4 categories: priority 1-3 and non-priority. In a pamphlet, the CDC defines COVID-19 symptoms as fever, cough, and shortness of breath.(17)

Asymptomatic patients with skin lesions fall into the non-priority category as “individuals without symptoms.”(17) Even if testing were to ramp up and more substantive studies support a possible COVID-19 skin manifestation, there are many other widely-documented symptoms that would likely supersede in priority, as some of them in isolation currently do not qualify for testing at many sites in the United States.(18) These symptoms include “myalgias (23.8%), diarrhea (23.7%), and nausea and vomiting (19.1%),” according to the “Clinical Characteristics of COVID-19 in New York City” study published in the *New England Journal of Medicine*, which performed a retrospective case series involving 393 consecutive patients admitted to two hospitals.(19)

Conclusions

Although there are many viruses that present with dermatologic manifestations in the lower extremities(20), the published data currently available to suggest such an association with the novel coronavirus are small in size and other reports have been mainly anecdotal across the globe. As healthcare practitioners during a global pandemic, our expert opinions come with an even greater sense of responsibility. The onus is on us to deliver accurate and beneficial information, as the general public looks for answers.

The literature available today suggests that although there may be a dermatologic component to the disease, this has mostly been observed in the trunk. The literature also suggests that these lesions improve over time with conservative therapy.(7) There is no analytical evidence at this time to draw any relationships between lower-extremity lesions in otherwise asymptomatic patients, COVID-19 infections, and an associated risk of SARS-CoV-2 infection transmissibility by proxy.

In addition to the guidelines for testing outlined by the CDC's website, it notes that "clinicians should use their judgment to determine if a patient has signs and symptoms compatible with COVID-19 and whether the patient should be tested." The CDC also states that "increasing testing capacity will allow clinicians to consider COVID-19 testing for a wider group of symptomatic patients." Until the country has reached such a capacity in testing, and until further data are published, it is important for practitioners to "continue to work with their local and state health departments to coordinate testing," as the CDC suggests.(17)

The ultimate question that remains is what should a practitioner do if a patient presents with lower-extremity skin manifestations in the absence of an obvious etiological course in the setting of this pandemic? The answer to that question depends on a multitude of factors. It is important for practitioners to understand the difference between social distancing, self-monitoring, quarantining, and isolating. At this time, all individuals should heed to the CDC's guidelines and partake in social distancing. However, the recommendation to self-isolate a patient with this symptomatology out of fear of transmission to healthy individuals is one that should be made in accordance with local health authority guidelines and in collaboration with the patient's primary-care provider. A serious discussion should be had with the patient about the effects of self-isolation on mental health, and on where the data to suggest an association between such lower-extremity lesions and COVID-19 stand.(21)

In the meantime, there are several efforts to keep an eye on as research in this space continues to grow. The Infectious Diseases Society of America (IDSA) is in the process of publishing guidelines on testing and infection prevention.(22) Additionally, The American Academy of Dermatology (AAD) has created an international COVID-19 dermatology registry that is IRB approved and only allowing healthcare workers to report lesions to "help us understand dermatologic manifestations of the COVID-19 virus."(23) Registries are very important tools in assessing patterns in populations and may serve as precursors to further studies. However, until the medical community can assess the fruits of these efforts, any definitive statements regarding a correlation between the novel coronavirus and dermatologic manifestations in the lower extremities should be reserved until more evidence is analyzed.

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