A CASE OF PERNIO-LIKE LESIONS ("COVID TOES") WITH HISTOLOGIC CONFIRMATION OF MICROTHROMBI

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The case report below supports the following three points:

- **"COVID toes" are different from idiopathic pernio**
- **Microthrombi are involved in the pathogenesis of "COVID toes"**
- **Microthrombi may occur in the absence of severe COVID-19 disease**

We have decided to publicize this case report on social media (which precludes publication in a peer-reviewed journal, but which does indeed allow for peer review) because we believe that this is the fastest way to disseminate new information, particularly as physicians and scientists at this moment are trying to get a grasp on the role of microthrombi in the pathogenesis of COVID-19 disease in order to develop better treatments. If this report sheds some light on

the pathogenesis of more severe disease (pulmonary, CNS, etc.) and one life is saved because of earlier understanding, then our mission will be accomplished. This is being posted first where dermatologists, pathologists, and dermatopathologists will view it, but we encourage sharing with experts in fields such as critical care medicine, vascular disorders, and immunology who may have interest in it. Thank you.

Case Report

"COVID toes" are pernio-like lesions that appear specific for COVID-19 disease. They were first reported in the medical literature by Mazzotta et al. after initial descriptions by dermatologists on social media (1,2). They occur mostly in children, particularly adolescents who are often otherwise asymptomatic but sometimes report preceding flu-like symptoms. The most common sites are the toes, plantar surface, and fingers. The lesions are often discrete and begin as red macules that progress to purpuric lesions, sometimes with blisters or crusting, resolving spontaneously after about two weeks. Mazzotta et al. postulated that microthrombi may be involved in their pathogenesis (1). A previous report of biopsy findings in "COVID toes" did not reveal microthrombi (3), but we suspect this may at least in part be due to the timing of the biopsy or the area that was sampled (the deepest dermis was not included in that biopsy, and microthrombi may be scarce). Herein we report a patient with "COVID toes" with histologic confirmation of microthrombi.

A 22-year-old otherwise healthy man was evaluated as a dermatology outpatient for a burning, pruritic, painful rash involving his bilateral toes for approximately 2 to 3 weeks. Approximately three weeks before lesion onset, he experienced a week-long period with fevers, chills, cough, and shortness of breath on exertion, consistent with COVID-19, with several college roommates experiencing similar symptoms; testing for SARS-CoV-2 was unavailable. Examination revealed erythematous macules and blisters involving the dorsal toes **(**Figure 1A**)** and very tender purplish lesions on the ventral toes. A biopsy specimen showed confluent epidermal necrosis, a moderately dense superficial and deep perivascular lymphocytic infiltrate, and subtle small vessel vasculopathy with microthrombi **(**Figure 1, B-D**).** Intralesional triamcinolone (5 mg/cc) and absorptive socks were implemented with marked improvement in two weeks.

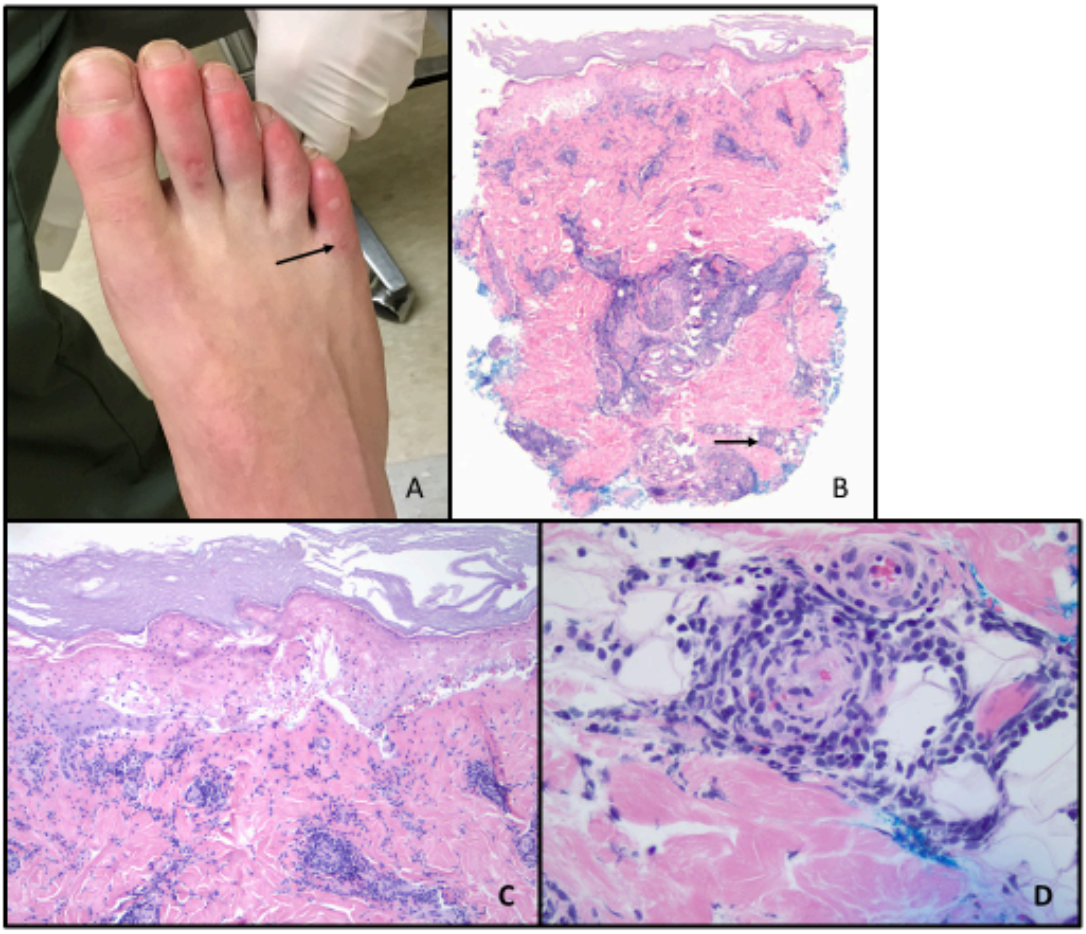
Our patient's clinical findings match those described by Mazzotta et al. and histologically confirm that vasculopathy is involved in the pathogenesis. Furthermore, the detailed clinical descriptions of Mazzotta et al. and our clinical and histologic findings suggest that these may be COVID-19-specific lesions. They seem to differ from idiopathic pernio clinically by having a greater tendency towards violaceous, dusky

lesions and true blisters (correlating with confluent epidermal necrosis, which almost never occurs in idiopathic pernio); furthermore, while thrombi may be found in a minority of biopsies of idiopathic pernio (4), such thrombi are almost always superficial, in contrast to the deep dermal thrombosis in our patient's biopsy. "COVID toes" are also distinguishable histologically from leukocytoclastic vasculitis (which shows neutrophils and karyorrhexis); hand-foot-mouth disease (which lacks thrombi and has significantly less inflammation); and primarily occlusive vasculopathies like antiphospholipid syndrome (which show relatively little inflammation).

It is noteworthy that Zhang et al. described 7 adult Chinese patients with severe COVID-19 disease and acral ischemic changes including gangrene (5). Furthermore, Magro et al. described microvascular thrombosis in lung and skin of adults with severe COVID-19 disease, with one patient having acral purpuric lesions, although that patient's biopsy findings differed from ours, being predominantly thrombotic without inflammation (6). It is unclear if our patient's acral lesions represent a different process or, alternatively, the same process with much milder clinical disease in healthy young individuals. Of particular note is the several week delay from the onset and resolution of our patient's respiratory symptoms to the development of microthrombotic disease manifested by "COVID toes". This may have implications for the pathogenesis of microvascular injury in older adults, who often experience a several week delay from the onset of respiratory symptoms to serious morbidity and death.

Figure 1. Clinical-pathologic correlation

Erythema on the dorsal toes with one or several blisters on each; arrow points to the pre-procedure biopsy site, the most subtle of three blisters on the 5th toe (Panel A). Panel B is scanning magnification of a hematoxylin and eosin-stained section from the punch biopsy specimen, showing a moderately dense, superficial and deep perivascular lymphocytic infiltrate. Panel C is a higher power view showing confluent epidermal necrosis and a subepidermal cleft (blister). Panel D shows a thrombosed small blood vessel in the deep dermis with a surrounding lymphocytic infiltrate (high magnification of the area indicated with arrow in Panel B).



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