Acrofacial purpura and necrotic ulcerations in COVID-19: a case series from New York City

Dear Editor,

As COVID-19 continues to spread worldwide, the prognostic significance of its cutaneous manifestations has been increasingly scrutinized, including that of retiform purpura. Additionally, an increased incidence of thromboembolism has been seen in COVID-19,1 and histopathologic evaluation of retiform purpura in COVID-19 patients demonstrated thrombotic vasculopathy suggestive of a hypercoagulable state.2 To better characterize purpura and necrotic ulcerations in hospitalized COVID-19 patients and examine incidence of systemic coagulopathy in this population, we performed a retrospective review of patients seen within a tertiary care center during peak incidence of COVID-19 in New York City.

After IRB approval, we reviewed patient charts for whom dermatology and wound care were consulted at NYU Tisch and Bellevue Hospital from March 1 to May 1, 2020. Over 3,800 patients were hospitalized for COVID-19 during this time. Inclusion criteria consisted of positive SARS-CoV-2 PCR (severe acute respiratory syndrome coronavirus polymerase chain reaction) and presence of purpura and/or necrotic ulceration. Salient laboratory values and clinical outcomes were documented (Table 1). In an attempt to exclude typical hospital-acquired sacral pressure ulcers, patients solely with sacral purpura/necrosis were excluded.

We identified 21 PCR-positive COVID-19 patients with purpuric and/or necrotic ulcerations on the ears, face, distal extremities, and/or genitalia (Fig. 1). Fourteen of 21 patients had multiple sites of involvement including eight patients who also had sacral ulcers. In 17/21 patients, sites in direct contact with medical devices including nasal cannula, endotracheal tube, urinary catheter, or pulse oximeter were involved; devices were in place for a range of 2–30 days (median 11 days) at the time of dermatologic evaluation, and time between hospitalization and first identification of skin manifestations ranged from 2 to 33 days (median 19 days). Case age varied greatly and was younger overall (25–88 years, median age 56) than in prior reports of retiform purpura in COVID-19.3 Only 3/21 patients were female. Most patients were critically ill; 19/21 required invasive mechanical ventilation and 18/21 required vasopressors within 2 weeks of lesion onset. All patients were intermittently prone.

In terms of systemic hypercoagulability, five patients developed deep vein thromboses and one experienced myocardial infarction. Sixteen developed acute kidney injury, possibly related to renal microthrombosis.4 Therapeutic anticoagulation was initiated in 16/21 (76%) for a thrombotic event or elevated D-dimer: 13 prior to the recognition of cutaneous findings, while the remainder were transitioned from prophylactic to therapeutic doses of anticoagulation after cutaneous eruptions were noted.

Recent reports document a high incidence of coagulopathic events in COVID-19.1 While the exact pathomechanism remains unclear, direct invasion of endothelial cells by SARS-CoV-2 virus and complement-mediated endothelial injury may promote a microthrombotic syndrome with potential for cutaneous involvement. In our review of 21 patients, we demonstrate a propensity for acrofacial purpura and necrotic ulceration in COVID-19, often associated with minor pressure (including intermittent proning or contact with medical devices) and occurring on nonsacral sites. Moreover, we identify a 29% rate of detectable thromboembolic events, 76% incidence of acute renal injury possibly related to microthrombosis, and 90% incidence of severe COVID-19 pneumonia in this cohort, despite a younger median age than previously reported.5 The majority of patients were men, likely reflective of increased COVID-19 disease severity as described in men compared with women.5

While sacral ulcerations are frequently seen in critically ill patients, acrofacial purpura and necrosis are less common. We posit that a microthrombotic syndrome associated with COVID-19 may result in acrofacial cutaneous purpura/necrosis and that pressure-associated tissue hypoxemia is an inciting factor in areas not typically prone to pressure-induced injury.

We highlight these cases to suggest increased vigilance for pressure-related cutaneous injury in severely ill COVID-19 patients. Further, observation of necrotic ulcerations may warrant heightened clinical suspicion for a procoagulant state and/or signs of other end-organ damage. These cutaneous findings may have implications regarding appropriate therapeutic anticoagulation targets, although additional prospective studies are needed.

The Ronald O. Perelman Department of Dermatology, New York University Grossman School of Medicine, New York, NY, USA

Conflict of interest: None.

Funding source: None.

Theodora K. Karagounis*, MD, MS
Katharina S. Shaw, MD
Avrom Caplan, MD
Kristen Lo Sicco, MD
Alisa N. Femia, MD

*E-mail: theodora.karagounis@nyulangone.org

Theodora K. Karagounis MD, MS
Katharina S. Shaw, MD
Avrom Caplan, MD
Kristen Lo Sicco, MD
Alisa N. Femia, MD
| Number | Sex/Age | Race       | Location of lesions                                                                 | Time of hospital admission to identification of lesions (days) | Time between possible inciting factor and onset of lesions, inciting factor | D-Dimer at time lesions noted (ng/ml, ref range <230) | Known history of coagulopathy | Deep vein thrombosis | Acute kidney injury | Arterial thrombus | Therapeutic anticoagulation | Invasive mechanical ventilation | Patient status at last encounter |
|--------|---------|------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------------------------------------|--------------------------------------------------------|-----------------------------|----------------------|----------------------|----------------------|-----------------------------|-------------------------------|-------------------------------|
| 1      | F/88    | White      | Upper and lower vermilion and cutaneous lips, columella                             | 7                                                                | 7 days, hi-flow nasal cannula                                               | 5,369                                                   | None                        | No                   | No                   | No                   | Yes, for elevated D-dimer     | No                            | Alive – not hospitalized        |
| 2      | M/68    | White      | L ear and R cheek                                                                   | 14                                                               | 10 days, intubation                                                         | 3,730                                                   | None                        | No                   | Yes, requiring RRT | No                   | Yes, for elevated D-dimer     | Yes                           | Alive – hospitalized           |
| 3      | M/77    | White      | L upper arm, sacrum                                                                 | 26                                                               | No known inciting factor                                                    | 6,022                                                   | None                        | No                   | No                   | Yes, requiring RRT | Yes, for elevated D-dimer     | Yes                           | Alive – not hospitalized        |
| 4      | M/55    | Asian      | L cheek, sacrum                                                                     | 5                                                                | 5 days, intubation                                                         | 6,694                                                   | None                        | Yes                   | No                   | Yes                   | Yes, not requiring RRT        | No                            | Alive – hospitalized           |
| 5      | F/67    | White      | L buttock, R shin                                                                   | 23                                                               | No known inciting factor                                                    | 1,918                                                   | Factor V Leiden             | No                   | Yes, requiring RRT | No                   | Yes, for elevated D-dimer     | Yes                           | Dead                         |
| 6      | M/40    | Hispanic or Latino | Glans penis                                                                       | 28                                                               | 12 days, Foley catheter                                                   | 2,746                                                   | None                        | Yes, identified 12 days after skin lesions | No                   | No                   | Yes, for DVT         | Yes                           | Yes                           | Alive – not hospitalized       |
| 7      | M/45    | Hispanic or Latino | Posterior ear, trunk, extremities, peri-orbital                                      | 2                                                                | 2 days, nasal cannula                                                      | 2,977                                                   | None                        | No                   | No                   | No                   | Yes, for elevated D-dimer     | No                            | Alive – not hospitalized        |
| 8      | M/56    | White      | L index finger, forearm, sacrum                                                     | 19                                                               | No known inciting factor                                                    | 2,223                                                   | None                        | Yes, identified 4 days prior to skin lesions | Yes, not requiring RRT | No                   | Yes, for DVT         | Yes                           | Yes                           | Alive – hospitalized           |
| 9      | M/79    | Hispanic or Latino | Upper cutaneous lip                                                               | 14                                                               | 12 days, intubation                                                         | -                                                       | Antiphospholipid syndrome | No                   | No                   | No                   | Yes – STEMI                  | Yes                           | Alive – not hospitalized       |
| 10     | M/43    | Hispanic or Latino | Upper and lower vermilion lips                                                     | 29                                                               | 24 days, intubation                                                         | 1,071                                                   | Antiphospholipid syndrome | No                   | No                   | No                   | Yes, requiring RRT           | No                            | Yes                           |
| 11     | M/55    | Hispanic or Latino | L ear, L cheek                                                                    | 33                                                               | 30 days, intubation                                                         | 2,866                                                   | None                        | No                   | Yes, requiring RRT | No                   | Yes, for elevated D-dimer     | Yes                           | Dead                          |
| 12     | M/35    | White      | Soles of feet                                                                      | 30                                                               | No known inciting factor                                                    | 410                                                     | None                        | No                   | No                   | No                   | Yes, for elevated D-dimer     | Yes                           | Alive – not hospitalized       |
| 13     | M/25    | Hispanic or Latino | L ear                                                                            | 33                                                               | Unknown, ear pulse oximeter                                                | 1,158                                                   | None                        | No                   | Yes, requiring RRT | No                   | Yes, for elevated D-dimer     | Yes                           | Alive – hospitalized           |
| Number | Sex/Age | Race      | Location of lesions                                                                 | Time of hospital admission to identification of lesions (days) | Time between possible inciting factor and onset of lesions, inciting factor | D-Dimer at time lesions noted (ng/mL, ref range <230) | Known history of coagulopathy | Deep vein thrombosis | Acute kidney injury | Arterial thrombus | Therapeutic anticoagulation | Invasive mechanical ventilation | Patient status at last encounter |
|--------|---------|-----------|-------------------------------------------------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------------------------|------------------------------------------------------|--------------------------------|----------------------|---------------------|------------------|------------------------|-----------------------------|----------------------------------|
| 14     | M/65    | White     | Bilateral cheeks, buttocks, sacrum                                                   | 12                                                              | 5 days, intubation                                                         | 533                                                  | None                              | No                   | Yes, not requiring RRT | No                | No                     | Yes                         | Alive – hospitalized            |
| 15     | M/49    | White     | R ear, sacrum                                                                         | 7                                                               | Unknown, ear pulse oximeter                                               | 744                                                  | None                              | No                   | Yes, not requiring RRT | No                | Yes, for elevated D-dimer   | Yes                         | Alive – not hospitalized         |
| 16     | F/63    | White     | Upper and lower vermilion and cutaneous lip, columella, chin, nasal tip              | 4                                                               | 3 days, intubation                                                         | 349                                                  | None                              | No                   | Yes, not requiring RRT | No                | Yes, for elevated D-dimer   | Yes                         | Alive – not hospitalized         |
| 17     | M/48    | Black     | R ear, inferior vermilion lip, glans penis, sacrum                                   | 30                                                              | Unknown, ear pulse oximeter                                               | >10,000                                               | None                              | No                   | Yes, requiring RRT   | No                | Yes, for atrial fibrillation | Yes                         | Alive – hospitalized            |
| 18     | M/56    | Black     | Nose, chin, sacrum                                                                    | 23                                                              | 22 days, intubation                                                       | 2,813                                                 | None                              | No                   | Yes, not requiring RRT | No                | Yes, for elevated D-dimer   | Yes                         | Alive – not hospitalized         |
| 19     | M/49    | Hispanic or Latino                      | Columella, superior vermilion lip, L cheek                                       | 24                                                              | 14 days, intubation                                                       | 1,725                                                 | None                              | No                   | Yes, not requiring RRT | No                | Yes, for elevated D-dimer   | No                          | Dead                           |
| 20     | M/64    | White     | Chin, neck, bilateral arms, heels                                                    | 6                                                               | 6 days, intubation                                                        | 2,537                                                 | None                              | Yes, identified 21 days after skin lesions | No                   | Yes, not requiring RRT | No                | Yes, for atrial fibrillation/ DVT | Yes                         | Alive – not hospitalized         |
| 21     | M/77    | Hispanic or Latino                       | Bilateral cheeks, upper cutaneous lip, nares, sacrum                              | 23                                                              | 23 days, intubation                                                       | 3,068                                                 | None                              | No                   | Yes, not requiring RRT | No                | Yes, for elevated D-dimer   | Yes                         | Alive – not hospitalized         |

F, female; M, male; L, left; R, right; RRT, renal replacement therapy; DVT, deep vein thrombosis; STEMI, ST-elevation myocardial infarction.
Theodora K. Karagounis and Katharina S. Shaw contributed equally to this manuscript.

IRB approval status: Reviewed and approved by NYU Langone Health IRB.

doi: 10.1111/ijd.15181

References

1 Cui S, Chen S, Li X, et al. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost* 2020; **18**: 1421–1424.

2 Magro C, Mulvey JJ, Laurence J, et al. The differing pathophysiology that underlie COVID-19 associated perniosis and thrombotic retiform purpura: a case series. *Br J Dermatol* 2020. (Epub ahead of print). https://doi.org/10.1111/bjd.19415

3 Freeman EE, McMahon DE, Lipoff JB, et al. The spectrum of COVID-19-associated dermatologic manifestations: an international registry of 716 patients from 31 countries. *J Am Acad Dermatol* 2020. https://doi.org/10.1016/j.jaad.2020.06.1016. (Epub ahead of print).

4 Su H, Yang M, Wan C, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney Int* 2020; **98**: 219–227.

5 Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020; **323**: 1574–1581.

Figure 1 Examples of purpuric and necrotic lesions in severely ill patients with COVID-19 – (a) purpura, erosion, and eschar on cheeks and upper cutaneous lip in areas of skin contact with endotracheal tube holder, (b) retiform purpura on ear in area of skin in contact with pulse oximeter, (c) purpuric and necrotic lesion on the chin, (d) sacral purpura.