

### Conflict of interest

Dr. Neri, Dr. Guglielmo, Dr. Viridi, Dr. Gaspari, Dr. Starace and Dr. Piraccini have nothing to disclose.

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## Introductory histopathological findings may shed light on COVID-19 paediatric hyperinflammatory shock syndrome

### Editor

The full clinical spectrum of SARS-CoV-2 disease (COVID-19) is not fully known.

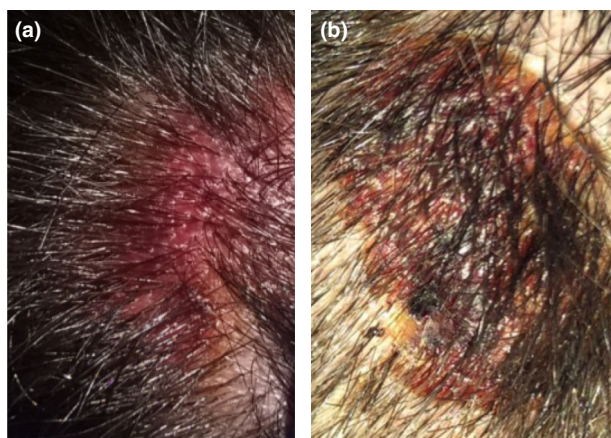
Numerous paediatric cases of hyperinflammatory shock syndrome (demonstrating features reminiscent of Kawasaki vasculitis) were recently associated with infection by COVID-19. Clinical presentation includes unrelenting fever, variable rash, conjunctivitis and abdominal pain, progressing to haemodynamic shock with severe myocardial involvement.<sup>1</sup> Recent report from Italy reported a 30-time increase in the rate of Kawasaki-like presentation during the COVID-19 pandemic among

children. In many cases, the nasopharyngeal swabs taken from these children were negative for COVID-19, and the association with COVID-19 infection is unclear.<sup>2</sup>

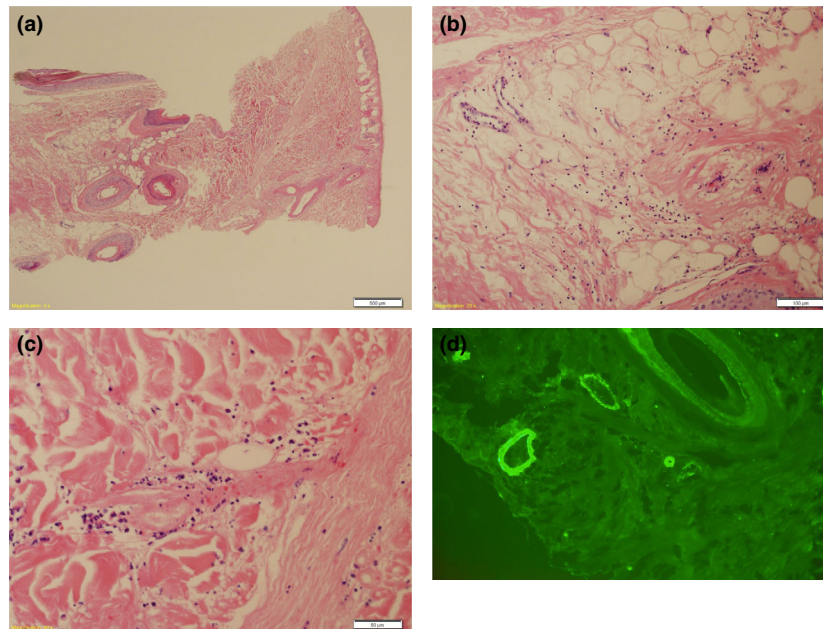
We hereby present an adolescent who developed distinctive scalp cutaneous lesions as part of COVID-19 hyperinflammatory shock syndrome.

A 16-year-old boy with unremarkable medical history was admitted due to 3-day history of severe abdominal pain and fever. A migratory rash composed of mildly oedematous and erythematous plaques was noted on the trunk and extremities. Echocardiography demonstrated impaired left ventricular function with dilatation. Laboratory workup revealed significant lymphopenia (up to 200 cells/ $\mu$ L) with mild neutrophilia, elevated creatinine levels (up to 2.65 mg/dL), elevated levels of C-reactive protein (up to 33.5 mg/dL) and D-dimer (1.61 mg/dL). Ferritin, fibrinogen and triglycerides' levels were mildly elevated. Empiric antibiotic treatment was initiated with no improvement. Expediently, the patient developed multiorgan dysfunction including cardiac failure requiring mechanical ventilation and inotropic support. High-dose intravenous methylprednisolone therapy was initiated, and the patient regained normal cardiopulmonary and renal functions. Extensive investigations failed to disclose an inflammatory or infectious aetiology, including repeated RT-PCRs for SARS-CoV-2 of nasopharyngeal, stool and bronchoalveolar lavage specimens. However, two serologic tests were positive for SARS-CoV-2 IgG.

Soon after cardiopulmonary stabilization was attained, two painful dusky erythematous plaques were noted over the posterior scalp (Fig. 1). A 3-millimetre punch skin biopsy revealed findings consistent with leukocytoclastic vasculitis including necrosis of the epidermis and most of the dermis with extravasation of erythrocytes and fibrin thrombi in the capillaries, as well as infiltration of neutrophils with nuclear debris in vessels' walls (Fig. 2). Direct immunofluorescence demonstrated deposition



**Figure 1** (a) Erythematous violaceous plaque over the posterior scalp, (b) hyperpigmented plaque with crusts over the posterior scalp, 5 days following the initial examination.



**Figure 2** (a) Extensive epidermal and dermal necrosis with thrombi in vessels (H&E  $\times$  40). (b) Neutrophils and fibrinoid thrombi in vessels' walls (H&E  $\times$  200). (c) Neutrophilic infiltration and nuclear debris surrounding the vessels (H&E  $\times$  400). (d) Direct immunofluorescence showing deposition of C3 in a vascular pattern in small size arterioles in the deep dermis.

of C3 and IgA in a vascular pattern. RT-PCR from affected tissue was negative for SARS-CoV-2, indicating an immune reaction rather than direct pathogen involvement.

The clinical course, as well as positive serology tests in our patient, is consistent with COVID-19-associated Kawasaki-like shock syndrome. To the best of our knowledge, this is the first report of histopathological findings in this novel paediatric disorder.

Multiple skin phenomena related to COVID-19 have been described, including maculopapular and vesicular eruptions, urticaria and chilblains.<sup>3</sup> Livedo reticularis or skin necrosis limited to the extremities has been correlated with more severe cases.<sup>4</sup> Non-specific rashes have also been described in COVID-19 Kawasaki-like shock syndrome<sup>1</sup>, but none has been studied meticulously and histologic data have not been given so far, although advocated repeatedly.<sup>5,6</sup>

Cutaneous leukocytoclastic lesions are typically seen in a symmetric distribution on the extremities and trunk, a manifestation previously reported in a COVID-19 patient.<sup>7</sup> Location only to the scalp is very unusual and has been rarely reported, such as in limited granulomatosis with polyangiitis.<sup>8</sup>


The pathological findings reported here may shed light on the yet unknown pathogenesis of the hyperinflammatory shock syndrome associated with COVID-19. The presence of IgA- and complement-mediated vasculitis with extensive necrosis may represent similar pathological abnormalities in affected internal organs and may be a key factor of understanding this novel disease.

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### Conflict of interests

The authors have no conflicts of interest to disclose.

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Authors have not published, posted or submitted any related papers from the same study.

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## Cutaneous autoimmune diseases during COVID-19 pandemic

### Editor

The pandemic of infection with the severe acute respiratory syndrome coronavirus (SARS-CoV-2) causing the atypical pneumonia coronavirus disease 19 (COVID-2019) has become a global health emergency. In parallel with the spread of the infection, there is new information on cutaneous involvement reminiscent to autoimmune diseases and concerns about the risk of disease

and management of patients with cutaneous autoimmunity under immunosuppression.

COVID-2019 mainly presents with fever, cough, loss of smell and taste, myalgia and fatigue.<sup>1</sup> Main complication of the infection is progression to acute respiratory distress syndrome (ARDS), coagulopathy, vasculopathy, cardiovascular failure and a cytokine storm syndrome requiring intensive care for days or even weeks.<sup>1,2</sup>

The risk factors for more severe COVID-19 infection are cardiovascular illnesses, diabetics, renal failure, respiratory failure, morbid obesity and older age (>65).<sup>3,4</sup>

Cutaneous symptoms of COVID-19 include petechial skin rash<sup>5,6</sup> or digitate scaly thin plaques<sup>7</sup> associated with severe respiratory disease (Table 1). A maculopapular urticarial rash may present as early sign of disease<sup>8–10</sup> or during disease<sup>11</sup> without a yet known association to severity.<sup>12,13</sup> There was also a case of pityriasis rosea like rash in one patient with mild febrile COVID-19.<sup>14</sup> In young children, infection with SARS-CoV-2 can be associated with Kawasaki syndrome including the maculopapular oedematous rash and conjunctival injection.<sup>15,16</sup>

Mild forms of disease in younger individuals seem to present with chilblain-like lesions on acral locations especially the toes<sup>17</sup> (Table 1). The skin appears shiny red and is painful (Fig. 1). The lesions resolve spontaneously after weeks and indicate a rather favourable outcome.<sup>17</sup> The symptoms may represent a form of inflammation induced by small vessel endotheliitis.<sup>17</sup> In histological section, these lesions may have a slight vacuolar

**Table 1** Cutaneous lesions associated with COVID-19

Cutaneous findings	Histopathology	COVID-19	Reference
Acral chilblain lesions	Vacuolar interface dermatitis and superficial and deep perivascular and periadnexal lymphohistiocytic infiltrates	Mild or none, late symptom	17–19,21,27
Violaceous papules and digital swelling	Diffuse perivascular involvement of the dermis and hypodermis by a dense lymphoid infiltrate	Mild or none, late symptom	20
Symmetrical petechial skin rash on buttocks, thighs that might be similar to dengue virus exanthema	Superficial perivascular infiltrate with erythrocyte extravasation, dermal papillary oedema, and scattered dyskeratotic keratinocytes	Associated with severe acute respiratory syndrome	5,6
Digitate scaly thin plaques	Spongiosis in the epidermis and mild papillary oedema with lymphohistiocytic infiltrate in the dermis	Associated with severe acute respiratory syndrome	7
Erythematous and oedematous non-pruritic annular fixed plaques involving the upper limbs, chest, neck, abdomen and palms	Superficial perivascular lymphocytic infiltrate, papillary dermal oedema, mild spongiosis, lichenoid and vacuolar interface dermatitis, dyskeratotic basilar keratinocytes	Mild	9
Maculopapular and urticarial rash		Early symptom	8,10
Maculopapular symmetrical rash	Superficial perivascular lymphocytic infiltrate, papillary dermal oedema, ectatic vessels, vacuolar interface dermatitis <sup>14</sup>	Mild, associated mild lung disease	11,13
Maculopapular rash in young children		Kawasaki syndrome associated with COVID-19	15
Pityriasis rosea		Mild	14