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LETTER TO THE EDITOR

Case reports of annular erythema: A diagnostic clue of multisystem inflammatory syndrome in children related to coronavirus disease 2019?

Dear Editor,

Contrary to adults, in children severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is mostly pauci-asymptomatic. Nevertheless, outbreaks of pediatric multisystemic illness overlapping with Kawasaki disease (KD) or KD-like have been described in pandemic areas, defining a new entity: multisystem inflammatory syndrome in children (MIS-C).[1] We observed two children with clinical and laboratory features of MIS-C, a direct link with SARS-CoV-2 infection, the same peculiar annular erythema, and histological lesions consistent with perivascular dermatitis.

A 6-year-old Caucasian boy was hospitalized for pneumonia with fever, vomiting, and annular erythematous lesions on the back and limbs, sparing hands and feet (Figure 1a). Skin biopsy showed a superficial perivascular dermatitis with edema, increased number of extremely dilated venules, no substantial differences between peripheral and central areas excepting a main mixed inflammatory infiltrate (lymphocytes and rare eosinophils) at the border of elements, and normal epidermis with basket-woven orthokeratosis. (Figure 1b–d). Two days later, he developed myocarditis with respiratory distress and shock, elevated cardiac enzymes, T-wave inversion on electrocardiography, and mild left ventricular dysfunction on echocardiography. Besides inotropic support, immunomodulatory therapy with i.v. immunoglobulin G (IVIG) was added, with global improvement and fading of skin lesions. History-taking revealed a strict coronavirus disease 2019 (COVID-19) contact 15 days prior, and his oropharyngeal swab and serology were positive for SARS-CoV-2.

Another 11-year-old Caucasian boy was hospitalized for fever, conjunctival hyperemia, and annular erythematous rash with fixed non-itchy, non-painful lesions on the hands' palmar surface and the right thigh (Figure 1e). Given a slightly elevated antistreptolysin O titer (ASO), suspecting an atypical acute rheumatic fever (ARF), a cardiac ultrasound was performed, showing normal coronary arteries and mild–moderate mitral and aortic valve regurgitation. Steroid therapy was started with rapid resolution of fever and valve regurgitations. The cutaneous rash disappeared after 3 weeks. ASO did not increase, excluding ARF. Despite a negative nasopharyngeal swab at

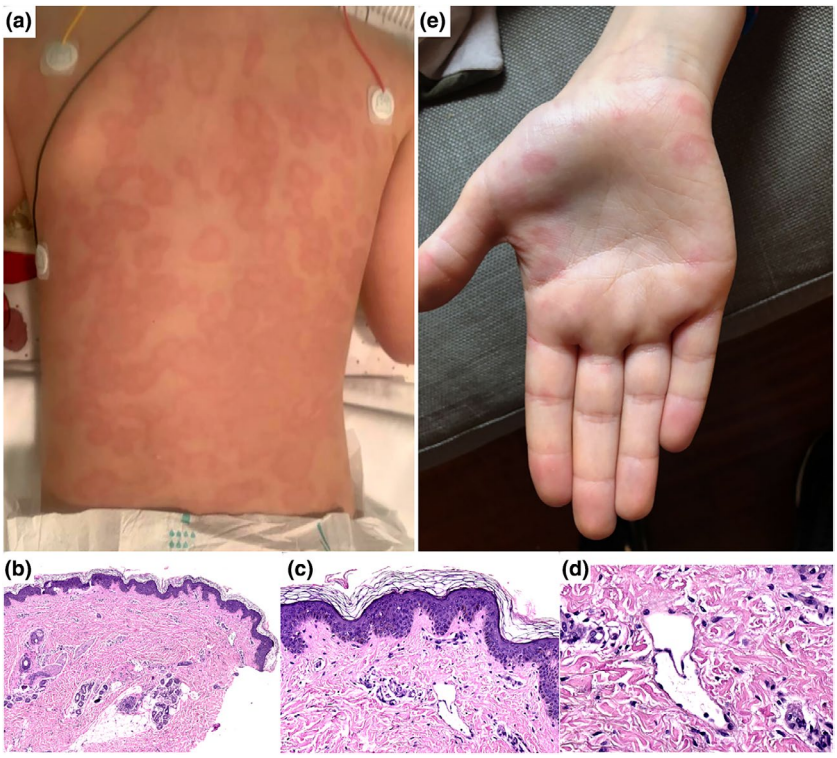

FIGURE 1 (a) The annular and erythematous lesions with central clearing of case 1, located on the back and limbs with sparing of hands and feet. (b) Superficial perivascular and interstitial dermatitis (hematoxylin–eosin [HE], original magnification ×4). (c) Proliferation of thin-walled vessels of swollen endothelial cells with the underlying basement membrane and jagged outlines (HE, ×13). (d) Edema, scant and perivascular infiltrates of lymphocytes, and rare eosinophils in the papillary and mid-dermis (HE, ×30). (e) The right hand of case 2 with annular erythematous lesions, fixed and asymptomatic, on the palmar surface

hospitalization, serology showed positive SARS-CoV-2 IgG. Notably, the father had presented an influenza-like illness 3 weeks before and had identical serology. The diagnosis was reconsidered as MIS-C.

Interestingly, both patients showed the same rash (not erythema multiforme, consisting of fixed macules with dusky central discoloration, but annular erythema, with polycyclic lesions with central clearing, as in our cases). Dermatological involvement in MIS-C has been reported in approximately 60% of cases, but poorly described, mainly as "maculopapular rash", although some published pictures of skin lesions are very similar to ours, suggesting that this could be a recurrent pattern in MIS-C. To date, given the paucity of well-detailed skin lesions, no correlation is known about this pattern and the prognosis of MIS-C.[1,2] The shorter duration of cutaneous manifestations in case 1, who received IVIG, may be related to the hypothesized superantigenic activity of SARS-CoV-2 S glycoprotein, comparable to other antigen targets of IVIG antibodies.[3]

The few published cases of MIS-C maculopapular eruptions' skin biopsies show perivascular dermatitis with lymphocytic infiltrate and vasculitis. Our findings seem to support what was previously hypothesized: cutaneous manifestations, just as visceral involvement, may depend not only on the direct effect of viral injury, but also on the immune responses and cytokine storm secondary to infection.[4,5]

CONFLICT OF INTEREST

None declared.

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