

## Re: Leukocytoclastic Vasculitis A peculiar presentation of scrub typhus

Dear Editor,

We read with interest the recent report of Vasireddy *et al.* about leukocytoclastic vasculitis (LV) associated with a Scrub typhus infection affecting a 28-year-old male, who presented with multiple, palpable purpuric eruptions mainly on the lower extremities.<sup>1</sup> The routine laboratory determinations were unremarkable and blood specific tests for autoimmune disorders, as well as malaria and bacterial and viral infections were negative; except for the Weil Felix test that was positive with a titre over 1:640 against OXK. Biopsy study of skin lesion showed the dermis with vasculo-centric infiltrate, and vessel walls with fibrinoid necrosis and dense infiltration by neutrophils, and leukocytoclasia. The final confirmed diagnosis was of LV, an uncommon manifestation of the *Orientia tsutsugamushi* infection, which is a zoonosis naturally transmitted by mite bites. Undergoing antimicrobial schedule of doxycycline, the patient improved in three weeks.<sup>1</sup> In fact, the authors emphasised the major infectious causes of leukocytoclastic vasculitis; but in the current global scenario one could include COVID-19 among the aetiologies.<sup>2–5</sup>

Capoferri *et al.* described a 93-year-old man who had COVID-19 infection and eight days later presented LV evolving with extensive skin necrosis in the lower extremities.<sup>2</sup> The lesions were erythematous and purpuric macules, hemorrhagic papules, and blisters. Skin biopsy study revealed the classic features of LV that was treated with corticosteroids. He evolved with dry gangrene of both legs and feet and declined the amputations; being discharged one month later, he died seven weeks after the initial diagnosis of COVID-19. The unfavorable evolution at least in part was due to risk factors including older age, arterial hypertension, peripheral artery disease and a heterozygous Factor V Leiden mutation.<sup>2</sup> Corrà *et al.* reviewed 19 cases with histological confirmation of LV, 68.4% were male with a median age of 48.4 (range: 13–93) years; three patients had diagnosis of IgA vasculitis, five had diagnosis of urticarial vasculitis and the 11 others were considered as LV.<sup>3</sup> Palpable purpura (with or without necrosis and haemorrhagic blistering) was the predominant manifestation; the commonest affected areas were the lower limbs and the trunk.<sup>3</sup> The span of time from the COVID-19 infection to the appearance of the skin rash ranged from concomitant until more than 30 days after the first positive nasopharyngeal swab. It is noteworthy that the SARS-CoV-2 was found in the vessel wall in three cases by polymerase chain reaction, supporting the direct virus role in the pathogenesis of cutaneous vasculitis.<sup>3</sup> After vaccination, 39 cases had vasculitis, 61.5% were female with a mean age of 53.2 (range: 22–94) years; the predominant manifestation was purpuric papules or maculae in the lower extremities. Direct immunofluorescence was not cited in 21 cases, and in five was negative; among the remaining 13 cases, five cases were of IgA vasculitis and three of vasculitis with C3 deposition.<sup>3</sup> Kutlu *et al.* compared 198 people (111 patients with COVID-19 and 87 age and sex-matched patients with other diseases) regarding the common dermatologic comorbidities.<sup>4</sup> In the COVID-19 group, the most common entities were pruritus (8.1%), eczema (6.3%), infections (3.6%), LV (1.8%) and urticaria (0.9%); while in the control group there were infections (9.2%), eczema (3.4%), pruritus (2.3%), urticaria (1.1%) and none of patients had LV; the findings showed that pruritus and LV are more common in severe COVID-19 cases.<sup>4</sup> The authors also emphasised the pathogenic mechanism of Th1 cells hyperactivation to produce interleukin (IL) 6, IL 2, and TNF- $\alpha$  is a major cause of death in severe COVID-19 cases.<sup>4</sup> Wong *et al.* reviewed nine cases of vasculitis secondary to COVID-19, with mean age of  $29.17 \pm 28.2$  years (range: six months to 83 years) and male to female ratio of 4:5.<sup>5</sup> The most common lesions were maculopapular, violaceous, popular and erythematous rash. The patients utilised heparin (n = 2), methylprednisolone (n = 6) and intravenous immunoglobulin (n = 4) showing significant improvement in 89% of patients. A seven-year-old patient who died due to hypoxia was the unique death in the studied group.

The high-quality report of Vasireddy *et al.* is really very useful, including for physicians out of the “tsutsugamushi triangle” who can have diagnostic challenges to care of infected travelers. Nevertheless, the current pandemic may be also included in the role of the LV differential diagnosis, because an earliest diagnosis will allow better outcomes. We strongly believe that descriptions of case studies may enhance the suspicion index about uncommon conditions, which favours prompt diagnosis and adequate management.

## AUTHORS' CONTRIBUTION

VMS and TAMS drafted the manuscript. VMS and TAMS reviewed the literature and performed the critical revision of the manuscript. All authors approved the final version of the manuscript.

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