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Re: Leukocytoclastic Vasculitis

A peculiar presentation of scrub typhus

Dear Editor,

We read with interest the recent report of Vasireddy A *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.[1] 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 titer over than 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 leukocytoclasis. 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.[1] In fact, the authors emphasized the major infectious causes of leukocytoclastic vasculitis; but in the current global scenario one could include COVID-19 among the etiologies.[2-5]

Capoferri G *et al*.[2] described a 93-year-old man who had COVID-19 infection and 8 days later presented LV evolving with extensive skin necrosis in the lower extremities. 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 risk factors including older age, arterial hypertension, peripheral artery disease, and a heterozygous Factor V Leiden mutation[2] Corrà A et *al*.[3] reviewed 19 cases with histological

confirmation of LV, 68.4% males, median age of 48.4 (13-93) years; 3 patients had diagnosis of IgA vasculitis, 5 had diagnosis of urticarial vasculitis, and the 11 others were considered as LV. Palpable purpura (with or without necrosis and hemorrhagic blistering) was the predominant manifestation; and the commonest affected areas were the lower limbs and the trunk.[3] 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. Worthy of note, the SARS-CoV-2 was found in the vessel wall in 3 cases by PCR technique, supporting the direct virus role in the pathogenesis of cutaneous vasculitis.[3] After vaccination, 39 cases had vasculitis, 61.5% women, mean age of 53.2 (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 5 was negative; among the remaining 13 cases, 5 cases were of IgA vasculitis and 3 of vasculitis with C3 deposition.[3] Kutlu Ö *et al*.[4] compared 198 people (111 patients with COVID-19 and 87 age and sex-matched patients with other diseases) regarding the common dermatologic comorbidities. In 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 control group 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.[4] The authors also emphasized the pathogenic mechanism of Th1 cells hyperactivation to produce IL 6, IL 2, and TNF-α is a major cause of death in severe COVID-19 cases.[4] Wong K *et al*.[5] reviewed 9 cases of vasculitis secondary to COVID-19, with mean age of 29.17 ± 28.2 years, age range from 6 months to 83 years, and male to female ratio of 4:5. Most common lesions were maculopapular, violaceous, popular, and erythematous rash. The patients utilized heparin (n = 2), methylprednisolone (n = 6), and intravenous immunoglobulin (n = 4); and significant improvement was obtained in 89% of patients. A 7-year-old patient who died due to hypoxia was the unique death in the studied group.

The high-quality report of Vasireddy A *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 roll 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 favors 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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