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# Leukocytoclastic vasculitis following coronavirus disease 2019 (COVID-19): A case report

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## ABSTRACT

Leukocytoclastic vasculitis (LCV) refers to the histopathological changes observed in a common form of small vessel vasculitis that can affect skin and/or internal organs. LCV can be precipitated by several causes (including infections, drugs, and collagen vascular diseases) or can be idiopathic. We report a 50-year-old man who presented with fever, parotid enlargement and skin rash (discrete and confluent erythematous macules, papules, and plaques and a few purpuric lesions on the back of trunk and upper limbs), 3 weeks after being diagnosed with coronavirus disease 2019 (COVID-19). The patient showed four out of the five features required to satisfy the working case definition of multisystem inflammatory syndrome in adults (MIS-A). Histopathology of rash was consistent with LCV. Whether, COVID-19 was the cause for LCV in our patient remains unclear. The fever, parotid enlargement and rash showed complete resolution following treatment with systemic corticosteroids and enoxaparin.

**Keywords:** Coronavirus disease-2019, Multisystem inflammatory syndrome in adults, Skin rash, Leukocytoclastic vasculitis, Histopathology

## INTRODUCTION

Cutaneous manifestations are not uncommon in coronavirus disease 2019 (COVID-19) and are widely variable. The skin lesions may precede, coexist, or succeed COVID-19.[1,2] Here, we report a man who manifested rash of leukocytoclastic vasculitis (LCV) following COVID-19.,

## CASE REPORT

A 50-year-old man presented with fever of 4 days and asymptomatic cutaneous rash of 2 days duration. He received cefixime 200 mg twice a day from a nearby hospital for fever. After the third dose of cefixime, the rash appeared on the trunk and limbs. He stopped the drug but subsequently developed bilateral conjunctival congestion and pain and swelling of both parotid glands. He did not manifest cough, breathlessness, chest pain, diarrhea, vomiting, edema of lower limb, or pain of lower limb.

He received a diagnosis of COVID-19 (reverse transcription polymerase chain reaction) 3 weeks before the onset of the present illness. The only drug he received was acetaminophen 500 mg 3 times a day per orally for 2 days. Ten days later, he tested negative for COVID-19 on rapid antigen test.

His medication history included aspirin (150 mg)-clopidogrel (75 mg) combination once daily (following cerebrovascular thrombosis), amlodipine 5 mg daily, atorvastatin 40 mg daily, and

metformin 500 mg twice a day (for diabetes mellitus). He was on these medicines since 11 months.

The patient was febrile (40°C), pulse and respiratory rates were 116/minute and 26/minute, respectively, and blood pressure was 112/70 mm of mercury. Oxygen saturation was 100% on room air. Dermatologic examination showed discrete and confluent erythematous macules, papules, plaques and a few purpuric lesions on the back of trunk [Figure 1a] and upper limbs with sparing of lower limbs, palms, and oral cavity. Other findings were bilateral conjunctival congestion [Figure 1b], erythema, edema, and tenderness of parotid glands [Figure 1c] on both sides, hepatomegaly and left-sided hemiparesis (which was persisting since the cerebrovascular accident).

Apart from the mild elevation of liver transaminases (alanine transaminase 40 IU/ml and aspartate transaminase 55 IU/ml) and prolongation of prothrombin time (15 seconds) and international normalized ratio (1.28) noted on liver function test, no other abnormality was detected in complete hemogram, urine microscopy, renal function test, serum electrolytes, blood and urine cultures, serum complement 3, thyroid function test, serum immunofluorescence test for antinuclear antibody, serology for dengue virus infection, and leptospirosis and chest radiography. Serum ferritin, D-dimer, and C-reactive protein (CRP) were 1253 ng/ml (upper limit of normal 300 ng/ml for men), 1 mg/l (upper limit of normal 0.5 mg/l), and 103.7 mg/l (upper limit of normal 10mg/l), respectively. Serum lactate dehydrogenase was elevated at 860 U/l. Serum triglyceride and fibrinogen levels were 200 mg/dl and 160 mg/dl, respectively. Ultrasonogram of abdomen confirmed the hepatomegaly. No significant abnormality was detected on cardiac evaluation. Throat swab and serology for ASO (antistreptolysin O titer) were not done.

Skin biopsy from a purpuric lesion on the back of the trunk showed small blood vessels in the dermis showing endothelial swelling, extravasated red blood cells, and perivascular inflammatory infiltrate of lymphocytes and neutrophils with occasional nuclear debri, consistent with LCV [Figure 2]. The patient was treated with dexamethasone 6 mg intravenously once a day, enoxaparin 40 units subcutaneously once daily (for 7 days) and doxycycline 100 mg twice daily (for 5 days) per orally. His regular medicines were continued. After 6 days of treatment, serum ferritin, D-dimer, and CRP reduced to 684 ng/ml, <0.05 mg/l, and 7.5 mg/l, respectively. After a week, the parenteral steroids were changed to oral corticosteroids and subsequently tapered and stopped over 14 days. Fever and parotid swelling subsided in 3 days. Rash resolved leaving a hyperpigmentation that attained normal skin color during the follow-up period of 1 month.

## DISCUSSION

Whether the LCV observed in our patient was associated with COVID-19 or not remains unclear. There are reports of LCV coexisting with or succeeding COVID-19 or following vaccination against COVID-19.[3-6] The different possibilities in our case were: COVID-19 acting as the infective trigger for LCV, LCV occurring as a manifestation of post COVID-19 hyper inflammatory syndrome, LCV induced by cefixime (taken for fever) or an idiopathic LCV following COVID-19.

Though we considered the possibility of Sweet's syndrome in view of fever, conjunctival congestion and lesions mainly affecting trunk and upper limbs, this seemed less likely since the skin lesions were asymptomatic and the patient did not show leukocytosis.

A working MIS-A (multisystem inflammatory syndrome in adults) case definition included five criteria as followed (after excluding patients with an alternative diagnosis like bacterial sepsis): A severe illness requiring hospitalization in a person aged ≥21 years, a positive test result for current or previous severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection during admission or in the previous 12 weeks, severe dysfunction of one or more extra-pulmonary organ systems, laboratory evidence of severe inflammation (elevated CRP, ferritin, D-dimer, or interleukin-6), and absence of severe respiratory illness. Our


**Figure 1:** (a) Discrete and confluent erythematous macules, papules, and plaques and a few purpuric lesions on the back of trunk of a patient, 3 weeks after diagnosis of coronavirus disease 2019; (b) Bilateral conjunctival congestion in the same patient; (c) same patient showing erythema and edema of parotid gland.

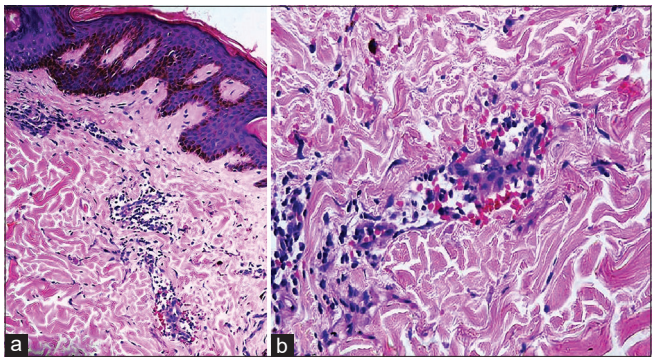


**Figure 2:** (a) Skin biopsy from a purpuric lesion on the back of trunk of a patient (the purpuric rash appeared 3 weeks after diagnosis of coronavirus disease 2019), showing small blood vessels in the dermis, extravasated red blood cells and perivascular inflammatory infiltrate with occasional nuclear debri (H and E, 100×); (b) higher magnification of the same showing endothelial swelling, extravasated red blood cells and perivascular inflammatory infiltrate of lymphocytes and neutrophils with occasional nuclear debri, consistent with leukocytoclastic vasculitis (H and E, 400×).

patient satisfied all except the criteria of severe dysfunction of one or more extra-pulmonary organ systems.[7] Whether MIS-A can present with variable severity and whether our patient represented a milder form of the condition remains unknown. The reported dermatologic manifestations in MIS-A include generalized maculopapular rash, transient palmar erythema, non-exudative, bilateral conjunctivitis, and mucositis.[3,7-10] Schnapp *et al*. reported a patient with MIS-C (MIS in children) who manifested LCV.[11]

The possibility of macrophage activation syndrome was less likely in our patient since the patient had recovered from COVID-19 and did not show any features of severe organ involvement (including severe pneumonia).[12]

The possibility of fever being a feature of LCV itself, (rather than that of MIS-A) cannot be ruled out. Whether the elevation noted in inflammatory markers was the declining phase from a higher level reached during COVID-19 also remains unclear since the serum levels of D-dimer, CRP, and ferritin, at the time of active infection were not available. Clinical findings in our case did not favor the possibility of a thrombotic episode as the cause for elevated D-dimer level. The presence and nature of immune deposits in our patient remain unknown since direct immunofluorescence analysis of skin lesion was not carried out.

In the absence of a drug re-challenge, we cannot rule out the possibility of LCV precipitated by cefixime in our patient. The previous authors have reported drug induced vasculitis manifesting as early as 1 day of drug intake.[13] The skin lesions appeared 36 hours after the intake of cefixime in our case. The persistence of symptoms despite discontinuation of cefixime (after 3 doses) was more in favor of an alternate etiology for LCV. It is suggested that an early withdrawal of the drug can attain complete recovery in drug induced vasculitis.[14]

The possibility of drug induced vasculitis by metformin, aspirin, clopidogrel, or amlodipine was unlikely in our case since the patient attained relief despite continuing all these drugs.

Previous authors have noted parotitis during COVID-19.[15-17] It is reported that the virus may gain entry since the gland shows expression of angiotensin converting enzyme 2 (identified as receptor for SARS-CoV-2).[17] Intra-parotid lymphadenitis has been cited as the reason for parotid swelling.[17] We cannot comment on the same in our case in the absence of imaging studies. Unlike the previous cases, where parotitis appeared during COVID-19, our patient manifested the same after recovery from the disease.[15-17] Whether the bilateral involvement of parotid glands (unilateral involvement in previous reports), favors the possibility of parotitis occurring as a manifestation of post COVID-19 hyper inflammatory syndrome in our case, remains unclear.

## CONCLUSION

With the surge in number of COVID-19 cases, we are seeing varying manifestations of the disease. More information through case reports and case series may help us to understand more about the pathogenesis of the disease, increase awareness about the manifestations (that can precede, coexist or succeed the disease), and improve the diagnostic definition of entities like MIS-A.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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