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LETTER

DERMATOLOGIC THERAPY WILEY

Possible association between IgA vasculitis and COVID-19

Dear Editor,

On 28 August 2020, a 22 years male developed fever, pain abdomen, vomiting, and painful swelling of both ankle and wrist joints. Two days later, he noticed multiple red raised lesions symmetrically over all extremeries. Nasopharyneal swab for Coronavirus disease 2019 (COVID-19) PCR testing was positive at admission. He had no respiratory symptoms. Examination revealed fever (100.8 °F), edema with tenderness over both wrist, hand and ankle joints. Cutaneous examination revealed multiple, discrete to confluent palpable purpura with few central vesicles distributed symmetrically over all extremities, gluteal region, and lower abdomen (Figure 1A-D). He denied history of any drug intake prior to onset of symptoms.

The patient was investigated on the lines of IgA vasculitis and systemic involvement of COVID-19. Urinalysis revealed a proteinuria of 2 g/day. Remaining investigations were as in Table 1. Skin biopsy from thigh lesion revealed features of leukocytoclastic vasculitis (Figure 2A,B). Direct immunofluorescence (DIF) from lesion was negative which could be due to biopsy from a lesion >48 h duration or sample processing error. PCR for SARS-CoV-2 from skin sample could not be done due to nonavailability. Because of the proteinuria, a kidney biopsy was done which showed features of focal necrotizing, mesangial, and focal endocapillary proliferative IgA nephropathy with mesangial granular deposits of IgA (Figure 3). Patient was promptly started on injection dexamethasone equivalent to 1 mg/kg of prednisolone for 10 days and shifted to oral prednisolone subsequently. Presence of poor prognostic findings on kidney biopsy with glomerular segmental tuft necrosis and cellular crescent formation prompted us to plan long-term immunosuppressants for at least three months duration. Hence, mycophenolate mofetil as steroid sparing agent was added to be continued for three months and oral prednisolone tapered off in one month. His cutaneous lesions, joint involvement and abdominal symptoms resolved, liver function tests, and urinalysis normalized over 2 weeks. The patient is under follow-up to look for long-term renal complications.

1 | DISCUSSION

Though lung involvement with alveolar damage and acute respiratory failure has been described as the hallmark presentation of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), further research has expanded its domain to other organs including kidney and skin where variable cutaneous manifestations including maculopapular exanthems, chilblain-like lesions, varicella-like eruptions, livedo reticularis, urticarial, erythema multiforme-like, and petechial lesions have been reported.[1] Recently, two cases have highlighted SARS-CoV-2 as a trigger for IgA vasculitis, one of which had renal involvement similar to index case.[2,3]

IgA vasculitis is a small vessel vasculitis owing to IgA immune complex deposits in skin and organs. It may be triggered by various micro-organisms including viruses.[4] Though, we cannot rule out the possibility that the IgA vasculitis is incidental in this patient and is independent in the setting of COVID-19, the presentation of symptoms with positive COVID-19 PCR points towards SARS-CoV-2 as trigger for IgA vasculitis here. SARS-CoV-2 induced endothelitis in various organs as a result of either virus directly invading the

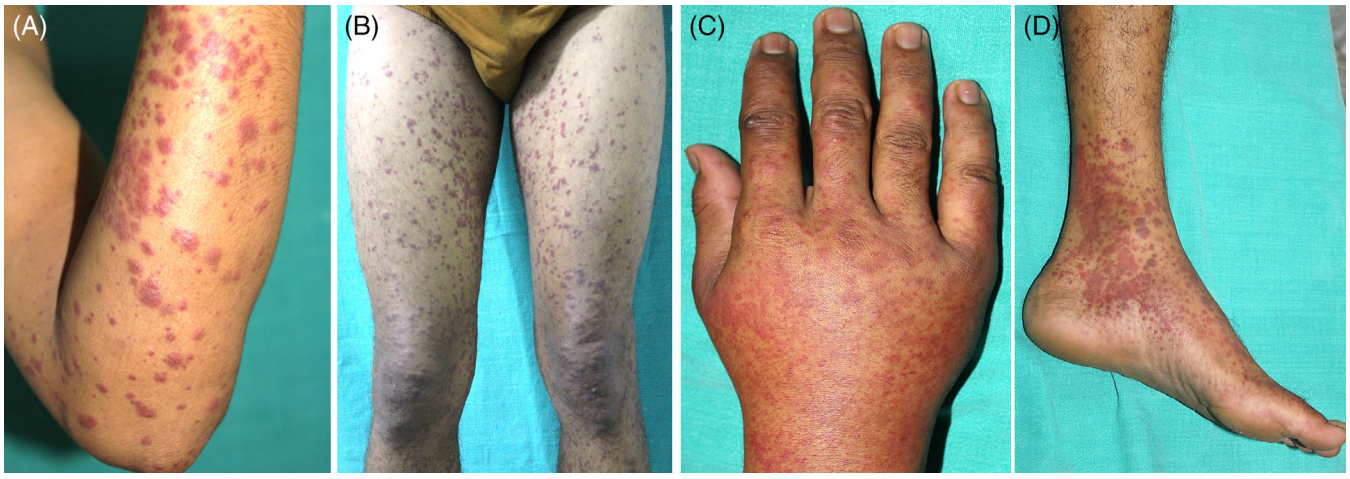

FIGURE 1 A,B, Multiple, discrete to confluent purpura seen over forearm, arm, and thighs. C,D, Edema over wrist, hand, and ankle also noted

TABLE 1 Initial laboratory parameters of the patient

Variables	Result	Variables	Result
Hemoglobin (g/dL)	13.2	Human Immunodeficiency Virus	Negative
Total leukocyte count (cells/μL)	4300	Hepatitis B surface antigen	Negative
Differential count (%)		Anti-hepatitis C virus	Negative
Neutrophils	54	EBV Viral capsid Antigen IgM	Negative
Lymphocyte	37	CMV IgM	Negative
Platelets (cells/μL)	1 78 000	Anti-Nuclear Antibody (ANA) by immunofluorescence	Negative
24 h urinary protein	2000 mg	ANA profile by immunoblot	Negative
Creatinine (mg/dL)	0.43	Anti-Neutrophilic Cytoplasmic Autoantibody (ANCA)	Negative
Sodium (mEq/L)	137	Perinuclear-ANCA	Negative
Potassium (mEq/L)	4.2	Cryoglobulins	Negative
Total bilirubin (mg/dl)	1.6	Complement levels (C3 and C4)	Within normal range
Aspartate aminotransferase (IU/L) (5-40)	62	Chest X-ray	No abnormality detected
Alanine aminotransferase (IU/L) (16-63)	122	Ultrasound abdomen	No abnormality detected
Alkaline phosphatase (U/L) (44-147)	108	Lactate dehydrogenase (U/L) (81-234)	236
Protein (g/dL) (5.7-8.2)	7.2	Creatine phosphokinase (U/L) (26-192)	46
Albumin (g/dL) (4.0-4.7)	4.4	Ferritin (ng/mL) (23-336)	145.7
Prothrombin Time (Control: 11.5 s)	11.7	d-Dimer ng/dL (0-200)	112
INR	1.01	Procalcitonin (ng/mL) (0-0.5)	0.02
Erythrocyte Sedimentation Rate (mm/1 h)	22		
C-Reactive Protein (mg/L)	Negative		

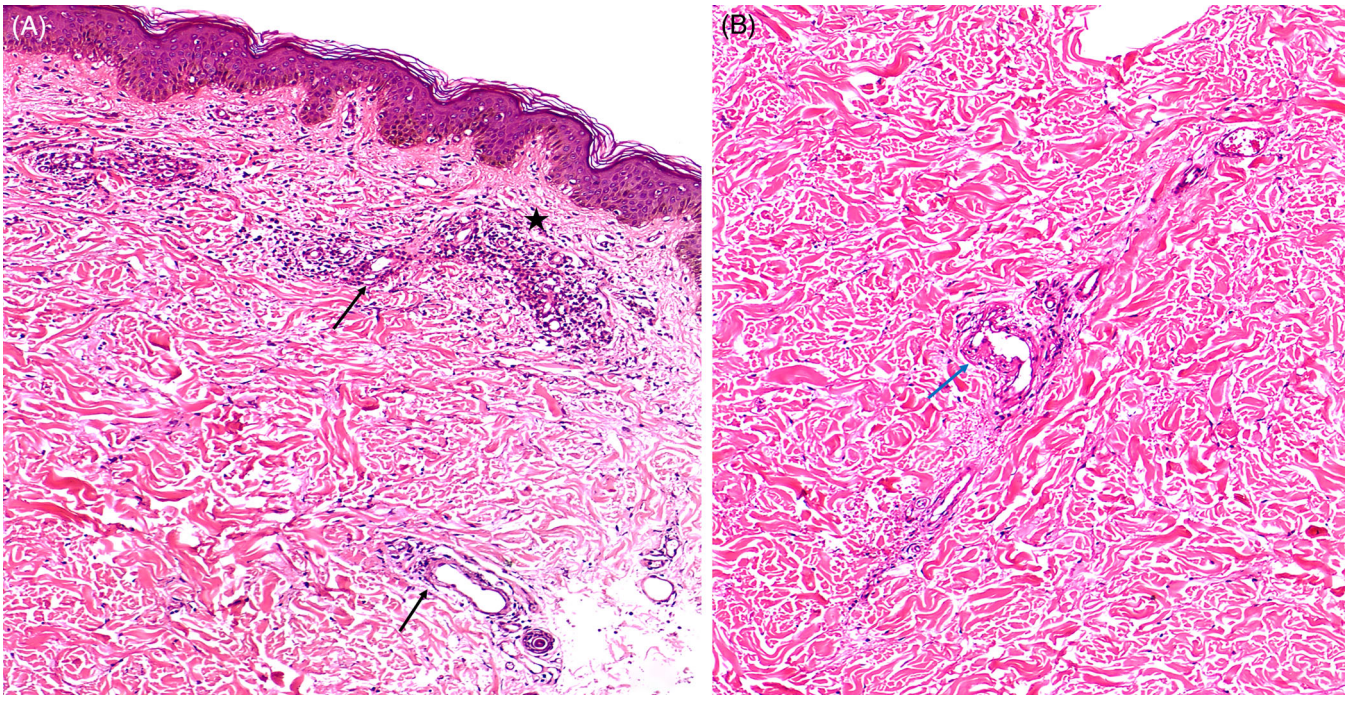

FIGURE 2 A, Histopathology was suggestive of leukocytoclastic vasculitis with features of plump endothelial cells (black arrow) with perivascular mixed inflammatory infiltrate comprising of neutrophils and lymphocytes and extravasation of RBCs in upper dermis (black star). B, Few capillaries show fibrinoid change of the vessel wall (blue arrow). (A: H&E, ×20 and B: H&E, ×80)

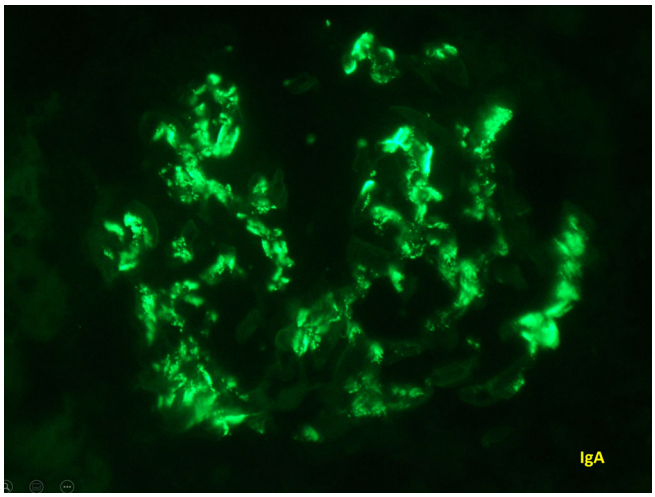

FIGURE 3 Kidney biopsy showed mesangial granular deposits of IgA

endothelial cells or because of inflammatory response has been suggested.[5]

Anti-SARS-CoV-2 IgA is the first immunoglobulin to be detected in COVID-19 as early as two days after onset while IgM and IgG seroconversion takes around 5 days.[6] A strong relationship has been suggested between chillblain-like lesions with possible vascular damage and COVID-19 based on detection of anti-SARS-COV-2 IgA and negative IgG in several cases.[7] Pathogenesis of IgA nephritis has been linked to increased levels of circulating form of IgA1 with aberrant glycosylation (Gd-IgA1) which forms circulating immune complexes with antigenic micro-organisms and subsequently gets deposited in the mesangium leading to kidney damage. Mucosal infections result in an upregulation of IL-6 as in COVID-19, which might trigger Gd-IgA1 development and subsequent renal damage.[8] This might explain the hypothesis of severe COVID-19 to be IgA mediated disease (related to IgA deposition and vasculitis) including IgA nephritis.[8] Patient here had severe kidney manifestation without evidence of respiratory manifestation which is being documented for the first time.

Kidney involvement ranges from proteinuria to acute kidney injury in COVID-19. Only one case had IgA deposits in the mesangium and capillary wall in a postmortem study of 26 patients of COVID-19.[9] Possible pathogenic mechanisms include direct renal infection owing to expression of ACE-2 receptors in tubular cells and podocytes and indirectly through "cytokine release syndrome" seen in COVID-19.[5]

Further research is required to delineate the role of SARS-CoV-2 in the pathogenesis of IgA vasculitis. This case highlights possible association of COVID-19 and IgA vasculitis where SARS-CoV-2 could be a trigger for it without any initial respiratory involvement.

The authors certify that they have obtained all appropriate patient consent forms for use of patient photographs and data obtained.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

The manuscript has been read and approved by all the authors. The requirements for authorship as stated earlier in this document have been met, and each author believes that the manuscript represents honest work.

DATA AVAILABILITY STATEMENT

The authors declare that data supporting the findings of this case are available within the article [and its supplementary information files].

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