COVID-19 associated immunoglobulin A vasculitis in an adult

Amanda M. Walker, BS, Ravi R. Patel, MD, Travis Vandergriff, MD, and Stephanie Savory, MD

Key words: COVID-19; Henoch-Schönlein purpura; IgA vasculitis; vasculitis.

INTRODUCTION

Immunoglobulin A (IgA) vasculitis is an immune complex mediated, small vessel vasculitis most often seen in children following upper respiratory or gastrointestinal infection. Herein, we report a case of IgA vasculitis and IgA nephropathy following COVID-19 infection in a previously healthy adult male.

CASE REPORT

A 39-year-old male with no significant past medical history presented to the Emergency Department (ED) with a persistent rash that began 8 days after receiving a positive COVID-19 antigen test. In the ED, the patient endorsed fever, cough, shortness of breath, diffuse arthralgias, nausea, vomiting, and upper abdominal pain. He denied hematuria or hematochezia. The patient was not on any medications or over the counter supplements at the time of admission, nor did he report any recent travel. On physical exam, he was found to have numerous nontender, purpuric papules covering the bilateral lower extremities, upper extremities, and lower trunk (Fig 1).

The patient was unvaccinated for COVID-19 at the time of presentation, and COVID-19 polymerase chain reaction test was positive. Additional labs at the time of ED admission were notable for elevated c-reactive protein (CRP, 4.4 mg/dL), erythrocyte sedimentation rate (20 mm/h), absolute neutrophil count (7.71 × 10^9/L), platelets (436 × 10^9/L), alanine transaminase (154 Units/L), and aspartate aminotransferase (99 Units/L). Urinalysis demonstrated subnephrotic range proteinuria (50 mg/dL). Two cutaneous biopsies were taken from the right upper extremity. Hematoxylin and eosin staining revealed an inflammatory infiltrate of lymphocytes, neutrophils with karyorrhexis, eosinophils, and extravasation of erythrocytes with fibrin deposition in the walls of small blood vessels. Direct immunofluorescence revealed granular deposits of IgA within papillary dermal blood vessel walls (Fig 2). Given the constellation of arthralgias, purpuric papules, abdominal pain, and histopathology, the patient was diagnosed with COVID-19 associated IgA leukocytoclastic vasculitis.[1]

Abbreviations used:

ALT:	Alanine transaminase
AST:	aspartate aminotransferase
CRP:	C-reactive protein
DIF:	direct immunofluorescence
ED:	Emergency Department
ESRD:	end-stage renal disease
ESR:	Erythrocyte sedimentation rate
EULAR/PRINTO/PRES:	European League Against Rheumatism/Paediatric Rheumatology International Trials Organisation/ Paediatric Rheumatology European Society
H&E:	Hematoxylin and eosin
HSP:	Henoch-Schönlein purpura
IgA:	Immunoglobulin A
PCR:	polymerase chain reaction

From the Department of Dermatology, University of Texas Southwestern Medical Center, Dallas, Texas.

Funding sources: None.

IRB approval status: Not applicable.

Declarations of interest: None.

Informed consent: Consent for the publication of all patient photographs and medical information was provided by the authors at the time of article submission to the journal stating that all patients gave consent for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available.

Correspondence to: Stephanie Savory, MD, Department of Dermatology, University of Texas Southwestern Medical Center, 5939 Harry Hines Blvd. Dallas, TX 75390-9069. E-mail: stephanie.savory@utsouthwestern.edu.

JAAD Case Reports 2022;30:35-7.

2352-5126

https://doi.org/10.1016/j.jdcr.2022.09.028

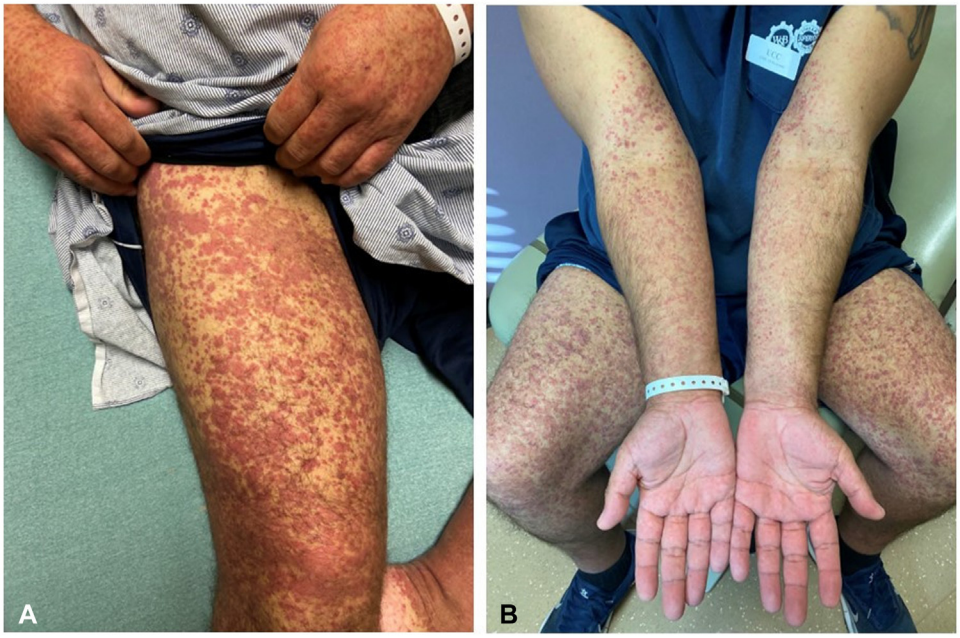

Fig 1. COVID-19 associated immunoglobulin A vasculitis. Erythematous-violaceous, non-blanchable papules coalescing into plaques. **A,** Right thigh and; (**B**) bilateral forearms and legs with sparing of the palms.

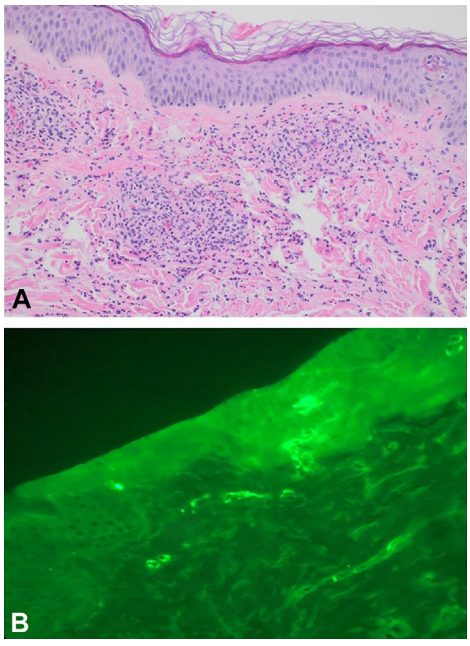

Fig 2. COVID-19 immunoglobulin A vasculitis skin biopsy findings. **A,** Punch biopsy of right arm stained with hematoxylin and eosin at 200× magnification. There is a perivascular infiltrate of lymphocytes, eosinophils, and neutrophils with leukocytoclasia with extravasation of erythrocytes and fibrin in the walls of small blood vessels. **B,** Punch biopsy of right arm stained with direct immunofluorescence at 200× magnification showing granular deposits of IgA within papillary dermal blood vessel walls.

At 1-month follow-up, patient noted resolution of all systemic and cutaneous findings, but reported new-onset hematuria. Repeat urinalysis demonstrated 3+ hematuria, 600 mg/dL protein, and a protein/creatinine ratio of 9.22. Serum creatinine was elevated at 2.6 mg/dL. Patient was referred to nephrology, and renal biopsy established a diagnosis of crescentic IgA nephropathy. He received treatment with methylprednisolone bridging to prednisone, and a total of 6 cyclophosphamide infusions. At the time of last clinic visit, patient continued to endorse clearance of all systemic and cutaneous symptoms. His creatinine and protein/creatinine ratio were steadily improving and approaching normal values.

DISCUSSION

IgA vasculitis is an immune complex-mediated vasculitis that classically presents with arthralgia, abdominal pain, and cutaneous purpura. Diagnosis is made through clinical symptoms, physical exam findings, and histopathological features. Although IgA vasculitis is frequently synonymous with Henoch-Schoenlein purpura (HSP), not all cases of IgA vasculitis meet criteria for HSP.[2] In 1990, the American College of Rheumatology developed guidelines to help differentiate HSP from other forms of systemic arteritis. Classification criteria for pediatric IgA vasculitis proposed in 2010 by the European League Against Rheumatism/Paediatric Rheumatology International

Table I. Classification criteria for immunoglobulin A vasculitis*

ACR classification criteria (1990)	EULAR/PRINTO/PRES classification criteria (2010)
Two of the following criteria: • Age ≤ 20 y • Palpable purpura • Acute abdominal pain • Biopsy showing granulocytes in the walls of the small arterioles or venules	• Purpura or petechiae AND • One of the following 4 criteria: - Abdominal pain - Arthritis or arthralgia - Renal involvement - Leucocytoclastic vasculitis with predominant IgA deposits or proliferative glomerulonephritis with predominant IgA deposits
Sensitivity 87.1%, Specificity 87.7%	Sensitivity 100%, specificity 87%

ACR, American College of Rheumatology; *EULAR/PRINTO/PRES*, European League Against Rheumatism/Paediatric Rheumatology International Trials Organisation/Paediatric Rheumatology European Society; *IgA*, immunoglobulin A.
*Table adapted from Hočevar et al.[1]

Trials Organisation/Paediatric Rheumatology European Society (EULAR/PRINTO/PRES) performed better than the older criteria established by the American College of Rheumatology. These guidelines, subsequently tested in an adult cohort, likewise demonstrated improved diagnostic sensitivity and specificity (Table I).[1] Applying the newer EULAR/PRINTO/PRES IgA vasculitis classification criteria, our patient meets criteria for IgA vasculitis given his abdominal pain, arthralgias, renal involvement, leukocytoclastic vasculitis with predominant IgA deposits, and palpable purpura.

HSP/IgA vasculitis is most frequently diagnosed in children after viral upper respiratory infections, including recent reports of HSP secondary to COVID-19 infection.[3] It is often self-resolving without lasting sequelae. However, adults with IgA vasculitis, regardless of COVID-19 status, are at increased risk of developing severe renal involvement, including permanent renal damage and progressive end-stage renal disease (ESRD).[4] In older adult patients, IgA vasculitis has also infrequently been a paraneoplastic syndrome related to lung and digestive cancers, or hematological malignancy. Presentation in this cohort may feature more necrotic purpura and/or alveolar hemorrhage, hematuria or high levels of serum IgA.[5]

COVID-19 has rarely been associated with new onset IgA vasculitis in adults, with even fewer cases reporting subsequent IgA nephropathy.[6] Five cases of COVID-19 associated IgA vasculitis (4 with renal sequalae) have been reported in adult patients to date, all of which were male.[6,7] A recent study showed that viral components of COVID-19 can induce endotheliitis and microvascular disruption in multiple organ systems, including the kidney.[8] Furthermore, it has been shown that COVID-19 can induce immune complex deposition in vascular beds by escalating a previously Th2 immune response to a type 3 hypersensitivity reaction.[9] Advanced age, male sex, and hypertension are all risk factors for endothelial injury that may make these patients more susceptible to IgA vasculitis by one or both of these mechanisms.

Herein we present a case of IgA vasculitis secondary to COVID-19 with subsequent development of IgA nephropathy in a previously healthy, middle-aged adult. Our case highlights the need for close monitoring of renal function in asymptomatic, adult patients with suspected IgA vasculitis, regardless of COVID-19 status.

The authors would like to thank the patient for allowing them to present his case as well as the Parkland Memorial Hospital Dermatology and Nephrology specialty teams.

Conflict of interest

None disclosed.

REFERENCES

1. Hočevar A, Rotar Z, Jurčić V, et al. IgA vasculitis in adults: the performance of the EULAR/PRINTO/PRES classification criteria in adults. *Arthritis Res Ther*. 2016;18:58.
2. Helander SD, De Castro FR, Gibson LE. Henoch-Schönlein purpura: clinicopathologic correlation of cutaneous vascular IgA deposits and the relationship to leukocytoclastic vasculitis. *Acta Derm Venereol*. 1995;75(2):125-129.
3. AlGhoozi DA, AlKhayyat HM. A child with Henoch-Schonlein purpura secondary to a COVID-19 infection. *BMJ Case Rep*. 2021;14(1):e239910.
4. Song Y, Huang X, Yu G, et al. Pathogenesis of IgA vasculitis: an up-to-date review. *Front Immunol*. 2021;12:771619.
5. Hankard A, Michot JM, Terrier B, et al. New insights on IgA vasculitis with underlying solid tumor: a nationwide French study of 30 patients. *Clin Rheumatol*. 2021;40(5):1933-1940.
6. Jedlowski PM, Jedlowski MF. Coronavirus disease 2019-associated immunoglobulin A vasculitis/Henoch-Schönlein purpura: a case report and review. *J Dermatol*. 2022;49(1):190-196.
7. Suso AS, Mon C, Oñate Alonso I, et al. IgA vasculitis with nephritis (Henoch-Schönlein purpura) in a COVID-19 patient. *Kidney Int Rep*. 2020;5(11):2074-2078.
8. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet*. 2020;395(10234):1417-1418.
9. Roncati L, Ligabue G, Fabbiani L, et al. Type 3 hypersensitivity in COVID-19 vasculitis. *Clin Immunol*. 2020;217:108487.