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New-onset lupus nephritis associated with COVID-19 infection

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Abstract

A dysregulated immune response plays a critical role in systemic lupus erythematosus (SLE) pathogenesis. Environmental factors such as viruses, including coronavirus 2 (COVID-19), have been described to play a role in SLE presentation and exacerbation. These viruses trigger a host's humoral and cellular immunities typically essential in elimination of the viral infection. We present a case of a Hispanic male who developed new-onset lupus nephritis class II after a COVID-19 infection.

Keywords

systemic lupus erythematosus, COVID-19, lupus nephritis

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Introduction

Systemic lupus erythematosus (SLE) occurs more commonly in women but tends to be more severe in males and in Hispanic patients.[1] Immune complexes are central players of tissue injury in SLE. Similarly, viruses can play a significant role in the pathogenesis of lupus, especially in genetically predisposed individuals.

Case presentation

During the summer of 2020, a 37-year-old Hispanic man was diagnosed with mild COVID-19 infection via a positive polymerase chain reaction assay of nasopharyngeal swab after presenting to an outside hospital with one week of fevers, dry cough, anorexia, but no hypoxemia. His course was mild and his symptoms self-resolved without treatment. His medical history was notable for a recurrent photosensitive rash, an episode of alopecia, and one self-resolving episode of interphalangeal joints discomfort in his hands 2 years prior to his presentation, at which time he had a negative anti-nuclear antibody (ANA) and rheumatoid factor. He had no history of prior COVID-19 vaccination or infection. His family history was notable for a mother and a sister with SLE.

Over the ensuing 6 weeks, he developed progressive nausea, generalized weakness, anorexia, and a diffuse skin rash. Repeat COVID-19 testing was negative. He was readmitted with acute onset vomiting, abdominal pain, and recurrence of fever. Documented physical examination included a Tmax 39.2°C, a tender abdomen and generalized erythematous papular rash on his arms, chest, back, abdomen, and legs (Figure 1).

He was empirically started on antibiotics for an initial concern for community-acquired pneumonia. However, further work-up showed positive ANA, positive double-stranded DNA antibody, hypocomplementemia, leukopenia, and proteinuria (Table 1). A kidney biopsy showed mesangial hypercellularity by light microscopy as well as minimal mesangioproliferation with electron dense deposits in the subendothelial, subepithelial, and intramembranous compartments, and numerous tubuloreticular inclusions, consistent with class II lupus nephritis (Figure 2). He was diagnosed with SLE and subsequently started on combination therapy of steroids and mycophenolate mofetil 1500 mg twice daily with resolution of his fevers, myalgias, arthralgia, rash, and abdominal pain. He remained asymptomatic at his first outpatient encounter with rheumatology 4 weeks after discharge. Hydroxychloroquine

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Table 1. Diagnostic evaluations confirming SLE in a male patient.

	Value two years prior to hospitalization	Value during hospitalization Day 1	Value during hospitalization Day 11 (on steroids and mycophenolate)	Normal range
Complete blood count				
White blood cell count (K/cu mm)	4.1	2.43	4.99	4.50–11.00
Absolute neutrophil count (K/cu mm)	2.45	1.70		1.50–7.80
Absolute lymphocyte count (K/cu mm)	1.17	0.46		1.10–4.80
Hemoglobin (g/dL)	11.2	9.2	9.3	13.9–16.3
Platelets (K/cu mm)	293	241	203	150–350
Chemistry				
Creatinine (mg/dL)	1.14	0.9	0.6	0.6–1.3
Aspartate amino transferase (U/L)	24	551	260	0–37
Alanine amino transferase (U/L)	19	193	173	0–41
Alkaline phosphatase (U/L)	56	174	260	30–130
Lipase (U/L)		764		15–63
Autoimmune testing				
Nuclear antibody (ANA), titer and pattern	Negative	1:160 homogenous		<1:40 (antibodies not present)
Anti-dsDNA antibodies		1:80		Antibody not present
Anti-RNP antibodies (units)		Negative		<20
Anti-Smith antibodies (units)		<3.3		<20
Complement (C3) (mg/dL)		46.3		81.0–157.0
Complement (C4) (mg/dL)		12.82		13.00–39.00
Rheumatoid factor ((IU)/mL)	Negative	Negative		0–14
Anti-cyclic citrullinated peptide 3 (CCP) IgG (units)		Negative		<20

(continued)

Table 1. (continued)

	Value two years prior to hospitalization	Value during hospitalization Day 1	Value during hospitalization Day 11 (on steroids and mycophenolate)	Normal range
Anti-neutrophil cytoplasmic antibody (ANCA) screen		Negative		Antibody not present
Creatine kinase (U/L)		2748		24–195
Renal studies				
Urinalysis		2+ protein, 6 RBCs/(HPF), 16 WBCs/(HPF)		Negative 0–5/(HPF)
Urine protein/creatinine ratio		1.4 g		0.00-0.19
CT chest/abdomen/ pelvis with IV contrast		Subtle bilateral infiltrates may be secondary to atypical pneumonia. Mild thoracic, abdominal, and pelvic lymphadenopathy, non-specific. Mild mesenteric stranding may be secondary to mesenteric panniculitis. Pancreatitis is possible.		

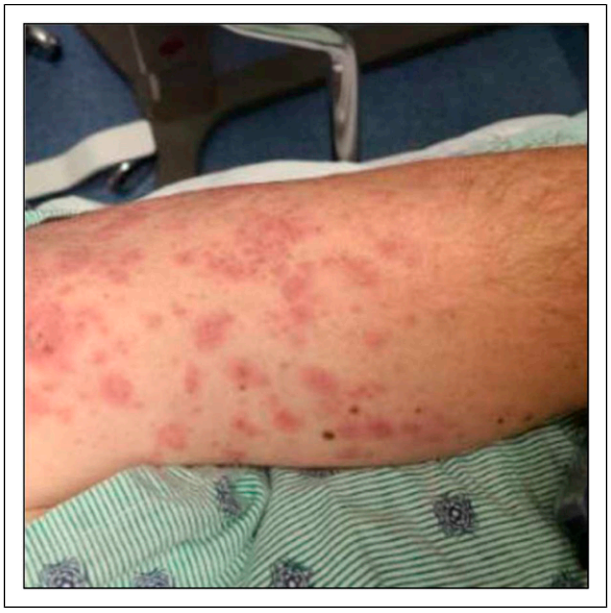

Figure 1. Image of rash on left upper extremity.

200 mg twice daily was added to his regimen and steroids were rapidly tapered. At his 3-months follow-up appointment, he was asymptomatic on combination therapy with mycophenolate and hydroxychloroquine. However, he failed to repeat regular lab monitoring and was later lost to follow-up.

Discussion

Lupus nephritis affects up to 60% of SLE patients within 10 years of diagnosis[2] and should be confirmed by renal biopsy unless a strong contraindication exists. Features suggesting muscle involvement in SLE have been reported in 30–50% of patients.[3] Although rare, SLE can also manifest as mesenteric panniculitis with a high associated mortality rate,[4] but significant improvement of panniculitis is typically seen with immunosuppressive therapy.[5]

The possibility that viruses, such as EBV or influenza, may trigger SLE or flares via molecular mimicry and epitope spreading has been considered for the past 40 years.[6,7] Understanding of COVID-19 is also continuously

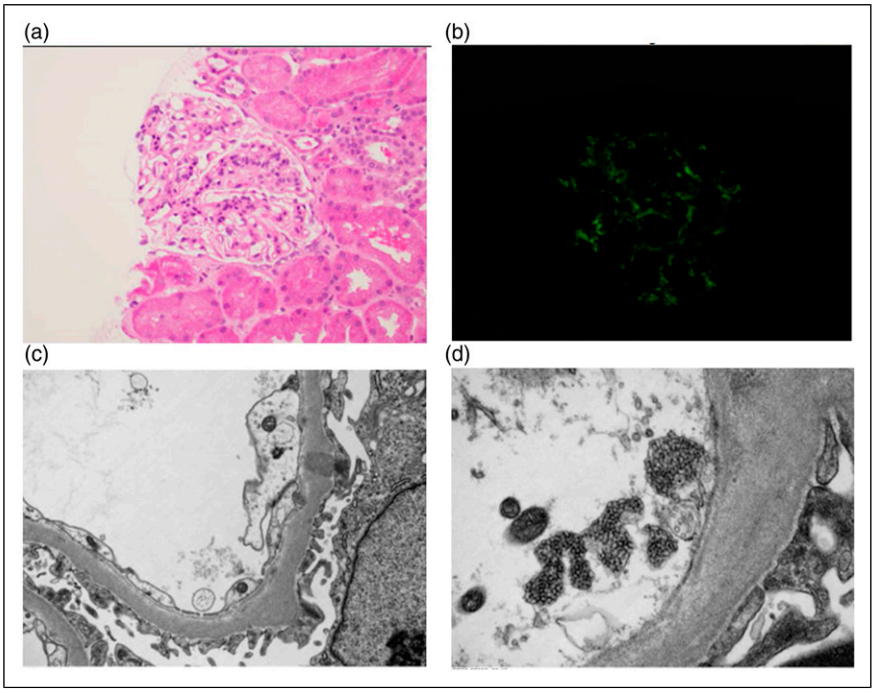

Figure 2. (A) Light microscopy showing mesangial regions with rare focal expansion and hypercellularity. (B) Immunofluorescence microscopy: Frozen sections stained with H&E contain one glomerulus. Immunoglobulin G: sparse trace to 1+ granular mesangial and capillary wall, immunoglobulin A: 1+, immunoglobulin M: trace, Kappa 2+, lambda 1+, C3: 3+, C1q trace with distributions to granular mesangial and capillary wall. There is non-specific linear glomerular and tubular basement membrane staining for albumin (2+). (C) Electron microscopy: Toluidine blue-stained thick sections contain three glomeruli. There are scattered small subendothelial, subepithelial, and intramembranous electron dense deposits. (D) Electron microscopy: There are frequent endothelial tubuloreticular inclusions in both glomerular and peritubular capillaries.

evolving. COVID-19 infection can cause a variety of clinical manifestations, from mild illness to severe disease with acute respiratory disease syndrome (ARDS), multi-organ failure, and death. Case reports describing new SLE diagnoses and particularly lupus nephritis triggered by COVID-19 remain scarce.[8–11] Zamani et al. describe a case of new SLE diagnosis associated with lupus nephritis class I presenting 2 months after COVID-19 infection.[10] Bonometti et al. described an incident diagnosis of SLE that developed following COVID-19 infection in an 85-year-old woman, who met EULAR 2019 criteria based on ANA positivity, thrombocytopenia, pleural effusion, and low complement.[11] COVID-19 infection has also been associated with SLE flares. In their case series, Kudosi et al. presented a case of SLE flare after COVID-19 infection, providing evidence for a role of coronaviruses in the exacerbation of SLE.[12] The mechanism of the wide range of COVID-19 immunologic manifestations remains unclear, and could be explained by autoreactivity, autoimmunity, or a mixed pattern physiology.[13]

Conclusion

COVID-19 may lead to autoimmune and autoinflammatory diseases. To the best of our knowledge, this is the first case report of COVID-19 infection associated with lupus nephritis class II. It is possible that COVID-19 may have led to the formation of immune complexes and the development of lupus nephritis in this patient with a genetic predisposition and a history of photosensitive skin rash, alopecia, and arthralgia with negative serology. Additional work is essential to decipher the mechanisms of COVID-19 modulation of the immune system in SLE.

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