IgA Nephropathy (Henoch-Schönlein Purpura) Associated with Recent COVID-19 Infection

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> t the end of 2019, the world faced a A rew virus–coronavirus disease 2019 (COVID-19)-which quickly became a pandemic. It has become clear that the COVID-19 virus can affect various body systems. Over time, we are finding more and more diverse manifestations of the course of the disease itself, its consequences, and complications. There have been several studies and reviews describing circulating antibodies in patients infected with COVID-19 (e.g., antinuclear antibodies [ANA], anti-cardiolipin, anti-B2 glycoprotein, perinuclear anti-neutrophil cytoplasmic antibodies [p-AN-CA], cytoplasmic ANCA [c-ANCA]). The development of autoimmune disorders has been reported (e.g., Graves' disease, systemic lupus erythematosus (SLE), immune thrombocytopenia [ITP], diabetes mellitus [DM] type 1, psoriasis). There are descriptions of COVID-19 associated vasculitis include Kawasaki-like symptoms in children and immunoglobulin A (IgA) vasculitis in children and adults [1].

> IgA vasculitis is small vessel vasculitis that most commonly affects children. It is characterized by IgA and complements C3 deposition in small vessels. Henoch-Schönlein purpura (HSP) is characterized by a classic triad of symptoms (purpura, arthritis, abdominal pain). About 40% of the patients develop some

degree of kidney injury. Half develop proteinuria. The prognosis is usually very good. Only 1% of patients develop chronic renal failure. The prognosis is generally worse with age.

We present a patient who developed IgA vasculitis a few weeks after being ill with COVID-19.

PATIENT DESCRIPTION

A 71-year-old patient with well-controlled diabetes was treated with metformin without target organ involvement, dyslipidemia, and inactive psoriasis. The patient had no history of heart or renal failure, and his general health was good.

The patient developed respiratory symptoms of dry cough, weakness, and muscle pain without fever, respiratory distress, and loss of smell.

A week later the patient was diagnosed with COVID-19 by polymerase chain reaction (PCR). He was not hospitalized, and he had no additional symptoms. He did not take any medications for the treatment of the COVID-19 infection.

After 6 weeks, purpura appeared all over his body, especially on his legs.

The rash resolved after a few days, and 2+ pitting edema appeared on both legs. He had no dyspnea, chest pain, or palpitation. He had no change in the amount of urine or urinary complaints.

Complete blood count showed mild anemia of hemoglobin 13 g/dl, low serum albumin (3.1 g/dl), and low serum protein (6.2 g/dl). The serum creatinine level was normal (0.88 mg/dl with eGFR

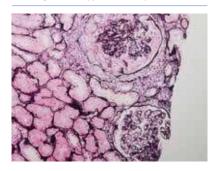
95 ml/min/1.73 m²). The level of serum triglycerides, C-reactive protein (CRP), potassium, and sodium levels were normal. Urinalysis showed proteinuria and red blood cells. The 24-hour urine collection showed nephrotic range proteinuria of almost 14 grams. Laboratory tests for hepatitis B, hepatitis C, and human immunodeficiency virus were negative. Cryoglobulin was negative, complement, CRP was normal. The free light chains were slightly increased with a normal ratio. p-ANCA, c-ANCA, ANA, DNA, and APLA antibodies were negative. The ESR was increased to 74 mm/h. There was no abnormality in the kidney ultrasound. Echocardiography shows normal left ventricular (LV) motion with impaired LV relaxation.

A kidney biopsy was performed. It showed precipitation of IGA compatible with IgA nephropathy [Figure 1].

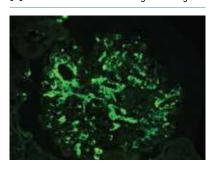
The patient was treated with highdose steroids in an out-patient clinic with quick tapering down. Proteinuria decreased to 6 grams, and the edema disappeared. After a few months, he was hospitalized because of dyspnea, worsening leg edema, and worsening hypoalbuminemia. Proteinuria worsened to 10 grams in 24 hours. He was treated with a course of pulse therapy of methylprednisolone with the improvement of proteinuria to 4 g/d, disappearance of leg edema, and dyspnea. The patient remained under supervision in the nephrological unit. The steroids were tapered down slowly without additional exacerbation of the disease.

Figure 1. A kidney biopsy showing precipitation of IGA compatible with IGA nephropathy

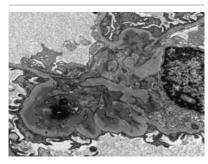
[A] Hematoxylin-Eosin shows glomerulus with segment of hypercellularity at 3 o'clock



[B] Immunofluorescence with IgA staining



[C] Electron microscopy shows mesangial deposits with increased mesangial matrix and cellularity



COMMENT

We described a 71-year-old patient with HSP associated with post-COVID-19 infection (typical rash, proteinuria, and renal biopsy with suggested IgA nephropathy).

In classical cases, IgA nephropathy most commonly affects children, and there is a predisposition to upper respiratory tract infection before the development of the disease. The common organisms associated with HSP are streptococcal bacteria, parainfluenza virus, and parvovirus. So, it seems logical to assume that COVID-19 infection could also be a trigger of IgA nephropathy. Furthermore, COVID-19 has already shown itself to be a virus causing an association with autoimmune diseases due to hyperstimulation of the immune system.

COVID-19 infection is being suggested as a trigger for the appearance of autoimmune diseases, including vasculitis. We provide a description of several cases of COVID-19 infection associated with Henoch–Schönlein purpura in adults.

A young Crohn's disease patient treated with adalimumab with positive PCR testing for COVID-19 with IgA vasculitis, which was manifested with abdominal pain, arthralgia, and typical rash. He responded well to steroid treatment [2].

A young, healthy man who was hospitalized due to IgA vasculitis and positive PCR testing for COVID-19 without respiratory symptoms. He had a typical rash, arthralgia, and proteinuria of 2 g/d. He was treated with steroids and mycophenolate-mofetil with complete recovery [3].

A 30-year-old man was diagnosed with impressive proteinuria due to IgA vasculitis, 2 weeks after COVID-19 in-

fection. He was treated with high-dose steroids and rituximab with the improvement of the condition [4].

An 88-year-old man was hospitalized with nephrotic syndrome 3 weeks after hospitalization because of COVID-19 infection with IgA-dominant infection-associated glomerulonephritis in kidney biopsy [5].

It seemed that there is an association between COVID-19 and IgA nephropathy in our patient, especially if considering his age and lack of predisposition to autoimmune diseases in most cases.

It should be noted that approximately 20 cases have been described so far, including those in children.

Our case is different from the others based on the age our patient. He was older than most of the patients. Moreover, our patient had a relapse, possibly suggesting a more severe illness.

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References

- 1. Halpert G, Shoenfeld Y. SARS-CoV-2, the autoimmune virus. *Autoimmun Rev* 2020; 19 (12): 102695.
- Allez M, Denis B, Bouaziz JD, et al. COVID-19related IgA vasculitis. Arthritis Rheumatol 2020; 72 (11): 1952-3.
- Sundhu S, Chand S, Bhatnagar A, et al. Possible association between IgA vasculitis and COVID-19. Dermatol Ther 2021; 34 (1): e14551.
- Suso AC, Mon C, Onate Alonso I, et al. IgA vasculitis with nephritis (Henoch-Schönlein Purpura) in a COVID-19 patient. Kidney Int Rep 2020; 5 (11): 2074-8.
- Perez A, Torregrosa I, Luis D et al. IgA-dominant infection-associated glomerulonephritis following SARS-CoV-2 infection. Viruses 2021; 13 (4): 587.

Capsule

PLK1 moves beyond mitosis in lung cancer

Increased levels of the mitotic kinase PLK1 in various cancers correlates with poor prognosis. **Kong** et al. identified a nonmitotic mechanism through which PLK1 fuels tumor growth. In Kras-mutant mouse lung adenocarcinoma cells, PLK1 kinase activity increased the expression of RET, which encodes a receptor tyrosine kinase. Together, KRAS and RET

activated the MAPK pathway, which promotes tumor growth. Combining clinically approved RET and MAPK pathway inhibitors induced tumor regression and prolonged survival in a mouse model of PLK1-overexpressing lung cancer.

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