ANCA-Associated Glomerulonephritis Following SARS-CoV2 Infection: A Case Report

Nefrologo in corsia

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ABSTRACT
Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) primarily affects small- and medium-sized arteries, including kidney vessels, thus causing rapidly progressive glomerulonephritis. The pathogenesis of AAV is intricate and several factors, including infections, are known to possibly trigger the autoimmune process. Numerous studies have reported that SARS-CoV-2 might cause acute kidney injury (AKI). To date, a modest number of AAV with COVID-19 cases has been reported. Herein, we discuss the case of a 61-year-old man with new-onset of diffuse proliferative ANCA-associated glomerulonephritis after COVID-19.

KEYWORDS: Vasculitis, ANCA, Acute Kidney Injury, Glomerulonephritis, COVID

Introduction

Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) is a systemic autoimmune disease that affects primarily small- and medium-sized arteries, including kidney vessels, thus causing rapidly progressive glomerulonephritis (GN) [1, 2]. The pathogenesis of AAV is intricate. Several factors (i.e. specific drugs, infectious agents, environmental exposures, etc.) are known to possibly trigger the autoimmune process in genetically susceptible patients [3, 4]. Numerous studies have reported that severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), responsible for the respiratory disease called Coronavirus disease-19 (COVID-19), may cause acute kidney damage (AKI) [5, 6]. To date, a modest number of AAV with COVID-19 cases have been reported [7]. Herein, we discuss the case of a 61-year-old man with new-onset of diffuse proliferative ANCA-associated glomerulonephritis (GN) after COVID-19.

Case Report

A previously healthy 61-year-old Italian man accessed to our Emergency Department in March 2022 because of a 1-month history of progressive bilateral leg pain and weakness. The patient was vaccinated with two doses of Comirnaty BNT162b2 (BioNTech/Pfizer) and had tested positive for SARS-CoV-2 in December 2021 with mild symptoms of COVID-19, not requiring hospitalization. Vital parameters were normal except for mild hypertension (B.P. 150/90 mmHg). Physical exam was unremarkable except for bibasilar crackles on chest auscultation. Initial serum laboratory tests showed: creatinine 6.2 mg/dl, BUN 161 mg/dl, Haemoglobin 8.4 g/dl, MCV 88.7 fL, c-reactive protein (CRP) 1.24 mg/dl, ferritin 404 ng/ml, fibrinogen 543 mg/dl, Interleukin-6 12.3 pg/ml. RT-PCR test for SARS-CoV-2 was negative while IgG for SARS-CoV-2 resulted positive (40 BAU/ml) on the CLIA test. At urine sediment analysis there was evidence of: proteins 300 mg/dl, numerous red blood cells and numerous hyaline-granular cylinders. Chest X ray showed bibasilar pleural effusion. Chest high-resolution CT scan confirmed the presence of bilateral pleural effusion with no evidence of parenchymal thickenings of inflammatory or cancerous significance. Abdominal ultrasound exam showed no alteration of liver, bile ducts, gallbladder, spleen, pancreas and bladder with normal appearance of both kidneys and urinary traits. The patient was transferred to our Emergency Medicine Unit. He denied any history of smoking, prior kidney disease, diabetes mellitus, alcohol intake and drug abuse. Family history was also insignificant and he was not taking any medication.

Additional laboratory tests were performed (Table 1) with evidence of: proteinuria (urinary total protein 5.6 g/24h), negative serum and urine immunofixation, negative serum tumor markers panel, normal complement C3 and C4 levels and negative ANA and ENA screening. ELISA test showed positive c-ANCA essay pattern (title 1:80), positive anti-proteinase-3 (anti-PR3) 1082 CU, negative anti-myeloperoxidase (anti-MPO, < 3.2 CU). Esophagogastroduodenoscopy only showed mild chronic superficial gastritis while colonoscopy showed no alterations.

Renal biopsy was performed with evidence of diffuse proliferative necrotising glomerulonephritis and acute tubulointerstitial nephritis (Figure 1). In particular, histological analysis showed glomeruli with both evidence of chronic (i.e. global sclerosis) and active lesions (i.e. cellular crescents) and marked inflammatory lymphomononuclear-granyulocytic infiltrate. Immunofluorescence (IF) staining for IgA, IgG, IgM, C1q, C3, kappa and lambda light chains was negative; fibrinogen was positive.

The patient was started on IV Methylprednisolone therapy (500 mg per day for six days) followed by oral Prednison (1 mg/kg/die) and Rituximab 375 mg/1,73 m^2 (one infusion every 7 days for 4 weeks). Prophylaxis for Hepatis B virus reactivation with Entecavir was also started.

During the subsequent follow-up serum creatinine values progressively decreased (Table 1). After 24 months, clinical conditions significantly improved. ANCA antibodies became undetectable, renal function remained stable (creatinine 2.4 mg/dl, proteinuria 2.3 g/24h). A chest CT was repeated with no evidence of pleural effusion.

Lab test	2022	24 months later
Haemoglobin (g/dl)	8.4	14
Creatinine (mg/dl)	6.2	2.4
GFR estimated by CKD-EPI equation (ml/min)	8.9	27.3
BUN (mg/dl)	161	62
Proteinuria (g/die)	5.6	2.3
PTH (pg/ml)	65	48
C3 complement (mg/dl)	120 (n.v. 90-180)	N/A
C4 complement (mg/dl)	38 (n.v. 10-40)	N/A

Table 1. Laboratory exams trend before and after treatment.

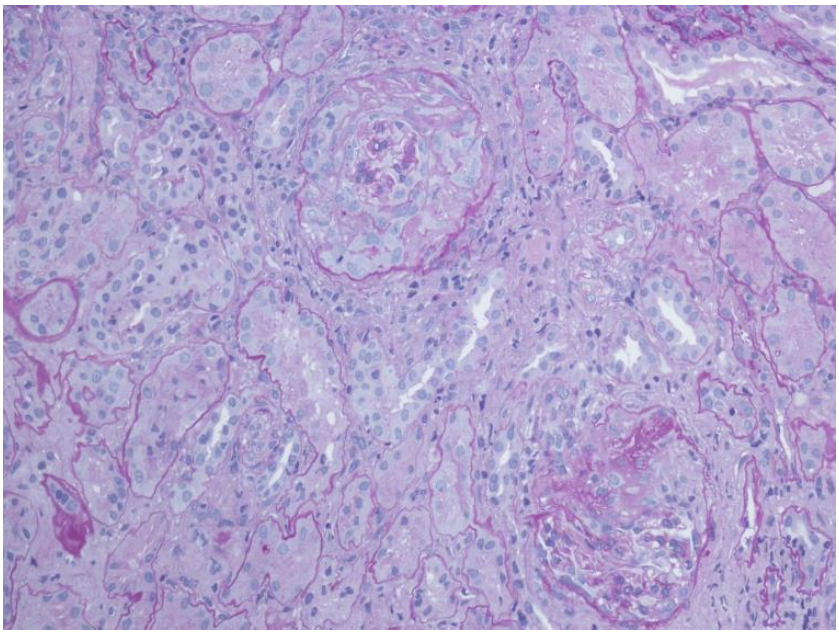

Figure 1. Renal biopsy, histological analysis. The figure shows 24 glomeruli, 11 with evidence of chronic lesions such as global sclerosis and 7 characterized by parcel necrosis of the convoluted tubules and active injuries as cellular crescents and cell-fibrous lesions. In the remaining glomeruli, variable ischemic wrinkling of the capillary walls can be observed. Arteries are free from significant alterations; arterioles show signs of focal intimal hyalinosis. Small areas of tubular atrophy associated with fibrosis of the interstitium and a marked inflammatory lymphomononuclear-granyulocytic infiltrate, also of the eosinophilic type, with images of tubulitis, are evident.

Discussion

Although Covid-19 presents primarily with respiratory symptoms, accumulating evidence demonstrated the potential severity of extrapulmonary involvement, including kidney injury [8, 9]. A higher rate of AKI was reported in critically ill Covid-19 patients with pre-existing conditions such as hypertension, diabetes mellitus and obesity [10]. A case of microscopic polyangiitis associated with SARS-CoV-2 infection was first described in 2021 by Allena et al. [11] and, to date, less than 25 cases of de novo ANCA-associated vasculitis with glomerulonephritis in Covid-19 patients have been reported. In November 2023 a systematic review was published by Banjongjit et al [7]: among the 21 patients included, the mean age of SARS-CoV-2 infection-associated ANCA-GN was 48 ± 19 years

with 56% of patients showing positivity for myeloperoxidase (MPO)-ANCA and 36% of patients showing concomitantly positive antinuclear antibodies. In this review, 11 out of the 21 cases (55%) were diagnosed with ANCA-GN during hospitalization due to SARS-CoV-2 infection while the remaining cases were diagnosed after a median of 2.1 months following COVID-19. Finally, 71% of patients showed improvement in kidney function following different treatments. Histological analysis, overall, showed signs of crescentic glomerulonephritis with glomeruli potentially displaying both cellular and fibrocellular crescents, fibrinoid necrosis, mesangial and endocapillary hypercellularity, interstitial fibrosis and tubular atrophy.

In this case, we present an otherwise healthy man who contracted Covid-19 with minimal respiratory symptoms; no specific antiviral medications or monoclonal antibodies were needed. He later developed new-onset, severe ANCA-associated glomerulonephritis and appropriate therapy was started with progressive improvement of clinical conditions and renal function. Based on the absence of recent COVID-19 vaccinations, we could discard the possibility of COVID-19 vaccine-induced ANCA-GN, a rare but possible event recently described in literature [12].

We believe our case report is of particular interest for many reasons. Firstly, the majority of patients included in the systematic review [7] were reported from United States of America (52%) while Europe contributed for 14% of cases and Italy only for one case. Secondly, our patient showed positivity for proteinase-3 (PR3) at ELISA analysis while only 6 of the patients included in the systematic review exhibited this peculiarity. Furthermore, most of the patients included in the review showed peak serum creatinine levels lower than 6 mg/dl with only 3 out 21 patients showing higher levels compared to our patient's. Finally, the majoriry of cases included in the review were diagnosed with ANCA-GN during hospitalization due to SARS-CoV-2 infection and the remaining cases were diagnosed after a mean interval of 2.1 months following COVID-19, while in our patient the diagnosis was done after almost 4 months. The histological aspects, on the contrary, were similar to those reported in the review.

Conclusion

While SARS-CoV-2 continues to be investigated for its acute manifestations, the long-term impact of COVID-19 is far from being completely known. With the increasing number of people who contracted the virus with mild to no symptoms, it is very important to consider that there is a potentially large number of patients who will need help beyond the infectious period. Routine laboratory tests might be useful to diagnose long-term Covid-19 complications in time.

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