Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

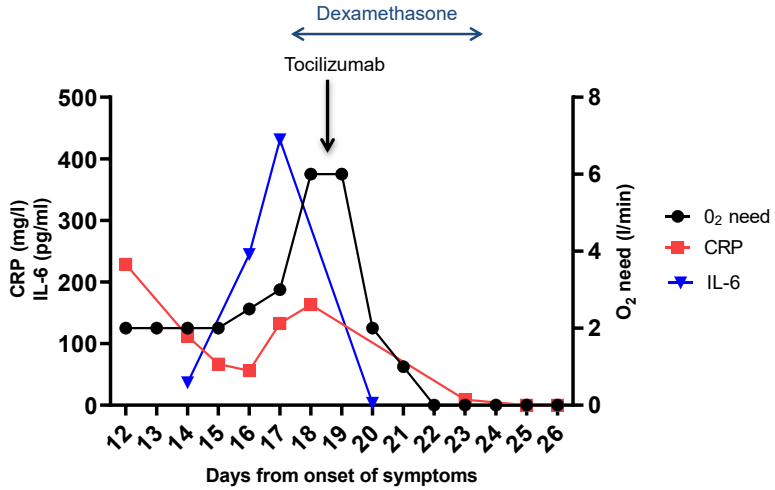

Figure 1 | Temporal course of serum inflammatory biomarkers—C-reactive protein (CRP) and interleukin (IL)-6—in relation to the patient's need for oxygen therapy. The timing of tocilizumab infusion and administration of dexamethasone is shown by the arrows.

cyclosporine. The patient was hydrated, and antibiotic prophylaxis was started (Table 1). Unfortunately, the patient's respiratory function further deteriorated, and laboratory findings were suggestive of cytokine release syndrome with remarkably elevated (431 pg/ml) serum interleukin-6 levels. A single i.v. infusion of tocilizumab (8 mg/kg per d) was attempted. Two days after, oxygen was no longer required (Figure 1). The patient was discharged home and completely recovered from acute kidney injury.

Early detection of cytokine release syndrome biomarkers is recommended and should prompt anti-inflammatory interventions. Larger studies are needed to confirm the utility and safety of interleukin-6 inhibition combined with dexamethasone in kidney transplant recipients with COVID-19.

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Thrombotic microangiopathy in a patient with COVID-19

To the editor: We describe a patient with coronavirus disease 2019 (COVID-19) and clinically significant kidney biopsy-proven thrombotic microangiopathy.

A 69-year-old Caucasian female with a past medical history of asthma presented to the emergency department with productive cough, fever, and shortness of breath of 2 weeks' duration. In the emergency room, she was afebrile, with a respiratory rate of 22 breaths per minute, and oxygen saturation of 89% on room air. Initial laboratory tests showed a normal white blood cell count, hemoglobin level, and platelet count. Inflammatory lab parameters were elevated (Table 1). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was confirmed in the patient by reverse-transcriptase polymerase chain reaction assay or serologic testing at our center. A chest X-ray showed bilateral diffuse patchy opacities.

The patient was admitted, and treatment with hydroxychloroquine, low-molecular-weight heparin, and oxygen was initiated. Over the next several days, she received anakinra and tocilizumab (dosages and details are given in Table 1). On day 12, the patient's labs demonstrated down-trending platelets, hemoglobin, and worsening kidney function.

Table 1 | Chronological treatment and laboratory data

	Day 1	Day 7	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21
Treatment given	Hydroxychloroquine/ low-molecular-weight heparin	Anakinra & tocilizumab	Convalescent plasma	Intubation	Dialysis started		Kidney biopsy	Eculizumab
Hemoglobin (11.5–15.5 g/dl)	13	11.5	12.9	11.8	8.0	8.3	8.6	6.9
Platelets (150–400 K/ul)	203	142	85	14	97	37	21	27
Serum creatinine, mg/dl	0.72	0.75	0.57	2.06	2.49	4.07	On dialysis	On dialysis
Fibrinogen (350–510 mg/dl)				62	159	128	117	166
D-dimer (<229 ng/ml DDU)	411				6068	14,568	12,193	5927
ADAMTS 13 activity level (>66.8%)					43.2			
Alkaline phosphatase (40–120 U/l)	137	118	292	296	194	212	204	294
AST (10–40 U/l)	70	44	63	316	404	254	173	148
ALT (10–45 U/l)	38	30	27	97	146	239	230	165
LDH (50–242 U/l)	459		1073		3518	5130	5183	4707
C-reactive protein (0–0.40 mg/dl)	10.35	2.46	6.85		18.54	20.73	13.61	8.02
Hep- PF 4 AB result (0.0–0.9 U/ml)			<0.6					
Hep- PF 4 AB interpretation			Negative					
Schistocytes in smear					Present	Present		
Haptoglobin (34–200 mg/dl)					<20	<20		

ADAMTS 13, disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Hep, heparin; LDH, lactate dehydrogenase; PF, endogenous protein platelet factor 4.
Medication dosages: anakinra 100 mg q6 × 8 doses; tocilizumab 400 mg i.v. × 2 doses; eculizumab 900 mg i.v.—1 dose was able to be given (patient expired).

There was concern for microangiopathic hemolytic anemia. Due to worsening hypoxemia, the patient received convalescent plasma treatment as part of an expanded access trial. On day 17, the patient was intubated due to worsening respiratory failure. In addition, the patient developed hemolysis (presence of schistocytes, undetectable haptoglobin levels, high lactate dehydrogenase level). Urinalysis showed hematuria, large blood, 30–40 red blood cells/high-power field, and 1.4 g of protein. The patient's kidney function worsened, requiring initiation of continuous renal replacement therapy. On day 20, the patient underwent a kidney biopsy that revealed severe acute thrombotic microangiopathy with cortical necrosis (Figure 1). Although beta 2 glycoprotein-1 IgM levels were elevated, other laboratory and clinical features of antiphospholipid antibody were absent (Table 2). The disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS13) level was not low. Complement 3 and 4 were in the normal range. Heparin-induced antibody testing was negative. Coagulation parameters were normal. A kidney sonogram was negative for renal vein thrombosis and arterial clots. The patient did not have any other systemic findings of macro thrombi. Subsequent detailed complement testing revealed a low factor H complement antigen, and elevated plasma CBb complement and plasma SC5b-9 complement levels, suggesting an activation of the alternative complement pathway (Table 2). Genetic testing was not performed. Given clinical instability, plasma exchange was not performed. Instead, the patient was given a single dose of eculizumab at 900 mg on day 21. Unfortunately, the patient expired on day 23 in the setting of worsening shock.

Coagulopathy associated with SARS-CoV-2 has been widely reported.[1,2] The profound hypoxia, inflammation, and disseminated intravascular coagulation have all been implicated as potential causes.[2] There has also been a report of coagulopathy secondary to development of antiphospholipid antibodies.[3] Our patient had no evidence of disseminated intravascular coagulation. Although we cannot completely rule out antiphospholipid antibody syndrome, it is less likely to have played a role in this case, as there was no prior history of autoimmunity and no other current stigmata of evolving connective tissue disease, such as lupus, or antiphospholipid syndrome in other body systems. Transient elevation of both beta-2 glycoprotein-1 IgG and IgM can be seen in the setting of infections and drug exposures.[4] Ideally, a confirmation of autoantibodies is needed at 12 weeks, which was not possible to do in this case. Collapsing glomerulopathy associated with SARS-CoV-2 has now been reported from several centers as the first described glomerular pathology in this setting.[5,6] To our knowledge, there have been no published cases of SARS-CoV-2–associated systemic thrombotic microangiopathy. We report the first case of thrombotic microangiopathy associated with SARS-CoV-2, with presence of diffuse cortical necrosis and widespread microthrombi in the kidney biopsy. It is not clear if the virus played a direct pathogenic role or unmasked a latent complement defect (as noted in our complement testing) leading to widespread endothelial damage and micro thrombi.[7]

Acute kidney injury is not uncommon in patients with COVID-19.[8] Causes of acute kidney injury can range from pre-renal azotemia, to acute tubular injury, to collapsing glomerulopathy.[5,6,9] Physicians treating patients with COVID-19 should keep microangiopathic disease in the differential

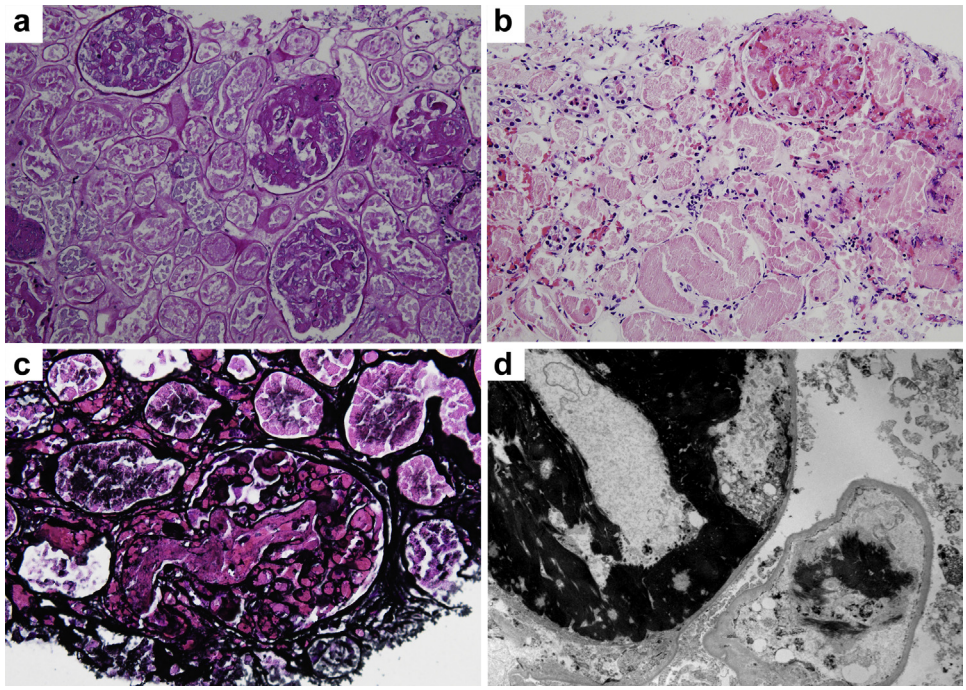

Figure 1 | Kidney biopsy findings. (**a**) Kidney parenchyma reveals diffuse coagulative cortical necrosis, with widespread glomerular thrombi (periodic acid–Schiff stain, original magnification ×200). (**b**) Glomerulus with multiple microthrombi in upper right aspect of the image and extensive coagulative necrosis of proximal tubules with ghost cells and nonviable nuclei (hematoxylin and eosin stain, original magnification ×200). (**c**) A thrombosed glomerulus with a large thrombus in the arteriole and vascular pole (Jones methenamine silver stain, original magnification ×400). (**d**) Electron micrograph with extensive crosslinked fibrin deposits in capillary lumens and partially denuded capillary due to ischemia and necrosis (original magnification ×4000). To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

diagnosis when systemic findings of hemolysis are present along with thrombocytopenia and acute kidney injury. Earlier diagnosis could perhaps lead to prompt treatment with plasma exchange or complement pathway inhibitors.

DISCLOSURE

KDJ serves as a consultant for Astex Pharmaceuticals and Natera. All the other authors declared no competing interests.

Table 2 | Antiphospholipid panel and complement panel

Comprehensive complement testing with results and reference ranges
Serum complement total—56U/ml (30–75)
Serum complement C3—105 mg/dl (75–175)
Serum complement C4—26 mg/dl (14–40)
Serum factor B complement antigen—28 mg/dl (15.2–42.3)
Serum factor H complement antigen—22 mg/dl (23.6–43.1)
Plasma C4d complement—2.3 mcg/ml (<9.9)
Plasma CBb complement—4.4 mcg/ml (<1.7)
Plasma SC5b-9 complement—875 ng/ml (<251)
Antiphospholipid antibody testing with results and reference ranges
Anticardiolipin IgG—13.6 GPL (0–12.5)
Anticardiolipin IgM—12.5 MPL (0–12.5)
Anticardiolipin IgA—6.7 APL (0–12.5)
Beta 2 glycoprotein—1 IgG—<5 SGU (<20)
Beta 2 glycoprotein—1 IgM—68.6 SMU (<20)
Beta 2 glycoprotein—1 IgA—8 SAU (<20)

APL, A phospholipids units; GPL, G phospholipids units; MPL, M phospholipids units; SAU, standard IgA aB2G2P1 unit; SGU, standard IgG aB2GPI unit; SMU, standard IgM aB2GPI unit.

ACKNOWLEDGMENTS

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The Northwell Health Institutional Review Board approved this case as minimal-risk research using data collected for routine clinical practice and waived the requirement for informed consent.

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Letter regarding "SARS-CoV-2 in the peritoneal waste in a patient treated with peritoneal dialysis"

To the editor: We read with interest the letter from Vischini *et al.* about the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the peritoneal effluent of a peritoneal dialysis (PD) patient.[1] Coronavirus transmission occurs primarily via respiratory droplets, and it has been found inconsistently in body secretions and excretions.[2] SARS-CoV-2 virion is 60–140 nanometers and could theoretically enter the peritoneal cavity via hematogenous diffusion or through the PD catheter after touch contamination.

This observation of Vischini *et al.* if confirmed, is important for daily clinical care of PD patients and handling of effluents. However, they found positive polymerase chain reaction tests in PD effluents in their patient 1 month after the first symptoms, calling into question whether the virus itself was present or whether it was just noncontagious RNA fragments. In our experience with serial PD effluent samplings from 3 PD patients with mild to moderate active coronavirus disease 2019 (COVID-19), we found results discordant with those of Vischini *et al.* We used quantitative reverse transcription polymerase chain reaction analysis based on the highly specific *RdRp* gene and *E* gene, in 2 independent laboratories. Although nasopharyngeal swabs obtained at admission showed high viral load in all 3 patients (cycle threshold value <30), decreasing during hospitalization, none of the 11 PD effluent samplings at days 0–3–4–7 taken after a 12-hour dwell time tested positive, even after dialysate centrifugation. A blood sample was positive in only one patient (A. Candellier, A. Scohy, N. Gillet, *et al.*, submitted for publication, 2020). Our data are also in line with the absence of SARS RNA in effluents from PD patients with SARS infection.[3]

The opposite results for both observations argue for performing a SARS-CoV-2 culture to confirm PD effluent contagiousness before imposing specific procedures in PD patients.

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Kidney transplantation trends in South Korea during the COVID-19 pandemic

To the editor: We read with interest the article by Banerjee *et al.*[1] reporting 7 cases of coronavirus disease 2019 (COVID-19) in kidney transplant recipients. Banerjee *et al.*[1] raised concerns about increased susceptibility to COVID-19 infection during the postoperative period; however, the impact of immunosuppression on susceptibility to COVID-19 remains unknown. Recent data on clinical outcomes of COVID-19 infection in kidney transplant patients are conflicting.[2] Furthermore, some preliminary reports suggest the reduced immune response due to immunosuppression may provide a protective effect against severe COVID-19.[3]

South Korea was one of the earliest countries to experience the COVID-19 outbreak, quickly becoming the country with the second highest number of COVID-19 infections after China. In response, South Korea carried out extensive virus testing and contact tracing. In cooperation with national-level efforts, most transplant programs adopted universal donor and recipient screening using reverse transcriptase polymerase chain reaction, in accordance with the Korean Transplantation Society recommendation. Thus, national kidney transplant activities in South Korea remained stable for both living and deceased donor transplantation compared with the same period during the previous year (Table 1).

During these unprecedented times, little is known about the safety of kidney transplantation. However, delaying or halting of kidney transplantation is not a safe option for patients with end-stage renal disease. Because they still