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BK polyomavirus infection following COVID-19 infection in renal transplant recipients: a single-center experience

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Coronavirus disease 2019 (COVID-19) has affected the transplantation community worldwide. Reports of transplant patients acquiring COVID-19 infections are extensive with diverse mortality rates [1]. Follow-up studies of COVID-19 in transplant communities are lacking. There are limited data on the association of the BK polyomavirus (BKPyV) with active COVID-19 infection in kidney transplant recipients (KTRs) [2,3]. Currently, theoretical concerns exist related to graft dysfunction or loss during the post-COVID-19 follow-up period in KTRs. This study aimed to explore the clinical profile, outcomes, and follow-up experiences of KTR patients who developed BKPyV after COVID-19. This was a single-center retrospective analysis of a study approved by our Institutional Ethical Board (ECR/143/Inst/GJ/2013/RR-19 with application No: EC/App/20Jan21/08) and was conducted in compliance with the Declaration of Helsinki. KTR patients admitted for COVID-19 infection during the study period from June 2020 to December 2020 who developed BKPyV after a positive COVID-19 diagnosis were included. We conducted extended and close monitoring and follow-up of the cohort in the physical, clinical, and psychological domains. Follow-up BKPyV testing was conducted at 1-month after discharge, followed by every 3 months thereafter. Testing also was performed in cases of increasing creatinine.

We identified 11 cases of BKPyV after infection in 167 total COVID-19 KTR cases. Table 1 shows the overall summary of the study. The median age of the cohort was 45 years (range, 29–56 years), with male predominance (90.9%). The majority of the cohort had comorbidities (72.7%), underwent live-related-donor transplantation (72.7%), and received thymoglobulin (81.8%) upon admission for COVID-19. The baseline median serum creatinine was 1.44 mg/dL (range, 1.3–1.9 mg/dL). COVID-19 severity was categorized as mild (9%), moderate (45%), and severe cases (46%) [4]. Acute kidney injury was reported in all cases, and acute respiratory distress syndrome developed in 18.2% of KTR patients, with one fatality during COVID-19 admission. Five cases (45.5%) received steroids during acute COVID-19 infection. At baseline, no cases showed BKPyV in the blood. Baseline polymerase chain reaction (PCR) urine testing of the cohort

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Table 1. Characteristics of the cohort with BKPyV following SARS-CoV2 infection

Characteristic	Case No.										
	1	2	3	4	5	6	7	8	9	10	11
Age (yr)	57	23	55	41	28	35	29	45	47	56	69
Sex	Male	Male	Male	Male	Male	Male	Male	Male	Male	Female	Male
Body mass index[a] > 30 kg/m^2	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes
Blood group	B+	B+	A+	O+	O+	B+	B+	B+	AB+	A+	B+
Comorbidity	DM, obesity	No	DM, HTN, obesity	HTN	No	HTN, obesity	No	HTN, obesity	HTN, obesity	HTN, CMV, TB, obesity	DM, HTN, obesity
Cause of end-stage renal disease	DM	Unknown	DM	Unknown	CGN	HTN	Unknown	Obstructive	Unknown	HTN	DM
Time from transplantation to COVID-19 detection (mo)	12	4	26	64	5	66	26	27	3	15	25
Transplant type	Living related	Living related	Living related	Living related	Deceased donor	Living related	Living related	Deceased donor	Living related	Living related	Deceased donor
Induction agents	ATG	ATG	ATG	ATG	IL-2	ATG	ATG	IL-2	ATG	ATG	ATG
Maintenance immunosuppression	S + Tac + MMF	S + Tac + MMF	S + Tac + MMF	S + Tac	S + Tac + MMF	S + Tac + AZA	S + Tac + MMF	S + Tac + MMF	S + Tac + MMF	S + Tac	S + Tac + MMF
Tac level (ng/mL)	8	7.2	6	5.2	8	4.2	NA	8	9.2	7.4	6.2
Baseline serum creatinine (mg/dL)	1.4	1.3	0.9	1.3	1.4	1.5	2.5	2	1.6	1.4	2.2
AKI during admission	1	1	1	1	1	2	1	1	HD	1	3
Follow-up creatinine (mg/dL)	1.4	1.2	1.1	1.3	1.4	1.5	2.2	2	3.1	1.6	HD
History of antirejection therapy	No	No	No	No	No	No	No	No	No	No	No
Presenting complaint	Fever	Fever, cough, dyspnea	Fever, cough, dyspnea, diarrhea	Cough, dyspnea	Cough	Dyspnea	Cough, dyspnea	Fever, cough	Fever, cough, dyspnea, diarrhea	Fever, cough, dyspnea	Fever, cough, dyspnea
COVID-19 severity	Mild	Moderate	Severe	Moderate	Moderate	Severe	Moderate	Moderate	Severe	Severe	Severe
Radiological abnormalities at admission	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Duration of hospital stay (day)	5	7	9	9	8	11	6	7	14	10	12
Anti COVID-19 therapy	Azithromycin	0	Steroids, remdesivir	0	R	Steroids, remdesivir	0	R	Steroids, remdesivir, plasma therapy	Steroids, remdesivir, plasma therapy, Tocilizumab	Steroids, remdesivir
Change in immunosuppression	MMF/CNI	MMF/CNI	MMF/CNI	CNI	MMF/CNI	AZA/CNI	MMF/CNI	MMF/CNI	MMF/CNI	CNI	MMF/CNI
Follow-up after BKPyV diagnosis (mo)	10	9	8	8	7	7	6	5	2	5	1
BKPyV quantitative (copies/mL)											

(Continued to the next page)

Table 1. Continued

Characteristic	Case No.										
	1	2	3	4	5	6	7	8	9	10	11
Baseline											
Blood	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Urine	63,795,828	ND	ND	ND	ND	2254	ND	ND	ND	ND	ND
Acute COVID-19											
Blood	41,746	30,686,658	77	294	1,878	280	7,800	89	2,509	240,900	20,364
Urine	1,898,962,063	100,846,288,896	4,433,366	3,313	-	7,602	323,136	198,681,183	2,460,617	35,608,162	150,220,635
Follow-up COVID-19											
Blood	104	ND	ND	ND	ND	ND	ND	ND	ND	ND	NA
Urine	331,931	2,077	ND	ND	ND	ND	ND	249,519,444	15,971	ND	
Immunosuppression modification for BKPyV	MMF stopped	MMF stopped	MMF tapered	CNI tapered	MMF stopped	AZA stopped	MMF stopped	MMF tapered	MMF stopped	MMF stopped	MMF/CNI stopped
Outcome and follow-up	Uneventful	Uneventful	Uneventful	Uneventful	Uneventful	Uneventful	Uneventful	Uneventful	Died 1 mo postdischarge	Uneventful	Died at day 14

AKI, acute kidney injury; ATG, thymoglobulin; AZA, azathioprine; BKPyV, BK polyomavirus; CGN, chronic glomerulonephritis; CMV, cytomegalovirus; CNI, calcineurin inhibitors; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; F, female; HD, hemodialysis; HTN, hypertension; IL-2, interleukin 2 blocker; M, male; MMF, mycophenolate mofetil; NA, not available; ND, not detected; O, other supportive therapy; R, remdesivir; S, steroid; SARS-CoV2, severe acute respiratory syndrome coronavirus 2; Tac, tacrolimus; TB, tuberculosis.
[a]Body mass index value > 30 kg/m^2 was defined as obesity.

did not detect BKPyV in most cases (81.8%). Table 2 shows the laboratory parameters of the cohort. The median BKPyV blood and urine PCR results during acute COVID-19 infection were 2,509 copies/mL (range, 280–41,746 copies/mL) and 4,433,366 copies/mL (range, 7,602– 198,681,183 copies/mL), respectively.

The follow-up period after BKPyV diagnosis was 7 months (range, 5–8 months). BKPyV was detected in the blood during the follow-up period in only one patient. The BKPyV PCR urine values of the cohort were less than those detected in 63.6% of the follow-up cases. No graft loss or graft dysfunction was reported in the cohort. No patient developed sensitization, urine microhematuria, or proteinuria during the follow-up period. Radiological resolution [5] of COVID-19 infection was defined as the absence of any chest radiographic abnormality potentially related to the infection; this type of resolution was seen in 91.6% of KTR cases and resolved after a median of 3 months of follow-up. No multisystemic sequelae were reported. One case was readmitted 1 week after discharge and died due to secondary fungal infection (aspergillosis) after 1 month.

Our report could simply indicate that the natural history and course of BKPyV happened to coincide with COVID-19 infection, and there might be no actual association between the two; however, reactivation of viruses like BKPyV is a high-risk factor for graft loss in transplant patients [6]. BKPyV causes complex changes in immunity and weakens the immune response, which could potentially aggravate the immune/graft injury often present in COVID-19 infection [7]. Elevated levels of inflammatory cytokines in COVID-19 infection can lead to greater transcription of the BKPyV genome [8]. The use of thymoglobulin as an induction agent could have been a confounding factor for BKPyV, but the institutional protocol of using a low dosage of thymoglobulin (1.5 mg/kg) hinders this connection. Moreover, at our center, the incidence of BKPyV in COVID-19 patients was 6.6% (11 of 167 patients), which was higher than the rate reported in normal follow-up or in non-COVID-19 admissions (1.3%). While we were unable to show a definite association of BKPyV with COVID-19 infection, the use of steroids to treat these patients and COVID-19 infection itself are both risk factors for an increase in number of BKPyV in KTRs. Therefore, we suggest screening for BKPyV in COVID-19 patients.

One limitation of this study was its small sample size. To date, this is the largest cohort of KTRs with BKPyV after

Table 2. Laboratory and inflammatory markers in the cohort at admission due to COVID-19 infectio

Laboratory parameter (normal range)	Case No.										
	1	2	3	4	5	6	7	8	9	10	11
Hemoglobin (13–16 g/dL)	10.6	12.5	13.1	11.4	14.8	14.4	17.1	9.3	17.1	8.5	7.8
Total leukocyte count (4–11 × 10^3 cells/L)	3,280	4,990	2,660	5,370	5,040	12,400	6,800	4,850	11,830	4,000	13,600
Polymorphs (60%–70%)	71	75	55	72	62	78	90	74	8	69	83
Lymphocyte (25%–33%)	26	23	42	25	35	19	8	23	16	27	15
Platelet counts (150–400 × 10^9 cells/L)	441	190	272	178	244	261	124	282	285	178	279
D-dimer (200–500 ng/mL)	3,360	630	9,870	NA	360	2,450	290	1,110	2,330	NA	2,880
Procalcitonin (<0.5 ng/mL)	0.05	0.05	0.05	NA	0.05	0.27	0.06	0.31	11.6	7.9	NA
Highly sensitive C protein (0–10 mg/L)	29	30.9	4.8	6.1	21.8	51.4	42.1	74.2	210	NA	189
Aspartate transferase (0–40 IU/L)	59	42	30	18	24	32	19	25	18	40	11
Interleukin 6 (<7 pg/mL)	8.2	58.3	NA	1,531	NA	NA	25.7	14.5	24.1	NA	470
Lactate dehydrogenase (100–190 IU/L)	387	510	272	322	391	523	550	292	NA	NA	534
Ferritin (13–400 ng/mL)	69.0	998.0	232.0	178.0	64.0	477.0	120.0	311.0	373.0	NA	465.0
Serum albumin (3.2–5.0 g/dL)	3.7	2.8	3	3.1	2.9	2.9	3.4	2.8	3.0	3.1	3.1
Blood urea nitrogen (13–45 mg/dL)	44	45	33	41	54	33	48	59	81	22	69

COVID-19, coronavirus disease 2019; NA, not available.

COVID-19 infection.

In summary, we report BKPyV following COVID-19 with no graft loss during the follow-up period. We suggest screening for BKPyV in all renal transplant patients with active COVID-19 infection (especially in patients with a history of BKPyV and in severe COVID-19 infection) as a safe option to avoid complications.

Conflicts of interest

All authors have no conflicts of interest to declare.

Authors' contributions

Conceptualization, Data curation, Formal analysis, Investigation: All authors
Writing–original draft: All authors
Writing–review & editing: All authors
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