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LETTER TO THE EDITOR

Belatacept, kidney transplantation and COVID-19: Successful management of the first reported case within the United Kingdom

Kidney transplant recipients may be at particular risk of acquiring SARS-CoV-2 infection with poor outcomes.[1] In a recent case report[2] it was hypothesized that kidney transplant recipients on maintenance belatacept, a cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) fusion protein, have a milder disease course due to belatacept mitigating the cytokine storm and resultant acute respiratory distress syndrome which have been linked to severity of COVID-19.[3] Here we present the first reported case in the United Kingdom of a kidney transplant patient on belatacept who on the contrary developed a severe COVID-19 pneumonia requiring intensive care admission and intubation.

Our patient is a 53-year-old man with end-stage renal disease secondary to polycystic kidney disease on mycophenolate mofetil (MMF) 250 mg twice daily and prednisolone (5 mg daily) along with monthly intravenous belatacept infusions (5 mg/kg) for the last 8 years, used due to post-transplant tacrolimus induced thrombotic microangiopathy (TMA). His last dose of belatacept was on 11th March. Baseline serum creatinine was 204 μmol/L (2.31 mg/dL) giving an eGFR of 31 mL/min. Six days after the last dose he developed a symptomatic cough (17th March) with gradually worsening shortness of breath followed by hospital admission (12th April). There was no history of travel or exposure to people with confirmed or suspected COVID-19. His body mass index was 29 kg/m^2. On admission his oxygen saturation was 94% on 60% oxygen as shown in Table 1. His due dose of belatacept (8th April) was withheld, MMF was also withheld as per British Transplant Society guidelines[4] and prednisolone was increased to 20 mg once a day.

Two serial SARS-Cov-2 reverse transcriptase-polymerase chain reaction (RT-PCR) swabs came back positive and the laboratory parameters and chest X-ray were also suggestive of COVID-19 (Table 1, Figure 1). The clinical condition started to deteriorate, and he required intubation in intensive care for 4 days. Other complications were a superadded bacterial pneumonia, urinary tract infection requiring antibiotics and a resolving acute kidney injury that did not require biopsy.

After transfer from intensive care to the ward, MMF was restarted and he was discharged after a negative repeat SARS-CoV-2

TABLE 1 Important laboratory and vital parameters, 60% FiO2 was through a humidified venturi system

Test	Units	Range	13/4	14/4	15/4	19/4	23/4	25/4	26/4
White cell count	$\times10^9$/L (/μL)	4.0-11.0 (4000-11000)	9.6	10.0		8.8	10.8	22.8	20.8
Neutrophil count	$\times10^9$/L (/μL)	2.0-7.5 (2000-7500)	8.2	8.7		7.1	8.7	20.1	18.6
Lymphocyte count	$\times10^9$/L (/μL)	1.0-4.0 (1000-4000)	0.8	0.6		0.7	1.0	0.9	0.7
D-Dimer	ng/mL	<500				1194	1795		1621
CRP		<5	107	88	48	57	26	106	111
Creatinine	μmol/L (mg/dL)	59-104 (0.67-1.18)	268 (3.03)	239 (2.70)	206 (2.33)	205 (2.32)	188 (2.1)	210 (2.3)	216 (2.4)
Ferritin	ng/mL	30-400			1050	1181	1077		1628
Procalcitonin	ng/mL	0.5			0.2				0.3
Oxygen Saturation	(%)	94-96	94	93	84	93	92	94	94
FiO_2	(%)	21-100	60	60	60	35	24	Air	Air

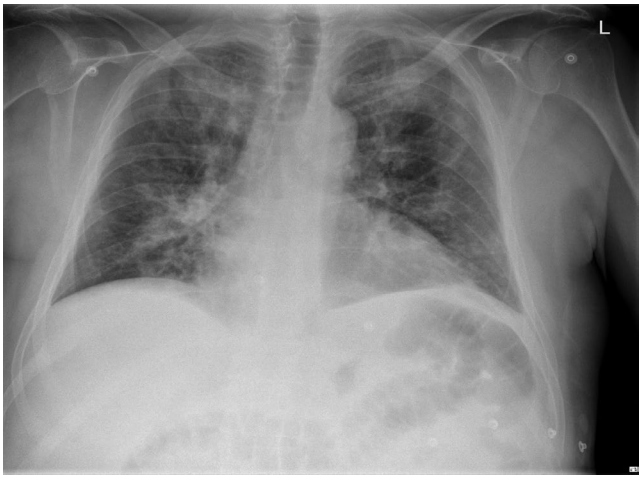

FIGURE 1 Chest X-ray of the patient showing peripheral interstitial infiltrates bilaterally

RT-PCR (Figure 2). The belatacept infusion was restarted on the 7th May and he is currently doing well and is being closely monitored as an outpatient (Figure 2).

Cytotoxic T cells are central to both transplant rejection and anti-viral immune responses. Drugs that prevent rejection may therefore also impair anti-viral responses. The immune response to SARS-CoV-2 appears to be a typical anti-viral immune response[5,6] and we suggest that avoidance of belatacept until viral clearance has been achieved is likely to be safest strategy. In our patient the clinical course was severe and unlike the case reported by Marx et al,[2] the option of restarting a calcineurin inhibitor was not available; however, recovery was achieved, despite belatacept being withheld. We postulate that belatacept may not have an important role in mitigating cytokine storm and parameters such as age, immunophenotype, and baseline co-morbidities play a dominant role in recovery from COVID 19 infection.

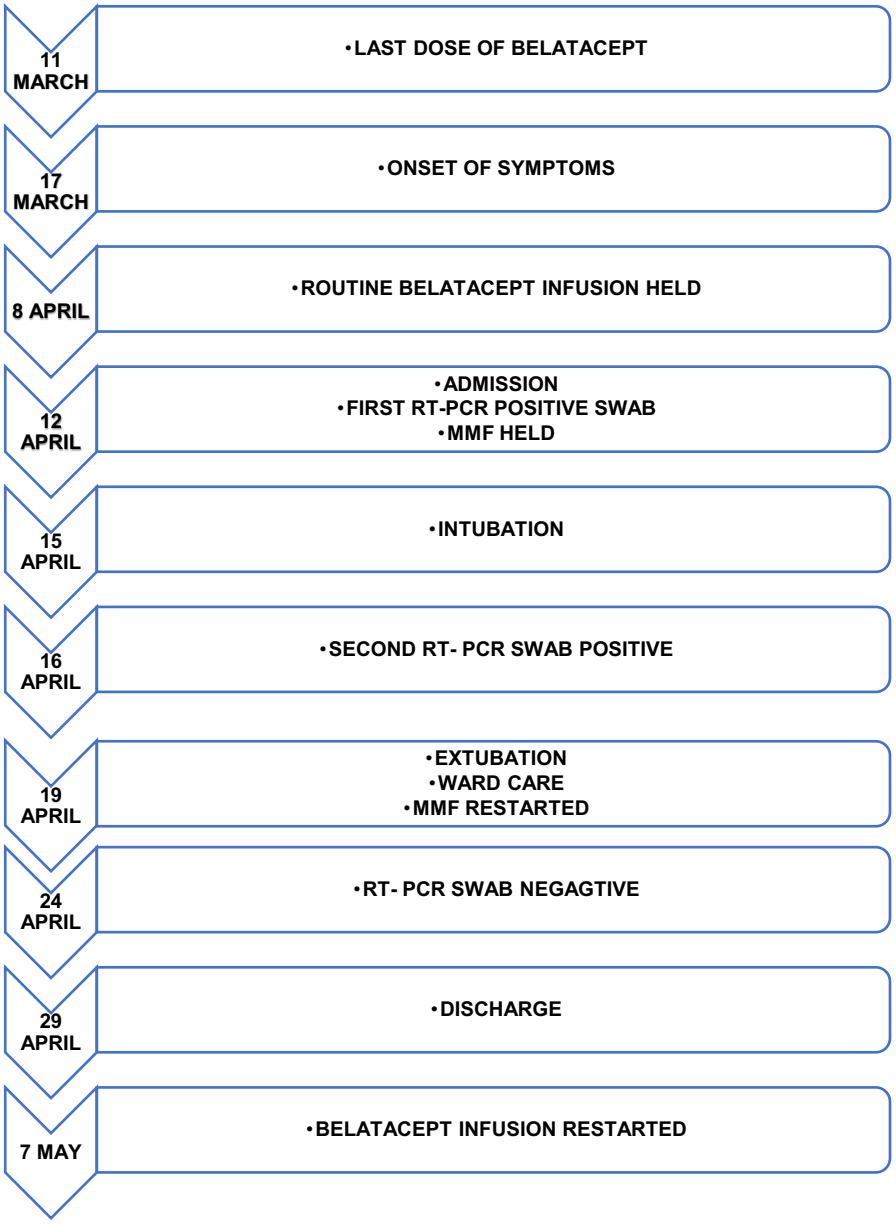

FIGURE 2 Treatment timeline

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

All authors contributed equally in all aspects of preparation of this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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