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ABOUT COVER

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CASE REPORT

Renal transplantation in gigantism: A case report

Jeevan Prakash Gopal, Sotirios Charalampidis, Jinpo Xiang, Frank J M F Dor, Vassilios E Papalois

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Abstract

BACKGROUND

Gigantism, characterized by excessive growth and height is due to increased secretion of growth hormone, most commonly from a pituitary adenoma. In addition to the surgical and anesthetic complexity, the extreme stature of these patients presents a unique challenge for kidney transplantation in deciding whether to proceed with a single or dual kidney transplantation. The lack of relevant literature further adds to the dilemma.

CASE SUMMARY

A 45-year-old patient with untreated gigantism and end stage renal failure on renal replacement therapy was waitlisted for a deceased donor dual kidney transplantation due to the extreme physical stature (Height-247 cm and weight-200 kg). He was offered 2 kidneys from a 1-0-1 HLA mismatched 24-year-old DCD donor (Height-179 cm and weight-75 kg), and was planned for a bilateral retroperitoneal implantation into the recipient external iliac vessels. The immunosuppression consisted of alemtuzumab induction (50 mg) and steroid-free maintenance with tacrolimus. The donor's right kidney was uneventfully implanted extra-peritoneally into the right external iliac vessels. On contralateral exposure, the left common and external iliac arteries were ectatic and frail. A complex vascular reconstruction was not preferred in order to preserve the arterial supply to the left lower limb, to minimise the cold ischemia time and prevent additional warm ischemic insult to the second kidney. Hence, it was decided not to proceed with dual transplantation. Amidst concerns of nephron mass insufficiency, the graft function was remarkable with a serum creatinine of 120 μmol/L within a month from transplantation and 94 μmol/L at 1-year post transplantation, and without proteinuria.

CONCLUSION
To our knowledge, this is the first case report on kidney transplantation in gigantism. Although it is believed that dual kidney transplantation is ideal, a single kidney transplantation from an appropriately selected donor can provide sufficient functioning nephron mass in patients with gigantism.

Key Words: Gigantism; Giantism; Renal transplantation; Kidney transplantation; Pituitary adenoma; Case report

Core Tip: We report a patient with untreated pituitary gigantism with end stage renal failure due to IgA nephropathy with secondary focal segmental glomerular sclerosis who underwent a successful deceased donor kidney transplantation. We have described the intra-operative challenges in deciding whether to proceed with a single kidney transplantation or dual kidney transplantation. To the best of our knowledge this is the first case report on kidney transplantation in gigantism.

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INTRODUCTION

Gigantism is a disorder resulting from increased growth hormone secretion before the fusion of growth plate, most often due to a pituitary adenoma and is characterized by excessive growth and height. In addition to the surgical and anesthetic complexity, the extreme stature of these patients presents a particular challenge for kidney transplantation in deciding whether to proceed with a single or dual kidney transplantation. So far there is no literature on kidney transplantation in patients with gigantism. To our knowledge, we are the first to report a patient with untreated pituitary gigantism characterized by uniquely extreme physical size and stature who underwent a successful kidney transplantation for end stage renal failure and discuss the dilemmas involved in his management.

CASE PRESENTATION

Chief complaints

Our patient, a 45-year-old African male presented with end stage renal failure and was awaiting a kidney transplant.

History of present illness

The end stage renal failure was due to IgA nephropathy which was biopsy proven and with secondary focal segmental glomerular sclerosis. He was established on haemodialysis.

History of past illness

He was diagnosed in his early teenage years to have pituitary gigantism but was left untreated.

Personal and family history

There were no relevant histories.

Physical examination

His physical stature [Height = 247 cm, weight = 200 kg, body mass index (BMI) was 33 kg/m^2, and body surface area (BSA) with the DuBois formula = 3.7 m^2], was twice than the normal upper limit.

Laboratory examinations

The laboratory investigations were not relevant apart from deranged kidney function due to end stage renal failure.

Imaging examinations

A pre-transplant computed tomography (CT) scan of the abdomen and pelvis showed normal iliac vessels bilaterally.

Multidisciplinary expert consultation

There was a therapeutic dilemma as to whether a single kidney transplantation would be sufficient for a patient of his body surface to alleviate his kidney failure to a degree that would not require further renal replacement therapy. With the above dilemma into consideration the patient was added to the United Kingdom deceased donor kidney transplant waiting list for dual kidney transplantation from a single deceased donor after discussion in our multidisciplinary team (MDT) meeting and approval by the NHS Blood and Transplant's Kidney Advisory Group.

Transplant characteristics

Less than a year after being waitlisted and after having received a few offers from extended criteria donors that were deemed unsuitable, the patient received and accepted a deceased donor dual kidney transplant offer from a 24-year-old male donation after circulatory death (DCD) donor who suffered irreversible hypoxic brain injury following a road traffic accident. The donor's past medical history was insignificant and had normal kidney function. His height was 179cm, weight was 75kgs, BMI was 23 kg/m^2, and BSA with the DuBois formula was 1.9 m^2 (almost half of our prospective recipient). Furthermore, there was a 1-0-1 HLA mismatch between the donor and recipient, the latter of which had a calculated reaction frequency of 0% (and therefore only a virtual crossmatch was performed). Immunosuppression consisted of induction with a depleting monoclonal antibody, alemtuzumab (50 mg) and steroid-free maintenance with tacrolimus as the only immunosuppressant. The organ retrieval in the donor hospital was uneventful.

Customised anaesthetic protocol

For the recipient, a customised anaesthetic protocol was implemented based on previous general anaesthetic experience with the patient. He was ventilated using a large (size 6) oropharyngeal airway and a large (size 6) face mask. A long Macintosh blade and size 10 endotracheal tube was used for intubation. Patient was anaesthetized on a hover mattress to enable safe transfer to the operating table, which can take up to 300 kgs body weight. The only issue was the patient's height; two table extensions were added to the operating table on either side and an instrument trolley was used to support the feet (Figure 1).

FINAL DIAGNOSIS

A bilateral extraperitoneal implantation in to the recipient's external iliac vessels was chosen as the preferred implantation technique. Initially the patient's right external iliac vessels were exposed and an uneventful implantation of the donor's right kidney was successfully completed with intraoperative urine production from the transplanted kidney. The cold ischemia time was 9 h and 52 min. On subsequent exposure of the recipient's contralateral iliac fossa, the left common and external iliac arteries were noted to be significantly ectatic and frail, which was not apparent from the pre-operative CT scan. In addition there were abnormal intraoperative Doppler signals (monophasic signals).

TREATMENT

Implanting the donor's left kidney in to the right common/internal iliac vessels was one of the options, but it would involve clamping the right common iliac artery which would potentially add an additional ischemic insult to the transplanted kidney. Implanting the donor's left kidney into the left internal iliac vessels or intra-peritoneal implantation into the aorta/inferior vena cava were the other options. In order not to further extend the duration of the procedure and the resultant cold ischemia time by performing a complex vascular reconstruction/implantation with potential compromise to the arterial supply of the recipient's left lower limb and in view of the already completed successful single kidney implantation of the donor's right kidney, the decision was made to not to proceed with the dual kidney implantation. The donor kidney was of average size without having taken proper measurements. According to the national allocation policy of NHS Blood and Transplant, the donor's left kidney was subsequently offered to another patient on the waiting list.

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Figure 1 Operating table with extensions on either side and an instrument trolley at both the foot end and head side.

OUTCOME AND FOLLOW-UP

The patient was extubated at the end of the operation and was cared in intensive care unit for one day and subsequently stepped down to our high dependency unit. There was primary graft function and following an overall uneventful recovery, he was discharged from the hospital at day 15, with an improving estimated glomerular filtration rate (eGFR) of 44 mL/min/1.73 m^2. Following discharge, his serum creatinine continued to improve to 120 μmol/L within a month from the procedure. His serum creatinine remained stable throughout the first year post-transplant and without proteinuria (Figure 2).

DISCUSSION

Although giants are depicted in literature as individuals with lionized capabilities, the description of patients with gigantism in medical literature is very limited due to the rarity of the condition. Overproduction of growth hormone by a pituitary adenoma or pituitary hyperplasia can lead to pituitary gigantism. They can be either sporadic or can occur as a part of several genetic disorders such as multiple endocrine neoplasia type 1, McCune-Albright syndrome and carney complex[1-5]. There is no bibliographic report of pituitary gigantism patients that required renal transplantation for end stage renal failure.

The underlining challenge in such patients with extreme stature is to ensure that the physiological capacity and the functioning nephron mass of the donor organ can meet the increased metabolic needs of this unique recipients so to alleviate their need for renal replacement therapy and have a significant positive impact on their overall health, quality of life, and life expectancy. Recent studies have confirmed that the graft kidney volume/recipient BSA ratio along with the donor age and recipient's gender are independent predictors of recipient GFR in the early post-transplant period[4-6]. Considering the above concern, the option of synchronous dual deceased kidney transplantation in such extreme stature patients seems reasonable and needs to be considered at the time of wait listing them for a deceased donor kidney transplant and weighted against depriving the second graft from another potential recipient given the current scarcity of deceased donor organs.

Although there are some variations between jurisdictions in the allocation policy of kidneys for dual kidney transplantation, the common theme is to allocate kidneys from extended criteria donors for dual transplantation[7]. There was a special consideration for our patient due to his body habitus following MDT discussions and discussions in the national kidney advisory group of NHS Blood and Transplant, and hence was listed for dual kidney transplantation and ultimately received an offer from a young donor. Various implantation techniques have been described for dual kidney transplantation[7]. Although it has been reported that the complication rates for bilateral and unilateral placement of kidneys are similar[8,9], a bilateral extraperitoneal approach was chosen based on the operating surgeon's preference.

Vascular calcifications and atherosclerosis are well established complications of end stage renal failure[10], but it is unusual for isolated arterial aneurysm or ectasia to occur due to renal failure. Despite the intra-operative finding of ectasia and frailty of the left common and external iliac arteries, we still had several options for proceeding with dual kidney transplantation. Implanting the donor's left kidney in to the right common/internal iliac vessels was one of the options, but it would involve clamping the right common iliac artery which would potentially add an additional ischemic insult to the transplanted kidney. Implanting the donor's left kidney into the left internal iliac vessels or intraperitoneal implantation into the aorta/inferior vena cava were the other options. In order not to further extend the duration of the procedure and the resultant cold ischemia time by performing a complex

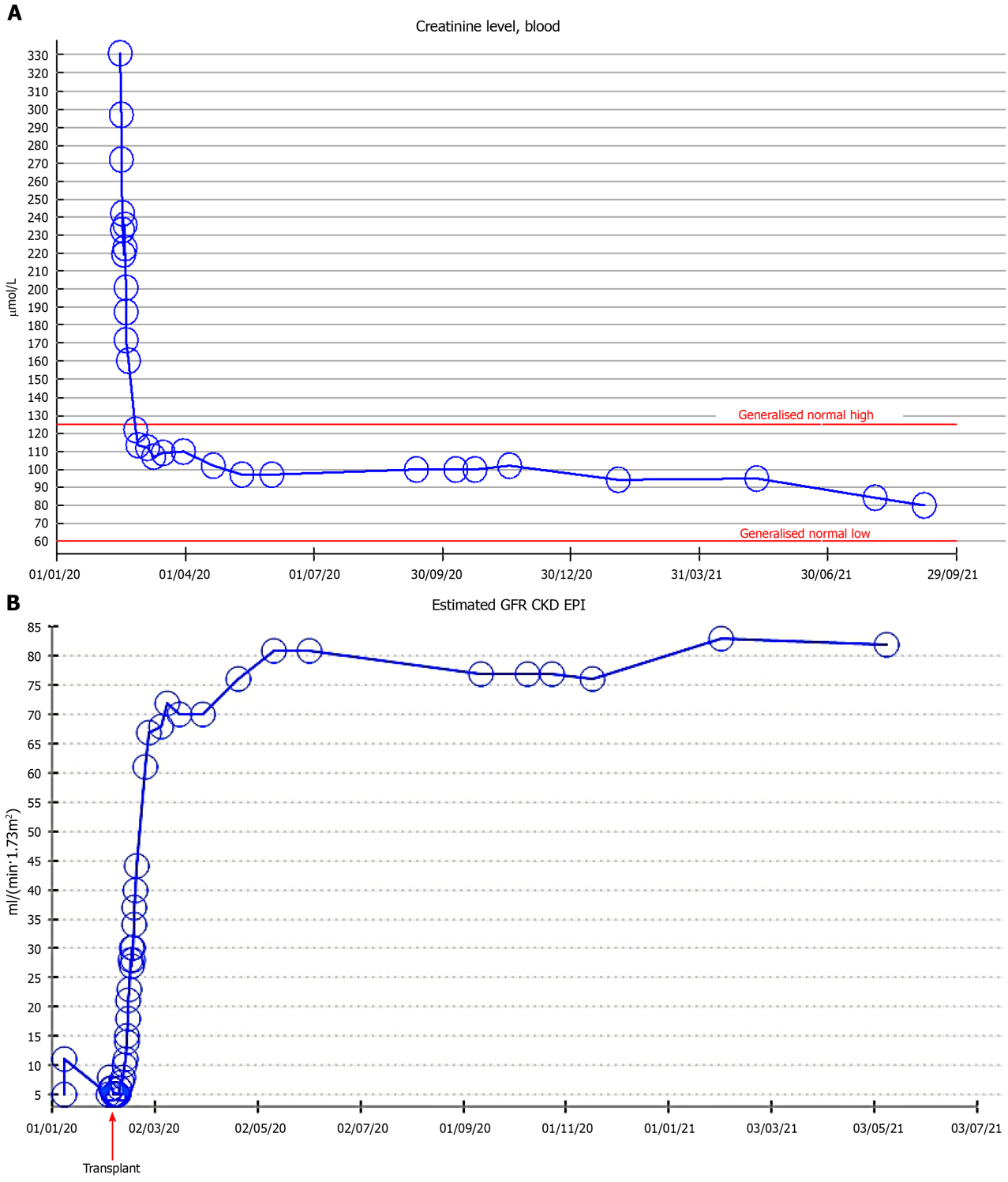

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Figure 2 Serum creatinine and estimated glomerular filtration rate trend post-transplant. A: Serum creatinine; B: Estimated glomerular filtration rate. GFR: Glomerular filtration rate; CKD-EPI: Chronic kidney disease epidemiology collaboration.

vascular reconstruction/implantation with potential compromise to the arterial supply of the recipient's left lower limb and in view of the already completed successful single kidney implantation of the donor's right kidney, the decision was not to proceed with the dual kidney implantation.

Although it has been reported that transplanting small kidneys in to large recipients (donor kidney weight/recipient body weight < 2 g/kg) causes hyperfiltration and results in decreased creatinine clearance and proteinuria 6-months after transplantation[11], in our patient, the single kidney graft has proved sufficient enough to keep him off renal replacement therapy and with normal serum creatinine levels as noted at 1-year post-transplant, and without proteinuria. Additionally, the second kidney from the same deceased donor was eventually implanted to a different recipient in our centre who benefited

from an equally good graft function.

Especially in rare cases such that of our patient with extreme physical stature and significant comorbidities one cannot overemphasize the importance of a detailed preoperative assessment and preparation. There are a few general considerations for people with gigantism undergoing transplantation such as a thorough multidisciplinary work up including anaesthetic pre-assessment before wait listing, the design of a customised anaesthesia protocol, modification of the operating table, and arranging an appropriately sized bed post-operatively. Furthermore, every individual organ offer needs to be assessed for suitability in regards to the donor's past medical history, renal function, age, as well as the body mass index and potentially total kidney volume calculated through any appropriate donor imaging available at the time.

CONCLUSION

This is the first case report on kidney transplantation in gigantism. Although it is believed that dual kidney transplantation is ideal for such patients based on body surface area, a single kidney transplantation from an appropriately selected donor can provide sufficient functioning nephron mass in patients with gigantism.

FOOTNOTES

Author contributions: Gopal JP, Charalampidis S and Xiang J wrote the manuscript; Gopal JP revised the manuscript; Papalois VE performed the transplant; Papalois VE and Dor FJMF made critical corrections to the manuscript; all the authors reviewed and approved the final version.

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CASE REPORT

Potential importance of early treatment of SARS-CoV-2 infection in intestinal transplant patient: A case report

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Abstract

BACKGROUND

Predispositions for severe coronavirus disease 2019 (COVID-19) are age, immunosuppression, and co-morbidity. High levels of maintenance immunosuppression render intestinal transplant (ITx) patients vulnerable for severe COVID-19. COVID-19 also provokes several gastroenterological pathologies which have not been discussed in ITx, so far.

CASE SUMMARY

During the second European COVID-19 wave in November 2020, an ITx recipient was admitted to the hospital because of electrolyte disturbances due to dehydration. Immunosuppression consisted of tacrolimus, azathioprine, and low-dose corticosteroids. During hospitalization, she tested positive on screening COVID-19 nasopharyngeal polymerase chain reaction swab, while her initial test was negative. She was initially asymptomatic and had normal inflammatory markers. Tacrolimus levels were slightly raised, as Azathioprine was temporarily halted. Due to elevated D-dimers at that time, prophylactic low-molecular weight heparin was started. Seven days after the positive test, dyspnea, anosmia, and C-reactive protein increase (25 mg/L) were noted. Remdesivir was administered during 5 d in total. High stomal output was noted in two consecutive days and several days thereafter. To exclude infection or rejection, an ileoscopy and biopsy were performed and excluded these. Four weeks later, she was discharged from the hospital and remains in good health since then.

CONCLUSION

Early eradication of severe acute respiratory syndrome coronavirus 2 in ITx recipients may be warranted to prevent acute rejection provocation by it.

Key Words: COVID-19; Intestinal transplantation; Outcome; SARS-CoV-2; Treatment; Case report

Core Tip: Acute rejection is often seen in intestinal transplant (ITx) recipients due to the high immunogenicity of the intestinal graft. However, it might also be provoked by latent presence of viruses, due to the high immunosuppression needs. Recently, chronic latency of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the intestine has been shown. Hence, early recognition, eradication, and follow-up on intestinal biopsies in ITx recipients might be warranted to prevent the potential acute rejection provocation of the intestinal graft by SARS-CoV-2.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19), provoked by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), poses a major challenge in intestinal transplantation (ITx) due to the high immunogenicity of the graft, requiring high levels of immunosuppression. In the early phase of the pandemic, patients were treated with hydroxychloroquine[1]. The treatment of SARS-CoV-2 in transplant patients was altered over time in favor of dexamethasone, antivirals, or only supportive therapy[2-4]. Next to this, it is known that SARS-CoV-2 provokes gastroenterological manifestations, due to its invasion of the enterocytes[5]. It has recently been shown that SARS-CoV-2 remained latent present in the upper gastrointestinal tract, as well as in the small intestine, until at least 3 mo post-COVID-19 positivity[6]. Several other latent gastrointestinal tract viruses are known to be able to provoke acute rejection of the intestinal graft, due to the high immunosuppression needs in these ITx recipients[7,8]. To our knowledge, the influence of SARS-CoV-2-related gastroenterological manifestations in ITx patients or the provoked risk for rejection have not been elucidated so far.

CASE PRESENTATION

Chief complaints

We recently encountered a SARS-CoV-2 infection in a 41-year-old female ITx-recipient, acquired during hospitalization for dehydration and electrolyte disturbances, during the second European COVID-19 wave in November 2020.

History of present illness

She underwent an isolated intestinal re-transplantation, combined with a kidney, in August 2019 for chronic allograft enteropathy. After her re-ITx, she underwent a conversion of her terminal ileostomy to a low ileorectal anastomosis with protective loopileostomy on September 29, 2020.

History of past illness

Her first isolated ITx was in December 2004 for chronic intestinal pseudo-obstruction with recurrent catheter sepsis. In between the two ITx procedures, she was in good health and never encountered an acute rejection, until she developed chronic allograft enteropathy for which she was back on parenteral nutrition since February 2019.

Personal and family history

Negative.

Physical examination

On admission, on October 28, 2020, she was on tacrolimus (3.5 mg bidaily, target trough level: 7-8 μg/L), azathioprine (50 mg/d), and methylprednisolone (4 mg/d). She had no fever, respiratory issues, nor recent contact with a potential COVID-19 positive patient.

Laboratory examinations

She tested negative on SARS-CoV-2 on a nasopharyngeal polymerase chain reaction (PCR)-test (Figure 1). Her lab values revealed an acute deterioration of kidney function and electrolyte disturbances. Six days after admission, on November 3, 2020, she tested positive for SARS-CoV-2 on a screening PCR-test.

Imaging examinations

There were no clinical nor biochemical signs of infection or chest X-ray alterations.

FINAL DIAGNOSIS

The final diagnosis of this presented case is mild COVID-19.

TREATMENT

Azathioprine was temporarily halted, and tacrolimus levels slightly raised towards target trough levels of 8-9 μg/L. Prophylactic low-molecular weight heparin was started as D-dimers measured 4110 ng/mL (normal ≤ 500 ng/mL). She was transferred to the COVID-19 low-care ward of our hospital. Five days later, on November 8, 2020, her stomal output increased with 227% up to 2830 mL/24 h. As rejection was suspected, ileoscopy *via* the stoma was performed on November 9, 2020, and ileal biopsies were taken (Figure 2). These excluded inflammation or rejection. That same day, anosmia and mild dyspnea with normal oxygen saturation developed. Body temperature increased until 37.8 °C and C-reactive protein level was 25 mg/L (normal < 5 mg/L). Remdesivir was intravenously administered for 5 d with 200 mg as loading dose and 100 mg daily thereafter. After the remdesivir treatment was finished, azathioprine was restarted, and tacrolimus trough levels lowered to standard levels.

OUTCOME AND FOLLOW-UP

Weekly SARS-CoV-2 PCR remained positive, until a cycle threshold (Ct)-value of 39.22 was found, 4 wk after her first positive test, on November 30, 2020, and she was removed from the COVID-19 ward as the internal hospital protocol states when the Ct-value is > 29. Stomal output kept fluctuating for 1 mo, with several days of high output (> 1200 mL/24 h). With adequate fluid replacement, renal function remained stable, and the patient could be discharged on December 2, 2020 remaining in good health since then. SARS-CoV-2 PCR remained negative since then, and 3 mo after discharge from the hospital

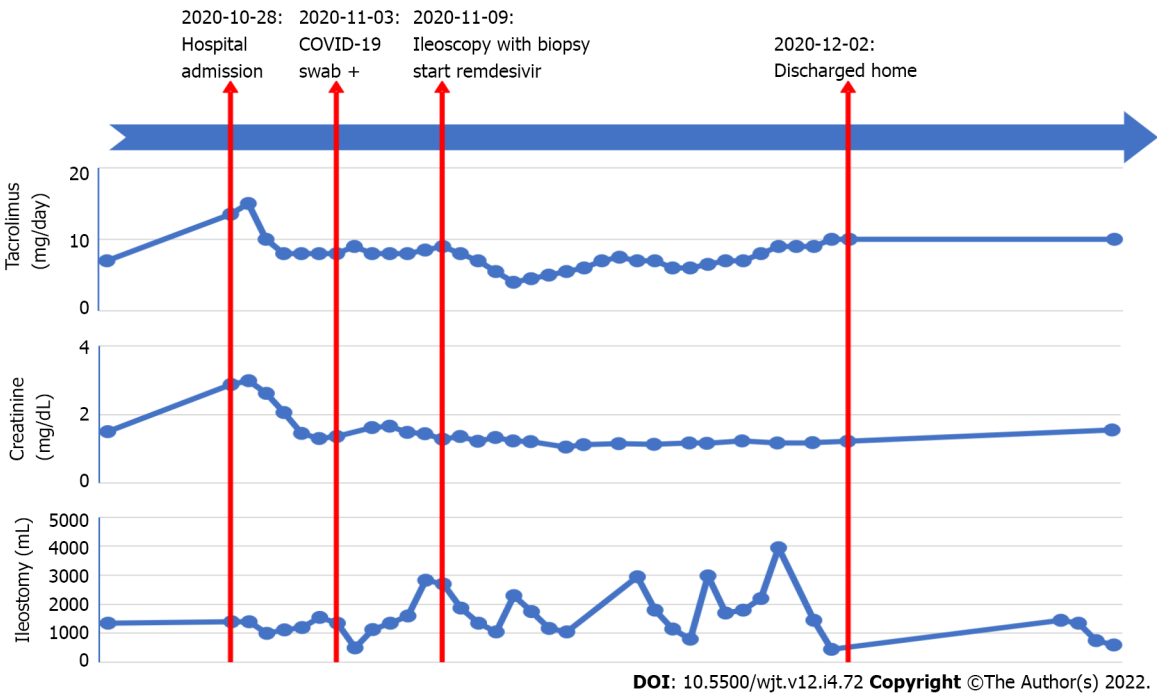

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Figure 1 Timeline of case report, with immunosuppressive regimen (total daily tacrolimus dosage; bidaily administration), serum creatinine (kidney function), and stomal output evolution. COVID-19: Coronavirus disease 2019.

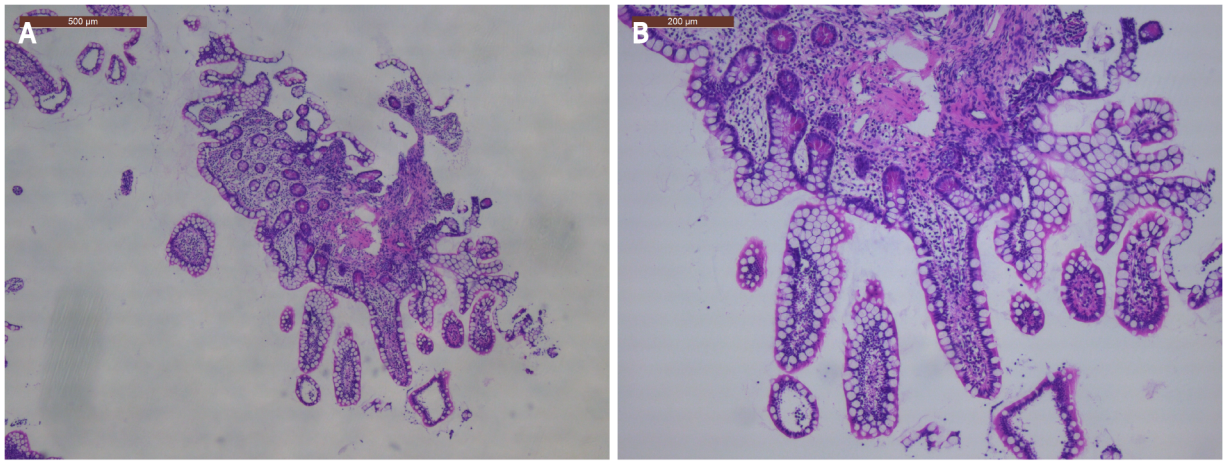

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Figure 2 Histology of the intestinal transplant biopsy showing normal intestinal mucosa, without arguments for rejection or infection. A: 500 µm; B: 200 µm.

SARS-CoV-2 immunoglobulin G (IgG) nucleocapsid antigen was negative. The patient gave informed consent, and ethical approval from the institutional review board was obtained (S64844).

DISCUSSION

We present the first report, to our knowledge, of mild COVID-19 in an ITx-patient treated with remdesivir, prophylactic low-molecular weight heparin, and temporary interruption of azathioprine. As according to the currently available evidence in transplant recipients, azathioprine was halted and tacrolimus slightly raised in return[9,10]. However, it has recently been shown that solid organ transplant recipients can also be successfully treated without adjustment of immunosuppressive therapy and without any antiviral treatment[4]. Our patient was preemptively treated with remdesivir as antiviral treatment. Up till now, there is not much yet known about remdesivir treatment in solid organ transplant recipients[11]. Recent reports have shown its tolerability and safety in kidney

transplant recipients, without effects on kidney or liver function[12,13]. However, it is strongly advised to monitor regularly liver biochemistry in patients treated with remdesivir, as hepatotoxic side effects have been described[11,14].

Although gastroenterological manifestations, including diarrhea, nausea, vomiting, and loss of appetite, are commonly seen in COVID-19 patients, symptomatology was mild in our case and limited to high stomal output[5,15,16]. These clinical symptoms might also be suggestive for an acute rejection in ITx recipients, which should be treated with an increase of immunosuppression or pulse corticosteroids, which is opposite in the case of an gastroenterological infectious process[8]. This symptomatic overlap renders the cause of the gastroenterological manifestations more difficult and hence influences the treatment strategy. If not treated promptly, acute rejection might eventually lead to intestinal graft loss[17]. Only endoscopic evaluation with histopathologic confirmation of acute rejection on biopsy can make a clear differentiation. A recent study showed that D-dimers > 1850 ng/mL, which was the case in our patient (up to 4110 ng/mL), is the best discriminator to find major intestinal mucosal abnormalities at endoscopy in COVID-19 positive patients[18].

It is known that viral entrance of SARS-CoV-2, by the angiotensin-converting enzyme 2 receptor, which is abundantly present in the enterocytes of the gastrointestinal tract, plays a major role[5,6,18]. This viral entrance provokes an acute inflammatory response, which coincides with ischemic damage due to the procoagulant state and endothelialitis, which has also been observed in ITx rejection[17,18]. Several other viruses have already been shown to mimic intestinal graft rejection by crypt apoptosis, such as cytomegalovirus, Epstein-Barr virus, adenovirus, and norovirus[7,8]. Close monitoring, during the postinfectious period of these viruses, is also important as the infection might provoke acute rejection of the intestinal graft[8]. For SARS-CoV-2, such a correlation has not been shown so far. However, as shown by Gaebler *et al*[6], SARS-CoV-2 can remain latent present in even asymptomatic patients at least 3 mo post-COVID-19[6]. As SARS-CoV-2 is able to enter the enterocytes by the angiotensin-converting enzyme 2-receptor and provoke an acute inflammatory response, it is hypothetically possible that SARS-CoV-2 might mimic or provoke acute rejection of the intestinal graft in ITx recipients as well. As such, follow-up of SARS-CoV-2 antigen on routine or screening , re-jection/infection suspicion, biopsies of the intestinal allograft might be performed in previous, current or suspected COVID-19 positive ITx recipients, as is currently the case for cytomegalovirus[7]. Early treatment and eradication of intestinal SARS-CoV-2 may be warranted to prevent the potential acute rejection mimicry or provocation.

SARS-CoV-2 nucleocapsid (N) antibodies assay, on the Abbott Architect system, was negative in our patient, despite SARS-CoV-2 positive PCR 3 mo earlier. However, it has been shown that SARS-CoV-2 IgG anti-N are positive in only 62% of SARS-CoV-2 PCR positive transplant recipients 1-2 mo post-infection, whilst these are decreasing towards only 55% at 3-4 mo and even 38% at 5-7 mo post-infection. This decline in anti-N is mainly seen in mild disease form[19]. SARS-CoV-2 spike (S) antibodies, on the contrary, are more durable with IgG anti-S present in 92% at 1-2 mo, 84% at 3-4 mo, and even 76% at 6-7 mo post-infection in transplant recipients[4]. Next to this, the analysis was run on the Abbott Architect system, of which it has been shown that it is less sensitive in transplant recipients, in comparison to non-transplant recipients and in comparison to other assets, due to a different targeting antigen[20]. It is proposed that the spike antigen is more immunogenic than the nucleocapsid antigen in immunosuppressed patients[20]. On top of that, there is evidence that spike antibodies may provide functional immunity information, as there is a correlation between spike antibodies and neutralizing antibodies[21,22]. As such, analyzing the anti-S might be clinically more relevant than the anti-N in immunosuppressed patients[20].

CONCLUSION

Early treatment of SARS-CoV-2 should be considered in ITx recipients in order to eradicate the virus and to prevent acute rejection mimicry or provocation and potential graft loss. SARS-CoV-2 antigen determination on ileal biopsies of ITx recipients might be routinely performed to screen for the hypothesis of SARS-CoV-2 acute rejection mimicry or provocation.

FOOTNOTES

Author contributions: Clarysse M contributed review of the clinical case, review of literature, and drafting of the article; Ceulemans LJ contributed critical review of literature and the article; Wauters L, Gilbo N, Capiau V, and De Hertogh G contributed review of clinical case and critical review of article; Verslype C, Laleman W, Monbaliu D, and Pirenne J contributed critical review of the article; Vanuytsel T contributed review of the clinical case, review of literature, and review of the article; All authors issued final approval for the version to be submitted.

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LETTER TO THE EDITOR

Can adequate hemodynamic management of brain-dead donors improve donor organ procurement?

Myat Soe Thet, Alessandra Verzelloni Sef, Davorin Sef

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Abstract

There is increasing evidence that adequate donor management with a goal of optimization of organ function is essential to maximize the number of organs that can be procured. Therefore, identification of the cause of hemodynamic instability is crucial in order to direct the right therapy. Several donor management goals for better hemodynamic management including serial echocardiography can guide hemodynamic management in potential donors to increase both number and quality of donor hearts.

Key Words: Brain-dead donors; Hemodynamic; Management; Organ procurement

Core Tip: There is increasing evidence that adequate donor management with a goal of optimization of organ function is essential to maximize the number of organs that can be procured. Early identification of potential donors and adequate donor management are essential in order to expand the donation pool and improve transplantable organ quality. The authors have summarized the available evidence on therapeutic strategies for hemodynamic management and monitoring.

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TO THE EDITOR

In the complex donation process, early identification of potential donors and adequate donor management are essential in order to expand the donation pool and improve transplantable organ quality[1,2]. Lack of evidence from randomized controlled trials still remains one of the main issues regarding the management strategies in donation after brainstem death (DBD) along with acceptance of more marginal donors with comorbidities and worldwide variability in donor management strategies due to various constraints. Most of the current guidelines are based on pathophysiological explanations, observational data and standard critical care practice[3]. Lazzeri *et al*[4] should be congratulated for aiming to summarize the available evidence regarding hemodynamic management of DBD in the era of consistently increased donor organ demand. In their article, authors focused especially on vasoactive-drug support and therapeutic goals[4]. The authors emphasized a loss of up to 20% of DBD organs due to inadequate intensive care management as one of the key concerns, which can be prevented with active donor management in intensive care[4]. Brain death can be often accompanied with considerable physiological instability, which, can induce deterioration in organ function before retrieval if not managed carefully[2]. In addition to a well-known rule of 100, the authors discussed several more donor management goals for better hemodynamic management including: (1) Invasive arterial pressure monitoring aiming mean arterial pressure ≥ 65 mmHg; (2) Urine output ≥ 1 mL/kg/h; (3) Central venous pressure monitoring (aiming 8-10 cm H_2O); (4) Lactate measurements; (5) Mixed venous oxygenation saturation; and (6) Serial echocardiography[4,5]. There is increasing evidence that adequate donor management with a goal of optimization of organ function is essential to maximize the number of organs that can be procured[5-7]. Therefore, identification of the cause of hemodynamic instability is crucial in order to direct the right therapy.

In this context, the role of pulmonary artery catheters (PAC) is not clearly described; whether the routine placement of PAC is warranted or not, since PAC insertion is not without risk of injury to the donor heart, including ventricular arrhythmias, bundle branch blocks, and even cardiac or pulmonary artery perforation[8]. However, appropriate hemodynamic monitoring is a prerequisite in assessment of volume status and response to therapy; therefore, the authors should have addressed the role of initial intravascular volume replacement and the need for assessment of volume status. Pathophysiological changes in DBD donors make the clinical assessment of volume status even more challenging, hence appropriate monitoring is of paramount importance in guiding fluid replacement. Recent guidelines suggest that the primary therapeutic goal should be to maintain euvolemia while isotonic crystalloid solutions should be the preferred when considering fluid replacement[9].

Serial echocardiography monitoring is suggested, yet it is not defined clearly whether we should rely on transthoracic echocardiography (TTE) or we should use more often TEE[3]. Interestingly, in a large study of 472 donor hearts, Casartelli *et al*[10] performed exclusively TTE for evaluation of ejection fraction. On the other hand, we would like to highlight that TEE can provide therapeutic benefits over TTE in critically ill, mechanically ventilated patients, even when the views with TTE are deemed adequate[11]. Importantly, serial echocardiography should be performed to evaluate recovery of function in neurogenic stunned myocardium and guide hemodynamic management in potential donors to improve availability and quality of donor hearts[3]. It is again highlighted that the benefits of the use of dopamine in renal transplant patients are not directly translated to donor hearts in heart transplantation[4]. Among vasopressor drugs, norepinephrine (NE) is the mainstay of cardiovascular support with the addition of vasopressin in cases of higher vasopressors requirements, and this is in line with current practices in many of the centers, as highlighted by the authors[4]. However, recent guidelines propose rather dopamine as the catecholamine of choice, and judicious NE usage due to concerns that it can increase both afterload and pulmonary capillary permeability and stimulate coronary vasoconstriction[9]. These guidelines recommend the use of dopamine as a first line therapy, with addition of NE when the requirement of dopamine exceeds 10 mcg/kg/min. However, the data on this is variable with a retrospective analysis stating otherwise[12]. Furthermore, NE may be associated

with worse cardiac graft function and worse post-transplant survival[13]. Moreover, vasopressin with its action on the V2 receptor will treat diabetes insipidus at the same time. It is also not evident whether it would require further therapy with selective V2 receptor therapy. However, as the authors did not perform systematic review, this could lead to extrapolation bias. Lastly, while there are many reasons why a significant number of potential organs are not donated and successfully transplanted, hemodynamic instability of the donor is an essential and modifiable factor.

FOOTNOTES

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