
*Case Report***COVID INFECTION AS DEVASTATING POST-TRANSPLANT COMPLICATION**

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Abstract

In march 2020 Covid 19 was declared as a pandemic by World Health Organisation. The marked risk group were older patients and patients with comorbidity such as hypertension, DM, obstructive pulmonary disease and chronic kidney disease. Patients on dialysis and kidney transplant recipients are among highest risk groups to be infected with Corona virus.

Since the very beginning, Corona virus pandemic have great impact on the transplant program worldwide.

There are recommendations for kidney transplant professionals that suggest the prioritization of patients for kidney transplantation.

We present an expanded criteria donor, and recipient with multiple vascular access problems as an indication for kidney transplantation. In the early posttransplant period vascular problems with implication on the graft function were diagnosed and surgically treated, and cholecystectomy was performed due to an uncalculous cholecystitis. Unexpected Corona virus infection early post transplantation occurred as a devastating complication for our kidney transplant recipient.

Keywords: kidney transplantation, Covid 19 infection, hydrops of the gallbladder, lethal outcome

Introduction

COVID-19 disease caused by the new coronavirus (SARS-CoV-2) was first recorded in Wuhan China in December 2019, in cluster of patients with severe pneumonia. On 30 January 2020, the World Health Organization (WHO) declared the outbreak of a Public Health Emergency of International Concern (PHEIC). Later, on 11 February 2020, WHO named the disease "coronavirus disease 2019" (COVID-19), and the International Committee on Taxonomy of Viruses (ICTV) named the

virus "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On 11 March 2020, COVID-19 was declared a pandemic by the General Secretary of WHO [1].

Older patients and also patients with chronic diseases are at highest risk of morbidity and mortality by COVID 19. Patients with Chronic kidney disease (CKD) have several comorbidities as diabetes mellitus, multiple cardiovascular diseases and hypertension. Considering these reasons, patients with CKD are highly susceptible to corona virus infection. Furthermore, CKD population undergoing chronic haemodialysis program and visiting dialysis unit three times per week are even at highest risk to be infected with Corona virus [2].

The fast spread of COVID-19 renders throughout the continents and countries significant restriction of the transplantation program in pandemic areas due to the high risk of infection in patients with immunosuppression, risk of transmission in health workers, and lack of medical resources especially in transplant units [3]. Such restrictions exclude transplanting only highly sensitized patients with negative cross match, eventually preemptive and those without dialysis access [4]. The American Society of Transplant Surgeons (ASTS), the American Society of Transplantation (AST), and The Transplantation Society (TTS) developed recommendations to promote donor and recipient safety [5-7].

Case report

A 68-years old female patient with CKD has been followed at the outpatient nephrology department with diagnosis of hypertension for 20 years and chronic pyelonephritis with frequent urinary tract infections. At the beginning of 2020 she experienced epistaxis and worsening of the CKD with increased blood urea nitrogen and serum creatinine (34 mmol/l and 840 µmol/L, respectively) and was hospitalized at the Department of Nephrology for dialysis initiation by femoral venous catheter on the right side.

At the following months she consulted several times for vascular access problems and exchanging of vascular catheters and in the meanwhile had created 2 AV fistulas that were primarily not successful. Exhausting the vascular access possibilities has led to consideration of kidney transplantation as a possibility, with her husband as a potential and compatible donor with 2 HLA matched antigens.

The patient was transplanted with the left donor kidney in the right iliac fossa. Relatively easy transplantation due to the presence of pronounced lymphadenopathy around the right iliac vein, on which after lymphadenectomy an end to side external iliac with renal vein anastomosis was created. The renal artery that was a bit sclerosed and tortuous with plaques that were released was also anastomosed end to side to the iliac external artery. The ureter is fused to the bladder by the Leach-Gregoire method. In the first postoperative days there was relatively satisfactory 1,5-2 L diuresis with a slow creatinine reduction

remaining around 570-620 $\mu\text{mol/L}$ at postoperative day (PO) 3 and 4. Doppler ultrasonography was performed at day 1 after transplantation and was with 67 cm/sec that felt down to 45 cm/sec at the fourth PO day. Thus, an indication for vascular revision was brought. A kink of the tortuous artery was found and the decision was taken not to re-anastomose de novo, but for reposition of the external iliac artery placing it in a Goretex prosthesis providing an adequate flow. The patient diuresis increased to 2-2,5 L based on an improved Doppler flow of 72 cm/sec and the creatinine slowly decreased to 440 $\mu\text{mol/L}$ at the ninth PO day. However, the patient's clinical condition was not improved, she was passive in bed and begun to complain of a severe abdominal pain, especially positioned under the right costal arch and back. Laboratory examination was with elevated WBC and CRP. An ultrasonography and computed tomography (CT) was performed that revealed an enlarged gallbladder-hydrops vesicae fellae (13 x 6 cm) (Figure 1).



Fig. 1. Ultrasonography (left panel) and computed tomography of the enlarged gallbladder (right panel).

The next day cholecystectomy was performed and the samples taken for microbiological cultivation of strains of microorganisms revealed *Pseudomonas* and *Enterococcus* species that were treated with appropriate antibiotics. Postoperatively, there was a local bleeding from the operative wound of the performed cholecystectomy because of the infection and hemostatic disorder that also provoked bleeding from the wound of the transplanted kidney. Hence, for the regulation of hemostasis and anemia the patient was treated in the following 2 days with fresh frozen plasma and cryoprecipitates, as well as with filtrated erythrocytes transfusion and low molecular weight heparin (LMWH). Thus, the bleeding was successfully managed. The patient vital signs were stable with good diuresis and subsequent decrease in

serum creatinine.

Nevertheless, the patient developed fever and marked decrease in oxygen saturation. The pneumo-physiologist was consulted setting an indication for RTG of the lungs and a COVID test. RTG revealed an atypical interstitial pneumonia (Figure 2), and the COVID test resulted as positive. In the meantime, the graft function remained stable with normalized values of creatinine.

In the following days, the patient's condition worsened and she was transferred back to the intensive care unit and intubated with COVID protocol treatment, accordingly. All measures were taken for substitution, stimulation and support of the cardiorespiratory system but after 3 days patient died.

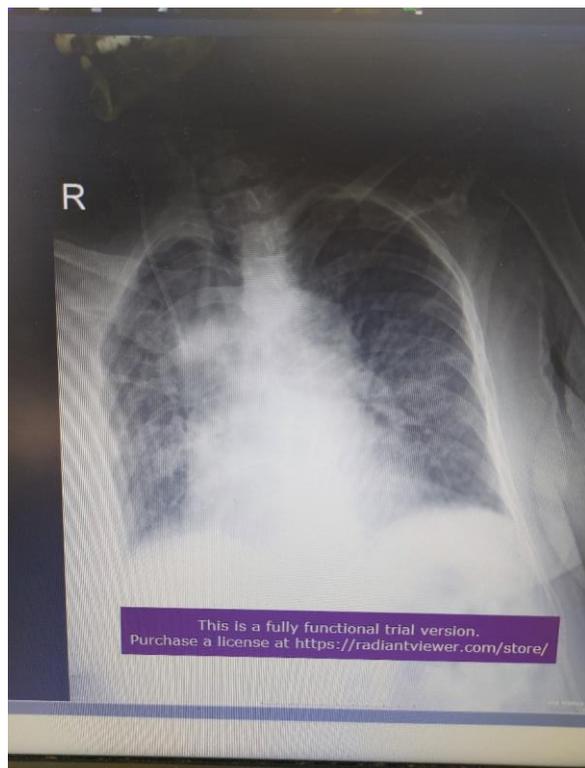


Fig. 2. Rtg of the lung with atypical interstitial Covid-associated pneumonia

There are two possibilities for positive Covid test in early posttransplant period, falls negative test or hospital-acquired infection due to multiple diagnostic and treatment procedure that were performed.

Discussion

Since the very beginning, Covid 19 pandemic have made great impact on the nephrology activity in general, especially on solid organ transplantation including kidney transplantation. In the end of March 2020, a survey of 88 US transplant institutions reported that 71.8% had completely suspended live donor kidney transplantation and 84% had implemented restrictions for deceased donor kidney transplantation [4].

The other study reported reduction in solid organ transplantation predominantly in kidney transplantation with 51% and 90% in the United States of America and France, respectively [8].

In our transplant center at the beginning of Covid pandemic from end of march 2020 complete kidney transplant program was stopped. However, some specific patients especially with vascular access problems were ranged as priority cases. The patient we presented was with multiple vascular access problems and inability to provide successful dialysis treatment. Because of these reasons we have completed all pretransplant investigations and taking in account the age of the donor and recipients we decided to perform kidney transplantation. We suggested two weeks stay at home period and pre-

transplantation COVID 19 testing according to the TTS Guidance [7].

Our patient experienced early posttransplant vascular problem with impact on the graft function. Based on the literature, vascular complications were presented in about 1-5% of kidney transplant recipients, with possible increased morbidity and mortality risk. Immediate vascular complications occurred within few hours and days after transplantation procedure. The most prevalent complications are kinking of the renal artery or vein and torsion of the kidney allograft with stenosis or thrombosis of the vessels. In order to minimize morbidity and mortality caused by vascular complications, quick diagnosis and appropriated surgical treatment are necessary [9]. Posttransplant surgical complications in general are divided in three groups: Vascular complications, typical urological complications such as ureteric anastomosis complications and uretero- and lymphocele formation and surgical complication such as bleeding and/or infection. Different studies report different rate of vascular complications. The highest rate of posttransplant surgical complications was reported by Safa *et al.* (37%) but not specific reasons were explained [10]. The other studies reported relatively low rate of vascular complications (between 1.29% to 8,8%) [11,12]. In our report the vascular complication was associated with presence of CKD as well as age related blood vessels changes. Both, donor and recipient were in the group of expanded criteria donors and recipients. Additionally, vascular problems for dialysis access were the main reason for kidney transplantation. The problem with renal artery in our patient were timely diagnosed and promptly treated getting an optimal graft function in the follow up period.

In the postoperative period hydrops of the gallbladder was an unusual complication found. Our patient was surgically treated. This kind of complications were reported in Varga *et al.* study [13]. They have explained that acalculous cholecystitis is more frequent in transplant recipients than in the general population. Clinical presentation could have been milder when compared with severity of gallbladder affliction. Also, majority of patients require surgical treatment [13].

Unfortunately, when all actual problems in the recipient were solved and optimal graft function established, the most unexpected problem appeared. After prolonged episode of fever, positive COVID 19 test was obtained. Despite all preventive measurements overtaken from the medical staff the transmission of corona virus was diagnosed in our kidney transplant recipient with a fatal outcome. Unfortunately, acquired COVID 19 infections in hospitals have been reported permanently. According to several reports, the SARS-CoV-2 hospital-acquired infection rate is 12-15% [14].

The article of Marago *et al.* analyzed the prevalence of hospital-acquired COVID-19 [15]. A retrospective case analysis presented a total of 239 patients tested positive for COVID-19, where the percentage of hospital-acquired

cases reached 16.2%. Patients with hospital-acquired infections underwent longer hospital stays [15].

Another study described a case series of 138 patients with COVID 19 [16]. Hospital-associated transmission was suspected in 12.3% of patients initially admitted for other health problems. Approximately 26% of the patients received intensive care treatment. Patient-to-patient transmission was considered the cause of infection in several cases [16].

A review and meta-analysis of cases in China-based databases of hospital-acquired infection in patients with COVID-19, SARS, and MERS. Among the confirmed patients, the proportions of nosocomial infections with early outbreaks of COVID-19, SARS, and MERS were 44.0%, 36.0%, and 56.0%, respectively. Of all confirmed cases, the medical staff and other hospital-acquired infections accounted for 33.0% and 2.0% of COVID-19 cases, 37.0% and 24.0% of SARS cases, and 19.0% and 36.0% of MERS cases, respectively. Nurses and doctors were the most affected among the infected medical staff [17].

Multiple aspects must be considered in order to understand whether the infection is a result of "malpractice" or may be considered as "inevitable" condition [14].

The other option is possible initial false negative test especially in hemodialysis patients. Studies of false-negative results from respiratory samples for SARS-CoV-2 are variable, and ranging from 1 to 30% [18]. There are multiple reasons for false negative results including suboptimal specimen collection, testing too early in the disease process, low sensitivity and low viral load [19].

Finding the reasons for false-negative tests until now had priority due to the devastating consequences of undetected cases in health-care and social care settings.

In systematic review involving 34 studies enrolling 12,057 COVID-19 confirmed cases, there was substantial and largely unexplained heterogeneity in the proportion of false-negative RT-PCR results. The findings reinforce the need for repeated testing in patients with suspicion of SARS-Cov-2 infection given that up to 54% of COVID-19 patients may have an initial false-negative RT-PCR [20].

Conclusion

During Covid 19 pandemia transplant team should carefully select the priority patients especially if resources of transplant center may be constrained. Priority cases are highly sensitized patients and without vascular access for dialysis. Besides all medical staff efforts sometimes Covid 19 infection could occurred due to a nature of the disease and specificity of testing. Hospital-acquired COVID-19 is a serious public health issue. This problem may result in unwillingness of patients to seek hospital treatment for fear of becoming infected. Medical staff should undertake all necessary preventive measures to stop further spreading out of an in-hospital infection, especially COVID 19 transmission.

Early posttransplant vascular problems could be presented especially in expanded criteria donors and recipients. Despite all mentioned possible complications transplant program should continue even in Covid 19 pandemic with careful pretransplant patient selection.

Conflict of interest statement. None declared.

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