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Cytomegalovirus nephritis in a lung transplant recipient: A case report

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INTRODUCTION: Cytomegalovirus (CMV) infections are frequent in solid organ transplant recipients and associated with increased allograft dysfunction.
CLINICAL STORY: We report the case of a 58-year-old lung transplant recipient (CMV mismatched) who presented with severe acute kidney injury (AKI) without any other organ involvement. Urinalysis showed moderate proteinuria, leukocyturia, and hematuria suggestive of interstitial nephritis, while renal/urinary tract ultrasound was normal. Anamnesis excluded iatrogenic AKI causes including contrast- and non-steroidal anti-inflammatory drugs-induced AKI, while dedicated blood tests excluded other AKI causes such as vasculitis, hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infection, thrombotic microangiopathy, tacrolimus overdosage, rhabdomyolysis. Urine and serum CMV polymerase chain reaction (PCR) were strongly positive, while urine BK virus was negative. A renal biopsy could not be performed due to anticoagulation and logistic reasons.
DIAGNOSIS: Based on the existing literature, we made a presumptive diagnosis of CMV nephritis and initiated intravenous antiviral therapy with ganciclovir. Within a few weeks, renal function improved but did not fully recover.
CONCLUSION: CMV nephritis is very rare in nonkidney solid organ transplant recipient but should be investigated in case of acute kidney injury as it may lead to chronic renal impairment.
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Case report

We present the case of a 58-year-old female lung transplant recipient who was admitted in our hospital in August 2022 for acute kidney injury (AKI) with metabolic acidosis, hypocalcemia, and hyperphosphatemia.

The patient beneficiated from sequential bilateral lung transplantation in December 2021 for a Gold stage IV/E chronic obstructive pulmonary disease. Her medical history included pretransplant appendectomy, cholecystectomy, and cesarean, as well as bladder polyps' resection for a transitional cell carcinoma in 2016. At the time the transplantation was performed, the recipient was cytomegalovirus (CMV) seronegative and the donor seropositive (D +/R-, CMV mismatch) and therefore at higher risk of developing CMV infection.[1] Thus, immediate post-transplantation CMV prophylaxis was ensured by intravenous

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Table 1 Main Biological Values at Admission

Readout	Value	Unit	Reference values
Hemogram			
Hemoglobin	8.1	g/dl	12.0-15.8
Red blood cells	2,550 × 10^6	/µl	3,500-5,300 × 10^6
Hematocrit	24.4	%	33.0-46.0
Mean corpuscle volume	95.7	µm³	80.1-99.8
Leukocytes	5,580 × 10^3	/µl	3,900-11,100 × 10^3
Neutrophils	4,486 × 10^3	/µl	2,100-7,500 × 10^3
Lymphocytes	0.642 × 10^3	/µl	1,000-3,000 × 10^3
Monocytes	0.290 × 10^3	/µl	0.240-0.910 × 10^3
Platelets	274 × 10^3	/µl	150-400 × 10^3
Reticulocytes	22.4 × 10^3	/µl	25.0-75.0 × 10^3
Ionogram			
Natrium	132	mmol/l	137-145
Potassium	4.9	mmol/l	3.5-5.1
Chloride	104	mmol/l	98-107
Bicarbonate	21	mmol/l	22-30
Calcium	1.91	mmol/l	2.10-2.55
Magnesium	0.58	mmol/l	0.66-0.94
Proteins			
Creatinine	3.60	mg/dl	0.52-1.04
Urea	88	mg/dl	15-36
Estimated glomerular flow rate	13.8	ml/min/1.73 m²	
Uric acid	7.2	mg/dl	2.5-6.2
Total proteins	59.5	g/l	63.0-82.0
Albumin	31.0	g/l	35.0-50.0
Total bilirubin	0.25	mg/dl	0.00-1.30
Haptoglobin	2.13	g/l	0.34-2.00
Liver enzymes			
LDH	323	UI/l	120-246
Alkaline phosphatases	98	UI/l	38-126
Aspartate transaminase	43	UI/l	14-36
Alanine transaminase	37	UI/l	< 35
Gamma-GT	77	UI/l	12-43
Toxicology			
Tacrolimus	8.60	ng/ml	10-12

gamma-GT, gamma-glutamyl transferase; LDH, lactate dehydrogenase.

Table 2 Urinalysis at Admission

Readout	Value	Unit	Reference values
Urine test strip			
pH	5.5		4.5-8.0
Glucose	Negative		
Ketone	(+)		
Hemoglobin	+++		
Protein	+		
Nitrite	Negative		
Urobilinogen	Negative		
Ascorbic acid	Negative		
Leukocyte esterase	+		
Urine specific gravity	1.010	IR	1.010-1.030
Urinalysis			
Glucose	< 20.0	mg/dl	
Osmolality	290	mOsm/kg	
Natrium	49.0	mmol/l	
Kalium	22.9	mmol/l	
Chloride	43.0	mmol/l	
Calcium	0.30	mmol/l	
Urea	812.0	mg/dl	
Protein	1.68	g/l	0.00-0.10
Creatinine	65.8	mg/dl	36.0-130.0
P/C ratio	2.55		< 0.20
Urinary sediment analysis			
Leukocytes	96	/µl	< 13
Erythrocytes	11,832	/µl	< 13
Hyaline casts	Rare		
Nonsquamous epithelial cells	Rare		

P/C, protein/creatinine.

ganciclovir, followed by oral valganciclovir for 6 months after transplantation.

In August 2022, the patient was seen in a follow-up consultation. No clinical complaints were reported on any aspect. Pulmonary function tests and chest X-ray were normal. The follow-up blood tests (see Table 1) revealed a stage III acute kidney injury, with an estimated glomerular filtration rate of 13 ml/min/1.73 m². Other laboratory abnormalities included slight liver enzymes elevation, grade II normocytic anemia, grade I hyponatremia, hypobicarbonatemia, and hyperphosphatemia. Tacrolemia was slightly below the required therapeutic range at 6 to 12 months post-transplant (i.e., between 10 and 12 ng/ml). The plasmatic CMV quantification by polymerase chain reaction (PCR) was ongoing at the time of the consultation, and the patient was hospitalized to further investigate the acute renal failure.

Additional tests were performed to investigate AKI etiology. No signs of urinary obstruction were observed by renal/urinary tract ultrasound. Urinalysis revealed moderate proteinuria, leukocyturia, and marked hematuria (see Table 2), and urine culture was negative. There was no recent administration of iodine contrast medium, nor non-steroid anti-inflammatory drugs intake since the lung transplantation. Rare causes of AKI including vasculitis, cryoglobulinemia, HIV or HCV infection, thrombotic microangiopathy, or rhabdomyolysis were investigated. However, dedicated blood tests were normal with, respectively, negative antineutrophil cytoplasmic antibodies and glomerular basal membrane antibodies, normal complement and serum protein electrophoresis, negative cryoglobulin screening, negative HIV and HCV serology, normal haptoglobin levels, normal platelets and schistocyte count, and normal creatine kinase levels. Human BK polyomavirus infection was investigated, and dedicated PCR in urine was negative.

Finally, the CMV PCR in both the serum and urine were highly positive, with 560,407 and 157,247 copies per milliliter, respectively. Serum CMV immunoglobulin G were

negative, while CMV immunoglobulin M were positive, suggesting CMV primo-infection. By taking all elements into account, we concluded to a CMV-related nephritis based on current diagnostic criteria.[2] No other organ injury was detected (e.g., CMV-pneumonitis and retinitis). Of note, urine positive CMV PCR does not necessarily reflects renal CMV infection, as urine is the primary site for CMV excretion. Although histological diagnosis would have been preferable, a transcutaneous renal biopsy could not be safely performed directly due to ongoing anticoagulation, while a transjugular biopsy was not available in a reasonable timeframe.

Anti-CMV treatment was rapidly started with intravenous ganciclovir adapted to the renal function, with oral substitution 5 days later by valganciclovir. In the next weeks, the renal function improved slowly, along with electrolytes abnormalities, while the number of CMV copies in the blood diminished, reaching negativity 2 months later. Four months after the acute episode, a chronic kidney disease persisted, with an estimated glomerular filtration rate of 40 ml/min/1.73 m², while the patient had a normal renal function prior to CMV nephritis.

CMV infection and tissue invasive diseases are among the most frequent infectious issues affecting solid organ transplant recipients and are associated with negative consequences in terms of allograft function and patients' survival.[3] The emergence of a pre-emptive prevention strategy has nevertheless allowed the peak incidence of CMV infections to be delayed beyond the first 3 months after transplantation and improve these unfavorable outcomes.[4] Besides CMV infection, defined as "virus isolation or detection of viral proteins (antigens) or nucleic acid in any body fluid or tissue specimen,"[5] tissue invasive CMV disease may theoretically involve any organ, with more common involvement of the gastrointestinal and respiratory tracts.[4] CMV nephritis is rare and has so far been exclusively described in isolated case series of kidney transplant recipients, where it is associated with poorer recipient and organ outcomes.[6,7] Although CMV nephritis formal diagnosis is based on the immunohistochemical demonstration of CMV inclusions in the kidney parenchyma,[5] we describe the case of a presumed CMV nephritis without final histological proof,[2] in a lung transplant recipient presenting with CMV primo-infection and AKI for which other causes than CMV have been excluded. To our knowledge, this is the first time that a CMV nephritis is described after lung transplantation.

In conclusion, we describe the case of a presumed CMV nephritis in a lung transplant recipient, as an isolated organ complication of a CMV primo-infection in a CMV-mismatched lung transplant recipient. Although CMV nephritis is well-described after kidney transplantation,[7] this is, to the best of our knowledge, the first time a CMV-nephritis is reported in a lung transplant recipient. In our patient, this acute episode was followed by chronic kidney impairment, and attention should be given to AKI in mismatched solid organ recipients in this regard.

Disclosure statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Patient's consent

The patient gave her informed consent for the publication of this case-report.

Author contributions

FMC collected clinical data and wrote the manuscript, MD was involved in the patient's management, MD and PE revised the manuscript.

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