Adenovirus Infection in a Kidney–Pancreatic Transplant Recipient: Case Report

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ABSTRACT

Adenovirus infection in transplant recipients may present from asymptomatic viremia to multisystemic involvement. Most frequently, it occurs in the first year after a kidney transplant, and it is secondary to the reactivation of latent disease. However, primary infection may occur, and disseminated disease is more common when related to primary infection. Kidney involvement may be confirmed by biopsy, although diagnosis may be presumptive. Reduction of immunosuppression and supportive care are important components of therapy.

Case Description. A 41-year-old female renal–pancreatic recipient 12 years before with chronic renal graft dysfunction and a functional pancreatic graft had a history of cytomegalovirus and polyoma virus infection 2 years after transplantation. She was taking tacrolimus, mycophenolate mofetil, and prednisolone. The patient was admitted after persistent uncharacteristic diarrhea 3 weeks before hospitalization without any relevant epidemiologic context. She was dehydrated, and the lab results showed worsened kidney function and leucocytosis. The viral culture revealed adenovirus. Vigorous hydration was implemented, and the mycophenolate mofetil dose was reduced. The patient was discharged, and renal function returned to previous values.

Discussion and conclusion. Adenovirus infection has a wide clinical presentation, and multisystemic involvement may occur in transplant recipients. Supportive care is paramount. The clinical features and viral culture confirm the diagnosis, although tissue samples and quantitative polymerase chain reaction may be required in more severe cases.

BACKGROUND

INFECTIOUS complications are a major cause of morbidity and mortality in the transplant recipient population [1]. Therefore, the diagnosis and management of infections should be optimized to achieve better clinical outcomes.

CASE REPORT

A 41-year female patient was submitted to a renal, pancreatic transplant 12 years before in the context of diabetes mellitus type 1. After transplantation, some complications occurred. Pancreatic antibody-mediated rejection occurred 1 year after transplantation and was treated with rituximab, after which pancreatic function improved. The patient also presented with an episode of urinary sepsis due to *Klebsiella pneumoniae*.

The patient took immunosuppression with stable levels of tacrolimus 11.0 mg daily, mycophenolate 500 mg twice daily, and prednisolone 5 mg daily. The patient was admitted with diarrhea and abdominal pain complaints for 3 weeks. She had no fever and no epidemiologic context. She was dehydrated, and the lab results showed worsening kidney function (serum creatinine of 3.43 mg/dL, baseline serum creatinine of 2 mg/dL) and an increase in the pancreatic enzymes (amylase 55 UI/L, lipase 100 IU/L, and C-peptide 7.4 ng/mL), with euglycemic state. The fecal cultures revealed the identification of adenovirus. Vigorous hydration was implemented, and mycophenolate mofetil was reduced with renal function improvement but stable pancreatic

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0041-1345/20
https://doi.org/10.1016/j.transproceed.2023.06.005

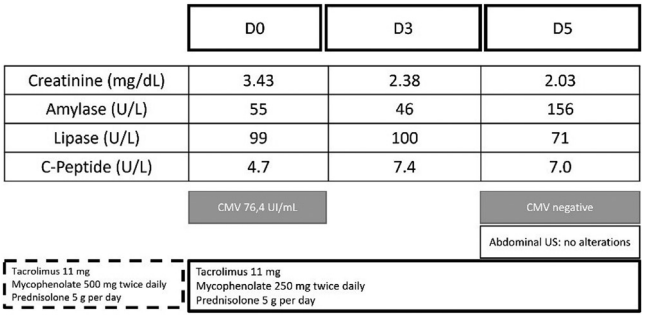

Fig 1. Laboratory and exam results during hospitalization. Immunosuppression scheme used. D0 = day of the hospitalization, D3 = day 3 after hospitalization, D5 = Day 5 after hospitalization. US, ultrasound; CMV, cytomegalovirus.

enzymes (Fig 1). The abdominal ultrasound excluded complications. Identification of cytomegalovirus was positive on admission, but after the measures were implemented, it was negative in the following evaluations.

DISCUSSION

Adenoviruses are associated with various clinical syndromes and present no seasonal variability [2,3]. Transmission may occur via aerosolized droplets, direct conjunctival inoculation, fecal−oral spread, or exposure to infected tissue or blood [2]. Although very common in the pediatric population, transmission in transplant patients may be acquired de novo due to the reactivation of a latent infection of the recipient or from the transplanted organ [3−5].

The incubation period may vary according to the viral serotype, and the transmission time may be from 2 days to 2 weeks, which demands droplet and contact precautions in hospitalized patients. The viral shedding can be prolonged in immunocompromised patients [2]. The incidence of infection is not well known in transplant patients, but transient self-limited viremia during the first year posttransplant is not uncommon [3]. Kidney transplant recipients have an estimated incidence of 4% to 5%, with most cases due to latent reactivation [1,3]. Reactivation occurs because the adenovirus may be latent in the lymphoepithelial tissues, renal parenchyma, tonsils, adenoids, and gastrointestinal tract, which correlates with the most frequent clinical manifestations—hepatitis, stomatitis, enteritis, necrotizing pneumonia, and hemorrhagic cystitis [1−3]. The literature review for this case is summarized in Table 1.

Screening for the virus in blood, urine, or stool may be enough to establish a diagnosis, which was the case in our patient. However, if clinical correlation is unclear, pathology diagnosis may be needed and remains the gold standard [3].

The renal findings include "smudge cells" with wide nuclei with basophilic inclusions and mixed inflammatory infiltrate with focal necrosis in the setting of the adenovirus interstitial nephritis [5]. A similar pattern can be found in adenovirus enteritis, although the "smudge cells" may be rare [3,14].

Treatment entails supportive care and immunosuppression reduction. There is no consensus about which drug to reduce, although reduction of the antimetabolite is the most common

Table 1. Case Report Revision of Adenovirus Infection in Kidney Transplant Patients

Authors	Case Report Description	Clinical Findings	Treatment
Saliba et al [6]	41-y-old man kidney recipient	Fever, dysuria and intermittency, mild graft dysfunction	Immunosuppression tapering
Mihaylov et al [7]	51-y-old man kidney recipient	General malaise, fever and leukopenia, acute adenoviral hepatitis with extensive necrosis	Immunosuppression tapering
Xu et al [8]	66-y-old man heart and kidney recipient	Fever, nausea, vomiting, urinary incontinence and leukocytosis, hemorrhagic cystitis and acute kidney injury	Immunosuppression tapering and cidofovir
Park et al [9]	32-y-old woman kidney recipient	Dysuria, hematuria and fever, dyspnea with pulmonary infiltrates	Immunosuppression tapering, ribavirin and endovenous immunoglobulin
Lachiewicz et al [10]	20-y-old woman kidney recipient	Fever, conjunctivitis, sinus congestion	Immunosuppression tapering, intravenous immunoglobulin and cidofovir
Ramírez et al [11]	26-y-old man kidney recipient	Fever, hematuria, dysuria and acute kidney injury	Immunosuppression tapering, intravenous immunoglobulin and ribavirin
Ramírez et al [12]	27-y-old man kidney recipient	Fever, dysuria	Immunosuppression tapering and intravenous immunoglobulin
Kozlowski et al [13]	44-y-old man kidney recipient	Fever, sore throat, donor-transmitted adenovirus infection	Immunosuppression tapering
Lim et al [14]	51-y-old man kidney recipient	Fever, hematuria, acute kidney injury	Immunosuppression tapering

measure in clinical practice, and it was our approach [2,3]. Immunosuppression reduction is maintained until the viral load is undetectable and the patient improves. However, this approach may be adapted according to the state of immunosuppression, site of infection, and degree of dissemination [2].

Some risk factors for adenovirus infection have been identified: age (more common in the pediatric population) [4], type of solid organ transplant received (more common in intestinal transplantation), and severity of immunosuppression [3].

Although they have been used before [15], antiviral agents are currently not widely recommended due to cidofovir and ribavirin adverse effects. Their use is reserved for serious and persistent cases [2,3].

CONCLUSIONS

Adenovirus infection may occur in kidney and pancreatic recipients, and supportive measures should be prioritized in managing these patients, despite coexisting risks of immunosuppression reduction, infection resolution, and rejection risk. Further research is needed to define the best approach in the setting of severe disease to achieve better outcomes.

DATA AVAILABILITY

The data that has been used is confidential.

DECLARATION OF COMPETING INTEREST

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

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