

CASE REPORT

Disseminated adenovirus infection in heart and kidney transplant

Kalp-böbrek alıcısında yaygın adenovirüs enfeksiyonu

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Summary– Presently described is a case of disseminated adenovirus infection in a heart-kidney transplant recipient that was successfully treated with cidofovir. There are several reports of adenovirus infections in adult solid organ transplant recipients and the prognosis is usually poor, with mortality rates of 40% to 60%. Severe disseminated adenovirus infections have been associated with increased risk of adverse transplant events, such as rejection, ventricular dysfunction, allograft vasculopathy, graft loss, and the need for re-transplantation. The patient's lack of clinical improvement, the onset of hemorrhagic cystitis and acute kidney injury were factors in our decision to temporarily discontinue administration of immunosuppressive agents and start an antiviral agent. It is important to suspect adenovirus in transplant patients when they do not respond to antibiotics and cultures are negative. Early diagnosis and treatment are critical to improving outcomes in immunocompromised patients.

Adenovirus infections usually cause respiratory or gastrointestinal illnesses, and in immunosuppressed patients, severe life-threatening disease may occur.^[1] Solid organ transplant recipients are susceptible to many complications, and adenovirus infection is a well-known complication of solid organ transplant recipients.^[1] However, adenovirus infection has not been widely reported in adult heart transplant patients.^[2-6]

CASE REPORT

A 66-year-old man who had a simultaneous heart and kidney transplant 3 years earlier, and who was on chronic prednisone, sirolimus, and tacrolimus for im-

Özet– Burada sidofovir ile başarıyla tedavi edilen bir kalp-böbrek alıcısında yaygın adenovirüs enfeksiyonu olgusunu tanımlıyoruz. Erişkin solid organ transplant alıcılarında prognozu genellikle kötü, ölüm oranları %40–60 arası birkaç adenovirüs enfeksiyonu olgusu bildirilmiştir. Ağır yaygın adenovirüs enfeksiyonları organ rejeksiyon, ventrikül işlev bozukluğu allograft vaskülopatisi, greft kaybı ve yeniden transplantasyon gerekliliği gibi giderek artan olumsuz transplant olayları riskiyle ilişkilendirilmiştir. Hastada klinik iyileşmemenin olmaması, hemorajik sistit başlangıcı ve akut böbrek hasarı geçici olarak bağışıklık sistemini baskılayıcı ilaçların uygulanmasını durdurup bir antiviral ilaca başlama kararımıza etkili faktörler olmuştur. Antibiyotiklere yanıt vermedikleri ve kültürlerin negatif olduğu durumlarda transplant hastalarında adenovirüsten kuşkullanması önemlidir. Bağışıklık sistemi risk altında olan hastalarda sonuçları iyileştirmede erken tanı ve tedavi önem taşır.

munosuppression, presented with a 2-day history of fever up to 39°C, nausea, vomiting, cough, urinary incontinence, and leukocytosis. Broad spectrum antibiotics were initiated. An echocardiogram showed normal left ventricular size and function. Despite empiric antibiotics, he continued to spike fevers up to 39.5°C. His course was complicated by respiratory failure requiring noninvasive ventilation, hemorrhagic cystitis, and acute kidney injury (AKI) with a creatinine peak of 4.5 mg/dL. Blood and urine cultures and polymerase chain reaction (PCR) for cytomegalovirus were negative. However, adenovirus was detected

Abbreviations:

AKI Acute kidney injury

PCR Polymerase chain reaction

Received: August 03, 2017 Accepted: October 07, 2017

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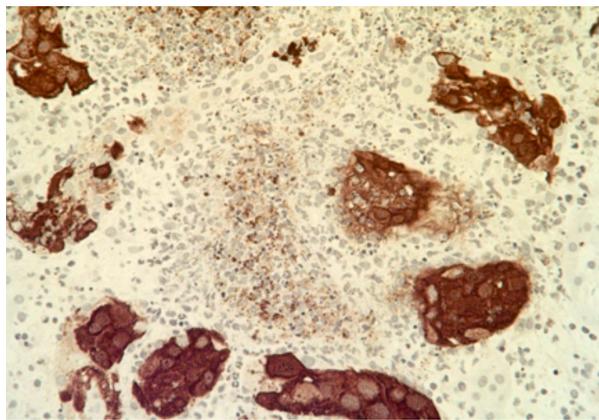


Figure 1. Renal biopsy illustrating acute pyelonephritis with suppurative and granulomatous features, marked tubular destruction, basophilic intranuclear inclusions, and positive immunohistochemical stain for adenovirus pyelonephritis. Diagnostic for adenovirus pyelonephritis.

in respiratory viral panel testing. Serum adenovirus PCR showed a viral load of >2 million copies. Kidney biopsy showed adenovirus pyelonephritis (Fig. 1). His immunosuppression treatment was withheld and he was treated with cidofovir for disseminated adenovirus infection. His fever curve improved and the creatinine level trended down. After 4 days, immunosuppression was restarted. He completed 7 days of cidofovir and subsequent serum adenovirus PCR showed zero copies.

DISCUSSION

The most common complications from heart transplants include bleeding, graft failure, cellular rejection, and infection.^[7] Complications due to infection may be bacterial, fungal, or viral in etiology. Adenoviruses are becoming more well known in the setting of hematopoietic stem cell as well as solid organ transplant recipients.^[8] Adenovirus diseases usually develop within the first 6 months after transplantation.^[8] There are several reports of adenovirus infections in adult solid organ transplant recipients and the prognosis is usually poor, with mortality rates of 40% to 60%.^[2-6] Using PCR analysis of myocardial tissue samples, one study of heart transplant patients demonstrated that 47% of heart transplant recipients were found to have a viral infection.^[9] The most common viruses found were enteroviruses (Group B Coxsackievirus) and adenoviruses while human cytomegalovirus and parvovirus B19 were found less frequently.^[9] There was 1 report of a fatal outcome for disseminated ade-

noviral infection in a heart transplant patient.^[2] Severe disseminated adenovirus infections have been associated with increased risk of adverse transplant events, such as rejection, ventricular dysfunction, allograft vasculopathy, graft loss, and the need for re-transplantation.

We report a case of disseminated adenovirus infection in a heart-kidney transplant recipient that was successfully treated with cidofovir. The patient's lack of clinical improvement, the onset of hemorrhagic cystitis, and AKI were factors in our decision to temporarily terminate the administration of immunosuppressive agents and initiate treatment with an antiviral agent. We believe that it is important to suspect adenovirus in transplant patients when they do not respond to antibiotics and cultures are negative. Early diagnosis and treatment are critical to improving outcomes in immunocompromised patients.

Informed consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying image.

Peer-review: Externally peer-reviewed.

Conflict-of-interest: None declared.

Authorship contributions: M.D. contributed in gathering information, writing introduction, case report and discussion. J.X., M.D., K.P., J.A., K.M., and D.I. manuscript editing. J.X. will act as guarantor.

REFERENCES

1. Humar A, Kumar D, Mazzulli T, Razonable RR, Moussa G, Paya CV, et al. A surveillance study of adenovirus infection in adult solid organ transplant recipients. *Am J Transplant* 2005;5:2555-9. [\[CrossRef\]](#)
2. Ivan D, Frazier OH, Abrams J. Fatal disseminated adenoviral infection in an adult heart transplant patient. *J Heart Lung Transplant* 2004;23:1209-12. [\[CrossRef\]](#)
3. Florescu DF, Kwon JY, Dumitru I. Adenovirus infections in heart transplantation. *Cardiol Rev* 2013;21:203-6. [\[CrossRef\]](#)
4. Duggan JM, Farrehi J, Duderstadt S, Turner NJ, Fekety R. Treatment with ganciclovir of adenovirus pneumonia in a cardiac transplant patient. *Am J Med* 1997;103:439-40. [\[CrossRef\]](#)
5. Refaat M, McNamara D, Teuteberg J, Kormos R, McCurry K, Shullo M, et al. Successful cidofovir treatment in an adult heart transplant recipient with severe adenovirus pneumonia. *J Heart Lung Transplant* 2008;27:699-700. [\[CrossRef\]](#)
6. Gupta A, Philip A, Ranga K, Cappa J, Dougherty J, Lawlor M. An interesting case of adenoviral hepatitis in a cardiac transplant recipient. *Transpl Infect Dis* 2010;12:84-6. [\[CrossRef\]](#)

7. Yusen RD, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, Goldfarb SB, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-second Official Adult Lung and Heart-Lung Transplantation Report-2015; Focus Theme: Early Graft Failure. *J Heart Lung Transplant* 2015;34:1264–77. [\[CrossRef\]](#)
8. Mehta V, Chou PC, Picken MM. Adenovirus disease in six small bowel, kidney and heart transplant recipients; pathology and clinical outcome. *Virchows Arch* 2015;467:603–8. [\[CrossRef\]](#)
9. Donoso Mantke O, Meyer R, Prösch S, Nitsche A, Leitmeyer K, Kallies R, et al. High prevalence of cardiotropic viruses in myocardial tissue from explanted hearts of heart transplant recipients and heart donors: a 3-year retrospective study from a German patients' pool. *J Heart Lung Transplant* 2005;24:1632–8. [\[CrossRef\]](#)

Keywords: Disseminated adenovirus; heart and kidney transplant; transplant recipient.

Anahtar sözcükler: Disemine adenovirüs; kalp-böbrek transplantı; transplant alıcısı.