

Case Report

Recurrent Oral Herpes Simplex Virus Infection in a Renal Transplant Recipient

Renal Transplant Alıcısında Tekrarlayan Oral Herpes Simpleks Virüs Enfeksiyonu

Meral Torun Bayram¹, Erkam Yıldırım², Esma Tuğba Kaşkçı Mermer³, Damla Seyhanlı³, Salih Kavukçu², Alper Soylu²

¹*Istanbul University, Institute Of Health Sciences , Pediatric Kidney Transplantion Research Doctoral Program, Istanbul, Türkiye*

²*Dokuz Eylul University Medical Faculty, Department Of Pediatric Nephrology, Izmir, Türkiye*

³*Dokuz Eylul University Medical Faculty, Department Of Pediatric Infectious Diseases, Izmir, Türkiye*

ABSTRACT

Herpes simplex virus (HSV) infection is common in solid organ transplant recipients due to viral reactivation under immunosuppression. We report a case of a 9-year-old renal transplant recipient who developed recurrent perioral HSV infection following discontinuation of antiviral prophylaxis. The patient presented with localized vesicular lesions without systemic symptoms, and each episode responded rapidly to oral antiviral therapy. However, recurrences occurred mainly during periods of increased immunosuppression, such as treatment for acute cellular rejection, or after cessation of prophylaxis, whereas no HSV-related episodes were observed during antiviral prophylaxis. Because of recurrent HSV episodes, long-term low-dose suppressive antiviral therapy was initiated. This case illustrates that HSV infection in pediatric renal transplant recipients may follow a recurrent course and underscores the importance of individualized management strategies given the uncertainty surrounding the optimal duration of prophylactic antiviral therapy.

Keywords: Recurrent Herpes Simplex Virus, renal transplantation, antiviral prophylaxis

ÖZET

Herpes simplex virus (HSV) enfeksiyonu, solid organ nakli alıcılarında sıkılıkla immünsüppresyon zemininde viral reaktivasyon sonucu ortaya çıkar. Burada, antiviral profilaksının kesilmesini takiben tekrarlayan perioral HSV enfeksiyonu gelişen 9 yaşında bir renal transplant alıcısı sunulmuştur. Hasta, sistemik bulguların eşlik etmediği lokalize veziküler lezyonlarla başvurmuş ve her atak oral antiviral tedaviye hızlı yanıt vermiştir. Ancak özellikle akut hücresel rejeksiyon tedavisi gibi immünsüppresyonun arttığı dönemlerde veya profilaksi kesildikten sonra nüksler gözlenmiş; antiviral profilaksi süresince HSV atağı izlenmemiştir. Tekrarlayan HSV enfeksiyon atakları nedeniyle hastaya uzun süreli düşük doz profilaktik antiviral tedavi başlanmıştır. Bu olgu, pediyatrik renal transplant alıcılarında HSV enfeksiyonunun tekrarlayıcı bir patern izleyebileceğini ve profilaktik tedavinin süresine ilişkin belirsizlik nedeniyle bireyselleştirilmiş tedavi yaklaşımlarının önemini vurgulamaktadır.

Keywords: Tekrarlayan Herpes Simpleks Virüsü, böbrek nakli, antiviral profilaksi

Received: 23.01.2025 · **Accepted:** 29.04.2025 · **Published:** 13.02.2026

Correspondence / Yazışma: Meral Torun Bayram · İstanbul Üniversitesi, Sağlık Bilimleri Enstitüsü, Pediatrik Böbrek Nakli Araştırmaları Doktora Programı, İstanbul, Türkiye · meralt.bayram@yahoo.com.tr

Cite this article as: Torun Bayram M, Yıldırım E, Kasıkçı Mermer ET, Seyhanlı D, Kavukcu S, Soylu A. Recurrent Oral Herpes Simplex Virus Infection in a Renal Transplant Recipient. Pediatr Acad Case Rep. 2026;5(1):8-11.

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INTRODUCTION

Herpes Simplex Virus types 1 and 2 (HSV-1 and HSV-2) are α -herpesviruses with a linear double-stranded DNA genome that cause infections affecting mucocutaneous surfaces, the central nervous system, and various organs [1]. HSV-1 is classically associated with orolabial disease, whereas HSV-2 is more commonly linked to genital herpes. However, genital infections caused by HSV-1 have been reported with increasing frequency and are generally associated with lower recurrence rates [2].

Herpes Simplex Virus is mainly transmitted through close contact with infected mucocutaneous surfaces or lesions, while donor-derived transmission is rare. Most infections are acquired from asymptomatic carriers, as viral shedding often occurs without overt disease. After primary infection, HSV remains latent within sensory ganglia and may reactivate intermittently [3].

Although only a minority of immunocompetent individuals develop clinically apparent disease, viral shedding from mucosal surfaces is common. In contrast, solid organ transplant recipients shed HSV more frequently, experience more severe disease, and exhibit a delayed response to antiviral therapy [3, 4]. In this high-risk population, early recognition and prompt treatment are critical to limit morbidity and prevent complications. However, the risk of recurrent infection and the optimal duration of antiviral prophylaxis remain poorly defined. Here, we describe a pediatric renal transplant recipient with recurrent oral HSV infection.

CASE REPORT

A 9-year-old male renal transplant recipient presented with complaints of perioral rash (Figure 1). It was reported that erythema and fluid-filled vesicles had appeared around the mouth one day earlier, without accompanying symptoms. In his medical history, he had undergone kidney transplantation from his mother due to end-stage renal disease secondary to dysplastic kidneys. He was on treatment with prednisolone, tacrolimus, and mycophenolate mofetil. Valganciclovir prophylaxis for cytomegalovirus (CMV) infection (both donor and recipient seropositive) had been administered for six months and was

discontinued approximately two weeks earlier. There was no consanguinity between the parents, and no family history of chronic kidney disease or other significant medical conditions.



Figure 1. Erythematous vesicular lesions at the left corner of the lip and below it

On physical examination, the patient was in good general condition and fully conscious. Body weight was 22 kg (3rd-10th percentile), and height was 121 cm (3rd-10th percentile). Body temperature was 36.5°C, and blood pressure measured 106/54 mmHg. Erythematous vesicular lesions were observed at the left corner of the lip and in the midline below the lower lip. Other systemic findings were normal.

The absence of a history of new drug use, fever, malaise, cutaneous herpetiform or target lesions, vesicles on the hands or feet, genital lesions, and lymphadenopathy suggested HSV-associated oral vesiculobullous disease. Oral acyclovir was initiated at a dose of 20 mg/kg/dose, four times daily. After 14 days, treatment was discontinued upon lesion resolution. Two weeks later, vesicular lesions recurred on the lips and surrounding area. This time, valacyclovir (20 mg/kg/dose, twice daily) was administered, and the treatment was discontinued after 14 days. One month later, following intensive immunosuppressive therapy given for acute cellular rejection, valganciclovir prophylaxis was reinitiated to prevent CMV and HSV infections. No HSV-related infection occurred during this prophylaxis. However, shortly after discontinuation, the patient again presented with vesicular lesions on the lips and perioral mucosa (Figure 2). Following retreatment with valacyclovir, due to recurrent infections, long-term lower-dose suppressive therapy was continued.



Figure 1. Vesicular lesions on the lip and perioral mucosa

DISCUSSION

Most symptomatic HSV infection in solid organ transplant recipients are attributed to reactivation of latent virus rather than primary acquisition, particularly during the early post-transplant period or during intensified immunosuppression, such as rejection therapy [5]. Although HSV-seronegative recipients may acquire infection through close contact, donor-derived HSV transmission is rare and has been reported primarily in liver, kidney, and other solid organ transplantations [1]. In our patient, the temporal relationship between the lesion onset and discontinuation of valganciclovir prophylaxis supports viral reactivation rather than donor-derived or newly acquired infection.

Several risk factors for symptomatic HSV infection in transplant recipients have been identified, including lack of antiviral prophylaxis, HSV seropositivity, episodes of rejection, and prior CMV prophylaxis [6]. In the present case, recurrent episodes occurred following cessation of antiviral prophylaxis and were temporally associated with periods of increased immunosuppression, particularly after treatment for acute cellular rejection. These findings suggest that fluctuations in immunosuppressive burden may play a key role in triggering HSV reactivation, even in the absence of severe clinical disease.

Clinically, primary HSV infection usually develops after an incubation period of 4-7 days, followed by painful vesicular lesions involving the oral-labial, genital, or perianal regions. These lesions generally heal within 1-3 weeks [1]. During reactivation, symptoms are generally milder and resolve more rapidly in immunocompetent individuals; however, in

immunocompromised patients, HSV infection may be more prolonged and present with atypical lesions during both primary infection and reactivation [1,6]. In both immunocompetent and immunosuppressed hosts, HSV may spread retrogradely to the central nervous system, causing meningoencephalitis or transverse myelitis. In more severe cases, disseminated mucocutaneous or visceral disease, esophagitis, hepatitis, and pneumonia may occur [1]. In our patient, recurrent perioral vesicular lesions occurred without systemic involvement, fever, or mucosal dissemination, indicating that HSV infection in pediatric transplant recipients may follow a recurrent yet clinically mild course rather than a fulminant presentation. Notably, prompt initiation of antiviral therapy at symptom onset during each episode may have played a role in limiting disease severity and preventing progression.

Diagnosis of HSV infection is often based on typical clinical findings; however, atypical or subtle presentations in immunocompromised hosts may hinder recognition. In such cases, laboratory methods, such as viral culture, detection of HSV DNA by PCR, direct fluorescent antibody testing, and serologic assays may be employed to establish the diagnosis [4, 7, 8]. In our patient, the absence of systemic symptoms, alternative mucocutaneous involvement, or a history of recent drug exposure in our patient suggested HSV infection. Therefore, no additional investigations were undertaken.

Early diagnosis and timely antiviral treatment are essential in immunocompromised patients to reduce morbidity and prevent complications. Limited mucocutaneous HSV infections are managed with oral nucleoside analogues (acyclovir, valacyclovir, or famciclovir), and therapy should be continued for at least 5-7 days until complete lesion healing. More extensive disease requires intravenous acyclovir. In severe cases, such as disseminated, visceral, or central nervous system involvement, high-dose intravenous acyclovir should be initiated promptly. In severe infections, treatment duration is generally 14-21 days. In life-threatening infections, the dose of immunosuppressive therapy should be reduced [1, 4, 9]. In the present case, oral acyclovir and valacyclovir were effective for acute management; however, repeated relapses following treatment discontinuation highlighted the challenge of long-term disease control.

The role and optimal duration of secondary antiviral prophylaxis in pediatric solid organ transplant

recipients remain poorly defined. Although antiviral agents administered for CMV prophylaxis are generally effective against HSV, there is limited guidance on the duration of suppressive therapy for recurrent HSV infection is lacking [1]. In our patient, recurrence consistently occurred after discontinuation of prophylaxis, whereas no episodes were observed during periods of antiviral suppression. These findings underscore the uncertainty surrounding the appropriate length of prophylaxis and support the need for individualized management strategies based on clinical course, immunosuppressive intensity, and recurrence pattern.

In pediatric patients, HSV prophylaxis is not applied as a universal approach. In patients with severe or recurrent HSV infections, there are no definitive guidelines regarding either chronic suppressive therapy or the optimal duration of such treatment. Clinical decisions should be based on factors, including the patient's HSV infection history, the degree of immunosuppression, and overall health status. In patients with frequent recurrences, prophylactic therapy may be considered, taking into account disease risk, drug toxicity, cost, and adherence.

Patient Consent Form / Hasta Onam Formu

The parents' of this patient consent was obtained for this study.

Conflict of Interest / Çıkar Çatışması

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

Financial Disclosure / Finansal Destek

The authors received no financial support for the research and/or publication of this article.

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