

Varicella Infection in an Immunized Pediatric Living Donor Liver-Transplant Recipient

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Abstract

Varicella-zoster virus (VZV) is a DNA virus belonging to the *Herpesviridae* family. Primary infection causes chickenpox followed by latency in the sensory ganglia, which can sometimes reactivate leading to herpes zoster. Chicken pox is generally a mild disease of childhood with a secondary attack rate of >85%, but disseminated VZV infection with visceral involvement and fatal outcome may occur in immunocompromised individuals. Indian Academy of Pediatrics recommends two doses of live-attenuated varicella vaccine in healthy unexposed children at 15–18 months and then at 4–6 years of age. The effectiveness of a single dose of vaccine is around 85% and with a two-dose schedule is as high as 92%. Despite the vaccine-induced protection, community-acquired VZV infections still remain a problem in immunocompromised population. We hereby report a case of a previously immunized pediatric liver-transplant recipient who acquired VZV infection. This case report clearly highlights the importance of strict environmental infection control practices, early suspicion, diagnosis, and management in such cases.

Keywords: Disseminated infection, DNA polymerase chain reaction, living donor liver transplantation, vaccine efficacy, varicella-zoster virus, varicella-zoster virus infection

INTRODUCTION

Varicella-zoster virus (VZV) is a DNA virus of *Herpesviridae* family, which causes both chicken pox as primary infection and herpes zoster as reactivation.^[1] Chicken pox is mild disease of childhood but has greater morbidity in adolescent and adult population.^[1] The overall seroprevalence in India was around 68.2% in 2000 with a seroprevalence rate of 29% in 1–5 years group to 71.2% at the age of 11–15 years and 91.1% at the age of 31–40 years.^[2]

Although the primary infection is benign in immunocompetent population, disseminated VZV infection may occur in children <1 year of age, immunocompromised individuals, and those with impaired cell-mediated immunity.^[3]

Varicella vaccination is an effective preventive tool (efficacy of >85%) [Table 1] for decreasing the burden and complications of varicella disease although it is less efficacious than natural VZV infection.^[4] Primary infection in such individuals often results in suspension or delay of surgery/chemotherapy, thus increasing the risk of progression of underlying disease.^[3]

We hereby report a case of an immunized pediatric liver donor liver-transplant recipient who acquired VZV infection.

CASE REPORT

A 6-year-old male child, 10 months prior, underwent an emergency live donor liver transplantation for acute liver failure secondary to hepatitis A infection. He now presented to the emergency with chief complaints of poor oral intake, high-grade fever with chills, and rigors (102°F) for 3 days and vesicular rashes of 2–3 days [Figure 1]. Vesicular rash was first noticed by the parents on the chest and shoulders which progressed onto the trunk, abdomen, face, and lower limbs; palms and soles were spared. The patient was on posttransplant immunosuppressive regimen with tacrolimus,

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Table 1: Seroconversion and efficacy of one and two doses of live-attenuated varicella vaccine (Oka strain)^[3-5]

Parameter	One dose (%)	Two doses (%)
Seroconversion	86	99
Efficacy - mild disease	70-90	98.3
Efficacy - moderate-to-severe disease	>95	100

cyclosporine, and mycophenolate mofetil. At the time of presentation, recipients' graft function was normal and no associated systemic abnormality was detected. Donor for the patient had pretransplant seropositive (IgG-positive) status for VZV, Epstein-Barr virus (EBV), and *Cytomegalovirus* (CMV) and no current active infection. The recipient's pretransplant serological status was also positive for VZV, EBV, and CMV. The recipient never had any history of natural infection to VZV before transplant nor has been exposed to any individual with chicken pox or varicella-zoster immunoglobulin, but parents gave the history of receiving VZV vaccination two doses (at 2 and 4 years of age), last dose taken 2 years before transplant. Anti-VZV IgG protective titers could not be measured. At present, the clinical presentation was generalized and not limited to any particular dermatome. We could not investigate the strain type so were unable to determine whether his/her infection was primary infection or vaccine strain re-activation. Hence, a clinical diagnosis of posttransplant VZV infection was made, despite the seropositive status.

Blood samples were sent to the virology laboratory for further workup and confirmation of diagnosis. VZV IgM was positive and plasma VZV-DNA load was $4 \log_{10}$ copies/mL by real-time polymerase chain reaction (PCR) assay. The patient received symptomatic treatment along with intravenous acyclovir (20 mg/kg/dose IV tds) and IV antibiotics (augmentin 20 mg/kg/day IV tds) for a 7-day period. All the immunosuppressant medications were briefly withheld. The patient clinically improved and the follow-up blood specimen was negative for VZV DNA after 7 days. The patient was eventually discharged, and written informed consent was obtained from the parents for the case report to be published.

DISCUSSION

Chicken pox is a self-limiting disease in healthy pediatric population, yet it carries the risk of dissemination in immunocompromised.^[1]

VZV disease is a frequent community-acquired (>6 months) infectious complication of solid organ-transplant (SOT) recipients. With high doses of immunosuppressants, fatal complications such as disseminated infections with visceral involvement are reported.^[5] However, varicella after transplantation is mild when patients are suspected and investigated early, hospitalized, and given immediate treatment.^[6]

Primary infection is rare in adult SOT recipients (seronegativity of 2%–3%) but more in pediatric transplant recipients (seronegativity ranges from 7% to



Figure 1: Vesicular skin lesions of the patient, at the time of presentation

50%).^[6] Various factors such as age of the child, prior vaccination, history of varicella disease, and level of immunosuppression before transplant may influence the serostatus of the pediatric group.^[7] Such cases are mainly community acquired, but still donor-derived varicella is reported but rare.^[1]

Vaccination is an effective prevention tool against VZV infection. Indian Association of Pediatrics recommends two doses of live-attenuated (Oka strain) vaccine to be administered, first dose at the age of 15–18 months and the second dose at the age of 4–6 years.^[4] The seroconversion rate and efficacy of the two doses of the vaccine are tabulated in Table 1. This vaccine is presently not given under the Universal Immunisation Programme in India, thus leading to decreased herd immunity and frequent outbreaks in immunocompromised patients.^[4] In SOT recipients, Infectious Diseases Society of America guidelines recommend completing pretransplant vaccination with live-attenuated vaccine in patients who are seronegative for VZV, >4 weeks before initiation of any immunosuppression.^[5]

Despite the vaccine efficacy, breakthrough varicella can still occur.^[1] This has a milder presentation among immunocompetent individuals; disseminated infection has been reported in immunocompromised, especially in those who did not develop immunity following vaccine or in whom the pretransplant-induced immunity waned off as a result of immunosuppression^[6] The present case is a case of breakthrough VZV infection in a vaccinated child post transplantation. This raises the question of exploration into the need of a third-dose VZV vaccine and justified routine evaluation for seroconversion after two doses. Studies in pediatric transplant recipients suggest that varicella vaccine is safe and immunogenic even after transplantation but must be performed only in selected patients with appropriate education and close follow-up.^[7]

Our literature search revealed few similar case reports of VZV infection in both immunocompetent and immunocompromised population reported from India [Table 2].

The present case highlights the importance of counseling the patients on environmentally acquired diseases and infection

Table 2: Breakthrough varicella cases reported from India in both immunocompetent and compromised patients

Authors	Age/sex	Underlying diagnosis	Serostatus before immunosuppression	Previous exposure (natural infection/vaccination)	Treatment	Prognosis
Immunocompetent population						
Suryam and Das, 2009 ^[8]	11/female	-	-	Vaccination (1 dose at 2 years of age)	Symptomatic	Good
	7/male	-	-	Vaccination (1 dose at 3 years of age)	Symptomatic	Good
Dubey <i>et al.</i> , 2015 ^[9]	10/female	-	-	Vaccination (1 dose at 3 years of age)	Symptomatic	Good
	5/male	-	-	Vaccination (1 dose at 2 years of age)	Symptomatic	Good
	19/male	-	-	Natural infection and vaccination (2 doses, at 15 years of age)	Symptomatic + acyclovir	Good
Immunocompromised patients						
Guru <i>et al.</i> , 2019 ^[10]	-	ALL on chemotherapy	-	1 st case - 48 days after vaccination 2 nd case - 61 days after vaccination		Good
Present case, 2020	6/male	Post LDLT on Immunosuppression	VZV IgG positive (seroprotective titers not measured)	Vaccination (2 doses at 2 and 4 years of age)	Symptomatic + acyclovir	Good

ALL: Acute lymphocytic leukemia, LDLT: Live donor liver transplant, VZV: Varicella-zoster virus, IgG: Immunoglobulin G

control practices. PCR-based early diagnosis and intensive treatment and effective monitoring may prevent disease and its dissemination.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Research quality and ethics statement

The authors followed applicable EQUATOR Network (<http://www.equator-network.org/>) guidelines, notably the CARE guideline, during the conduct of this report.

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Conflicts of interest

There are no conflicts of interest.

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