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JCN ISSN 2576-9529 JOURNAL OF CLINICAL NEPHROLOGY

Case Report

Clinical Decision Making Made Easy by Multiplex Polymerase Chain Reaction Technology in Case of Life-threatening Infections in Renal Transplant Recipients

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Submitted: December 08, 2025
Accepted: December 29, 2025
Published: December 30, 2025

Citation: Azad P, Rizvi Y, Jha L. Clinical Decision Making Made Easy by Multiplex Polymerase Chain Reaction Technology in Case of Life-threatening Infections in Renal Transplant Recipients. J Clini Nephrol. 2025; 9(12): 110-112. Available from: https://dx.doi.org/10.29328/journal.jcn.1001168

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Keywords: Multiplex polymerase chain reaction; Antibiotic resistance genes; Opportunistic infections; Post-transplant infections

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Abstract

Post-renal transplant recipients are very vulnerable to severe and life-threatening infections. This is due to ongoing immunosuppression, unusual clinical signs, and frequent involvement of opportunistic or multidrug-resistant organisms. Early and accurate identification of the pathogens, along with their resistance profiles, is crucial for timely and effective treatment. However, this task remains difficult with standard diagnostic methods. This article discusses the use of multiplex polymerase chain reaction (PCR) technology, based on a series of cases involving three renal transplant recipients with severe lung infections. In each case, multiplex PCR performed on bronchoalveolar lavage samples quickly identified the pathogens involved, including bacterial, atypical, and viral agents. It also detected important antimicrobial resistance genes like NDM, VIM, CTX-M, IMP, and OXA-48. The fast availability of these results allowed for targeted antimicrobial treatment, resulting in clinical improvement, successful discharge, and preservation of graft function in all patients. This case series highlights the value of multiplex PCR as a rapid, sensitive, and effective diagnostic tool. It helps inform clinical decisions for critically ill renal transplant patients, especially when quick detection of pathogens and resistance profiling are key to improving outcomes.

Introduction

Infection is the leading cause of mortality of post-renal transplant patients in developing countries [1]. Allograft dysfunction, rejection, and loss are also implicated by infections. Traditional as well as opportunistic infections are causative in such circumstances. Concurrent coinfections with multiple organisms and atypical presentation of immunosuppressed post-transplant patients make the clinicians more perplexed. An apt diagnosis is the only rescue for these patients [2].

Advances in PCR technology and other DNA signal and target amplification techniques have resulted in these molecular diagnostics becoming key role players for medical management [3-5]. In multiplex PCR, more than one target sequence can be amplified by including more than one pair of primers in the reaction. Multiplex PCR has the potential to produce considerable savings of time and effort within the laboratory without compromising test utility. In the field of infectious diseases, the technique has been shown to be a valuable method for the identification of viruses, bacteria, fungi, and/or parasites [6]. Another advantage of the multiplex PCR technique, apart from rapid identification of the causative pathogen, is the potential detection of genetic markers for clinically relevant antimicrobial resistances [7]. This method assesses the genotype of the organism compared to conventional susceptibility techniques, which assess the phenotype under artificial conditions. It is advantageous

for patients dealing with severe life-threatening infections, especially with organisms difficult to culture or organisms with slow growth [8]. Presence of the CTX-M gene in Gram-negative bacteria is responsible for resistance to several beta-lactam and non-beta-lactam antibiotics. This particular gene also renders the bacteria multi-drug resistant [9]. New Delhi metallo β-lactamase-1 (NDM-1) is a novel MBL that confers resistance to all β-lactam antibiotics except aztreonam [10,11]. Carbapenem resistance due to metallo-β-lactamases (MBLs) such as the Verona integron-encoded metallo-β-lactamase (VIM) is particularly problematic due to the limited treatment options. The acquisition of the VIM gene by bacteria is responsible for it [12]. Similarly, there are other resistance mechanisms like oxa-8-like, IMP [13].

Presentation of case series

Patient X: A 55 years old Post –renal transplant patient was admitted with chief complaints of fever, cough, and breathlessness. His chest x-ray was suggestive of left-sided pneumonia. Immunosuppression was reduced. Empirical antibiotics, other medications, and supportive measures were initiated. HRCT chest was done, which was s/o dense consolidation involving the left lingual region along with left-sided pleural effusion. Patient underwent bronchoscopy followed by bronchioalveolar lavage. BAL fluid was sent for multiplex PCR and Klebsiella pneumoniae group was detected, along with the detection of resistance mechanisms VIM, CTX-M, NDM, and Oxa-48. Ceftazidime plus avibactum was initiated as per multiplex PCR reports. The patient gradually improved and was discharged successfully.

Patient Y: A 69 years old Post –renal transplant patient was admitted with chief complaints of fever and cough. TLC was raised, and his chest X-ray was s/o left-sided opacity. Empirical antibiotics were started, and Immunosuppression was reduced. HRCT chest was done, which revealed areas of dense consolidation in the left upper, lower lobe, posterior segment of right upper lobe, posterior and medial basal segment of right lower lobe. Bronchoscopy was done bronchoalveolar lavage was done. BAL sample was sent for multiplex PCR. Mycoplasma pneumonia, pseudomonas Aeruginosa, and rhimovirus was detected. NDM, VIM, and IMP were detected as resistance mechanisms. Meropenem was initiated after multiplex pcr reports, and in a few days patient improved.

Patient Z: A 53 years old Post –renal transplant patient was admitted with chief complaints of on-and-off fever for 4 weeks, and breathlessness for 3 days. During the hospital stay, fever and breathlessness continued with increased need for oxygen and BiPAP support. Empirical antibiotics were initiated. Chest X-ray was normal, PET-CT was done. PET-CT was s/o metabolically active dense ground glass hazinessin b/l lungs with associated interstitial thickening in the bilateral lower lobes secondary to infection. Bronchoscopy was done bronchoalveolar lavage was done. BAL sample was sent for multiplex PCR. Haemophilus Influenzae was detected. Empirical antibiotics were continued, and within a week patient improved. Patient was discharged successfully.

Discussion

It has been estimated that 70% of kidney transplant recipients will experience an infection episode within the first 3 years after transplantation. After cardiovascular disease, infection is the second leading cause of death in recipients with allograft function [13,14]. The immunosuppressive therapy required to prevent organ rejection places the kidney transplant recipient at increased risk for donor-derived, nosocomial, and community-acquired infections as well as reactivation of latent pathogens [15]. Post-renal transplant patients, being immunocompromised, are always prone to serious life-threatening infections. Early diagnosis and management become necessary in such cases. Multiplex polymerase chain reaction technology isolates, amplifies, and detects the DNA of microorganisms that cause overlapping signs and symptoms. It also helps in the identification of microorganisms and antibiotic resistance genes. In all the 3 cases we encountered, multiplex polymerase chain reaction technology helped in the identification of infecting micro-organisms and the selection of antibiotics. Finally, all 3 patients were discharged with preserved graft function.

Conclusion

Infection is an important cause of morbidity and mortality after kidney transplantation. With the advent of newer imaging modalities focus of infection is not difficult to find, but early detection of the causative microorganism is still a challenge. In renal transplant patients, where both graft survival and immunity are equally imperative, an early diagnosis of infectious etiology along with its antimicrobial resistance becomes the priority. Multiplex polymerase chain reaction technology provides an apt answer to this situation.

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