Mucormycosis and Cytomegalovirus Co-infection in Renal Transplant Recipients

Opportunistic infections have a high incidence among hematopoetic and solid organ transplant recipients with compromised cell-mediated immunity induced by immunosuppression.[1] Cytomegalovirus (CMV) infection is frequently seen in the renal transplant recipients, especially those who have received T-cell depleting antibodies.[2] CMV infection produces immuno-modulatory effects, resulting in further immunosuppression that predisposes transplant recipients to develop serious non-CMV infections, like invasive fungal infections, following transplantation.[2] Mucormycosis is a rare and life-threatening invasive fungal infection caused by fungi of the *Zygomycetes* class and order *Mucorales*.[3] *Rhizopus*, *Mucor,* and *Rhizomucor* are the genera most frequently identified in the posttransplant setting.[4,5] Based on the route of infection and symptomatology, mucormycosis may present with different clinical syndromes with the rhino-cerebral and pulmonary being more common. Gastrointestinal (GI) mucormycosis is rare, accounting for only 7%, and has a high mortality rate of 85%.[6] GI mucormycosis may occur in any part of the alimentary tract, with the stomach being most commonly involved. In a recent issue of this journal, Nandwani *et al*. have described an interesting case of CMV and *Mucor* co-infection of the GI tract within 4 weeks of an ABO-incompatible (ABO*i*) renal transplantation.

In an earlier issue of the journal, Nandwani *et al*. had described a 45-year-old man with end-stage renal disease, who underwent a live-donor ABOi renal transplant after appropriate preconditioning with immunosuppressive medications and plasmapheresis.[7] Posttransplant course was marked by presumably tacrolimus-induced biopsy-proven diffuse thrombotic microangiopathy causing delayed graft function requiring dialytic support. His condition gradually improved, but worsened again four weeks posttransplant, when he developed GI symptoms that were proven to be related to co-infection with CMV and *Mucor* on gastric histopathology. Unfortunately, the patient succumbed to these fatal infections.

Two interesting aspects of this case include – early occurrence of CMV and *Mucor* co-infection as well as its occurrence in the setting of an ABO*i* renal transplantation. Of note, both donor and recipient were CMV seropositive (D+/R+) before transplant. However, per the case report, it does not appear that the patient received anti-CMV prophylaxis. Given that CMV is the most common opportunistic pathogen in solid organ transplant recipients, both CMV disease, and asymptomatic viremia pose a major challenge. Attributable to its immuno-modulatory effects, it can impair graft survival by facilitating acute graft rejection and interstitial fibrosis/tubular atrophy. Guidelines recommend that patients with asymptomatic CMV viremia should receive preemptive valganciclovir therapy for significantly better graft survival.[8] However, given that the patient described in the case report by Nandwani *et al*. did not receive anti-CMV prophylaxis, it could possibly explain early-onset CMV infection. This is also compounded by the fact that patient received aggressive immunosuppresive therapy in the pre- and post-transplant setting of ABO*i* transplantation. ABO*i* transplant recipients are at high risk for opportunistic infections because of enhanced immunosuppression.[9,10]

Mucormycosis and CMV infection can occur individually; a concomitant infection of the two as reported by Nandwani *et al*. is rare and was first reported by Ju *et al*. in 2001.[11] Independent risk factors for mucormycosis present in this patient include aggressive immunosuppression particularly with T-cell depleting agents, prolonged Intensive Care Unit stay, and renal dysfunction.[12] Initial graft dysfunction requiring augmented immunosuppression, as seen in this patient, has also been shown to be an independent predictor of mucormycosis.[12] Besides, further immunosuppressive effects of CMV infection could also have contributed to the development of this fatal invasive infection.

This case thus highlights the morbidity and mortality of mucormycosis and CMV co-infection in ABO*i* renal transplant recipients receiving aggressive immunosuppression. It also exemplifies the role of anti-CMV prophylaxis in patients, given the devastating effects of CMV infection on posttransplant outcomes. Improvement in patient outcomes entails preventive strategies with a high index of suspicion and early management of infection.

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