Original Article

Post-transplant human cytomegalovirus infection can lead to deterioration and dysfunction of renal allograft tissue

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Human Cytomegalovirus (HCMV) infection could lead to a renal allograft failure in post-transplant recipients even after a successful histocompatibility match and absence of donor specific preexisting antibody. The tentative possibilities lead to the theory of molecular mimicry as HCMV showed a sequence homology to the ß chain of human histocompatibility complex HLA DR. Therefore, viral peptide could induce antibodies that specifically recognized by human DR ß chain.Thus a regular post-transplant monitoring of HCMV and proper therapeutic intervention is highly warranted in case of renal allograft recipients. Moreover, CMV infection may precipitate acute rejection. Most transplant programs, use routine anti CMV prophylaxis 100 to 200 days.

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Key words **: HCMV, renal transplant, graft dysfunction.**

Human Cytomegalovirus (HCMV) is a member of the herpesvirus group. The transcription of HCMV can be divided into three separate phases: immediate early (IE), early(E) and late (L). From recent research it is now known that during viral latency transcription is restricted to (IE). The products of E and IE are recognized by HCMV specific cytotoxicT lymphocytes. The transcription of IE genes occurs in the absence of viral protein synthesis and is located in restriction areas 0.709 to 0.741 of the genome[1,2,3,4].

Others have reported the sequence homology and immunologic cross-reactivity of HCMV and HLA DR ß chain. Again post-transplant HCMV infection can lead to severe inflammation by elevating production of several inflammatory mediators, triggering immunological cascades and increased expression of MHC. Recent periodicals are well evidenced that there has been strong correlation between HCMV infection and allograft dysfunction and even leading to acute rejection[5,6,7,8].

In our present study we have focused on whether there is an association of post-transplant HCMV infection and clinical manifestation of degraded or dysfunctional renal allograft.

Materials and Methods

In this study the total 28 no of patients with manifestation of cytomegalovirus infection quantified by real time PCR assay and evidenced by histopathology has been included at Medica Superspeciality Hospital, a tertiary care hospital at Kolkata between the years 2015 to 2018.

Real time PCR assay has been done for the quantification of viral DNA from post-transplant recipient's EDTA plasma sample. The assay has been performed by Rotor Gene Q instrument from Qiagen with artus CMV RG RT PCR kit, cat. No. 4503263. To generate the standard curve, positive and negative controls were run along with the patient's sample.

Post-transplant allograft transplant recipients were underwent protocol biopsies to determine allograft dysfunction and rejection. Serum creatinine and total protein assay has been done by standard biochemical procedure.

All statistical analysis has been done by prism 4.1; origin 9.0 and Microsoft excel 2007.

Results

28 post-transplant recipients HCMV infected renal allograft recipients had been included in this study. Among those 17 patients are male 11 female. The mean age is 50.81 years. All patients had been evaluated histopathologically for graft degradation and rejection. The recipients had undergone all pretransplant histocompatibility testing and cross matching. There recipients had been screened for other infections and those with only HCMV infection had been included into the study.

Seven patients showed low viral count and no significant difference in graft function. Twelve patients showed moderate infection and again no apparent sign of graft dysfunction. Patients showed high viral load among those and all of them was detected with elevated creatinine and total protein and decreased albumin globulin ratio which

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signifies the deterioration of renal function. One patient lost because of bone marrow depression, retinitis and cmventero-colitis. He presented late in the course with fever and severe diarrhea (Table 1 & Figs 1-4).

Discussion

Recent research reveals that there is an association of post-transplant HCMV infection and worst allograft outcome. HCMV infected post renal transplant recipients showed a deteriorated graft function as the creatinine levels had been seen elevated along with proteinuria. All HCMV infected renal allograft transplant patients were screened for preexisting anti-HLA and non-HLA antibodies prior to transplantation. Therefore chances of donor specific antibody mediated immunogenicity trigger were improbable. Evidences of renal graft dysfunction and degradation had been seen histopathologically and biochemically.

Table 1 — *Total number of patents along with no of male and female and mean age*

Total no of Patients	28
Male	17
Female	11
Mean age	50.81 years
Percentage of patients with high viral load and graft deterioration	32.14%

It is already established that the viral IE and HLA DR Sequences were antigenically identical. Antibody to IE product could react with HCMV infected cells as well as on HLA DRAntigen-positive cells that were not infected with HCMV. The HLA DR and HCMV IE sequences are sufficiently similar and an immune response generated against the virus could also able to react with 'self' HLA DR. The more severe the disease, ie, HCMV replication could generate the greatest response against DR. Additionally, the enhanced micro circulation accompanying the transplanted site could attract lymphoid cells that can be transported to and accumulate at the area of local inflammation[9,10].

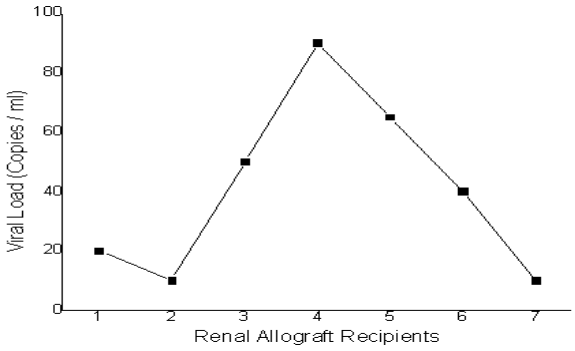

Fig 1 — Line graph showing low viral load in post-transplant renal allograft recipients

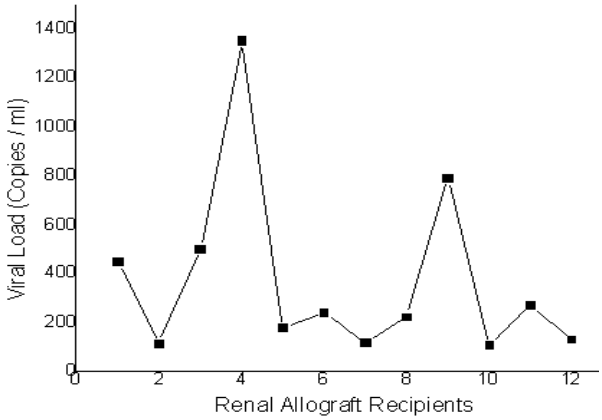

Fig 2 — Line graph showing moderate viral load in post-transplant renal allograft recipients

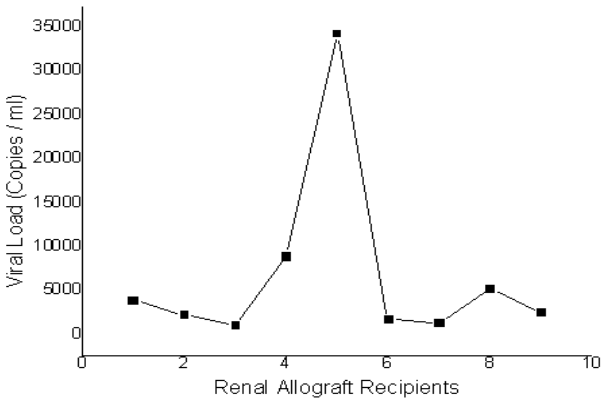

Fig 3 — Line graph showing high viral load in post-transplant renal allograft recipients

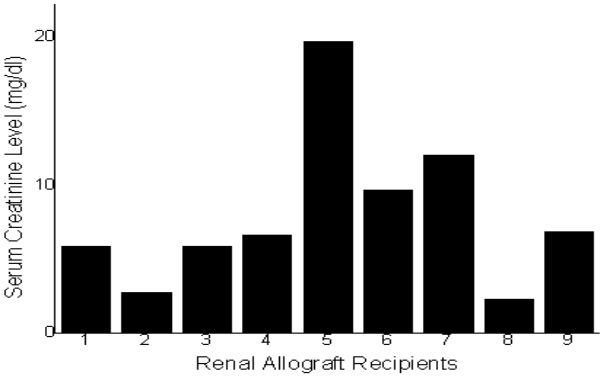

Fig 4 — Bar graph showing the serum creatinine level among patients with high viral load

The sharing of a microbial epitope with a host self-epitope from two dissimilar proteins has been termed molecular mimicry. Molecular mimicry is a common occurrence as judged by analysis of over 600 monoclonal antibodies to a wide variety of DNA and RNA viruses. Some studies showed that 4% of monoclonal antibodies against viruses also reacted with self-determinants[9,10,11].

Conclusion

Our study findings suggested that there is an association between post-transplant HCMV infection and deteriorated renal allograft function. The tentative mechanism behind the degradation of graft tissue and post-transplant

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HCMV infection could be immunogenicity attack and triggering of expression of inflammatory mediators which could lead to successive loss of tissue resulting graft deterioration and dysfunction.

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