Functional polymorphism in the promoter of NF-KB1 gene (-94ins/delATTG) is associated with a increased risk for CMV infection after kidney transplantation

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INTRODUCTION and OBJECTIVES

Nuclear factor-kB (NF-kB) regulates the transcription of many genes for immune response, cell adhesion, differentiation, proliferation, angiogenesis and apoptosis. Abnormalities in the NF-kB regulation are involved in multiple human pathologies including inflammatory diseases, immune deficiencies, infections, diabetes and atherosclerosis as well as tumors.

Previous data suggest that the activation of NF-kB can facilitate cytomegalovirus (CMV) viral replication through the activation of the promoter regulating immediate-early (IE) gene expression and so the IE-1 antigen itself. On the other hand, it can inhibit CMV replication by stimulation of the host immune response. Recently, a functional polymorphism in the promoter of NF-KB1 (-94ins/delATTG) was associated with a increased risk of developing inflammatory and infectious disease.

IN THIS STUDY WE EVALUATE IF NF-KB1 -94INS/DELATTG POLYMORPHISM MAY BE CONSIDERED A PREDICTOR FOR CMV INFECTION AFTER KIDNEY TRANSPLANTATION.

METHODS

We enrolled 106 kidney transplantation recipients (KTR) (F/M = 41/65; age 45.78 ± 13:48) pre-emptively treated for CMV.

Immunosuppressive regimen includes for every patients: steroids, CNI and mycophenolic acid. CMV infection was defined as detection of viremia > 650 copies/ml of whole blood. After extraction of DNA from venous blood, genotyping was carried out by Polymerase Chain Reaction (PCR) and digestion reaction with restriction enzyme PflMI (Van91I).

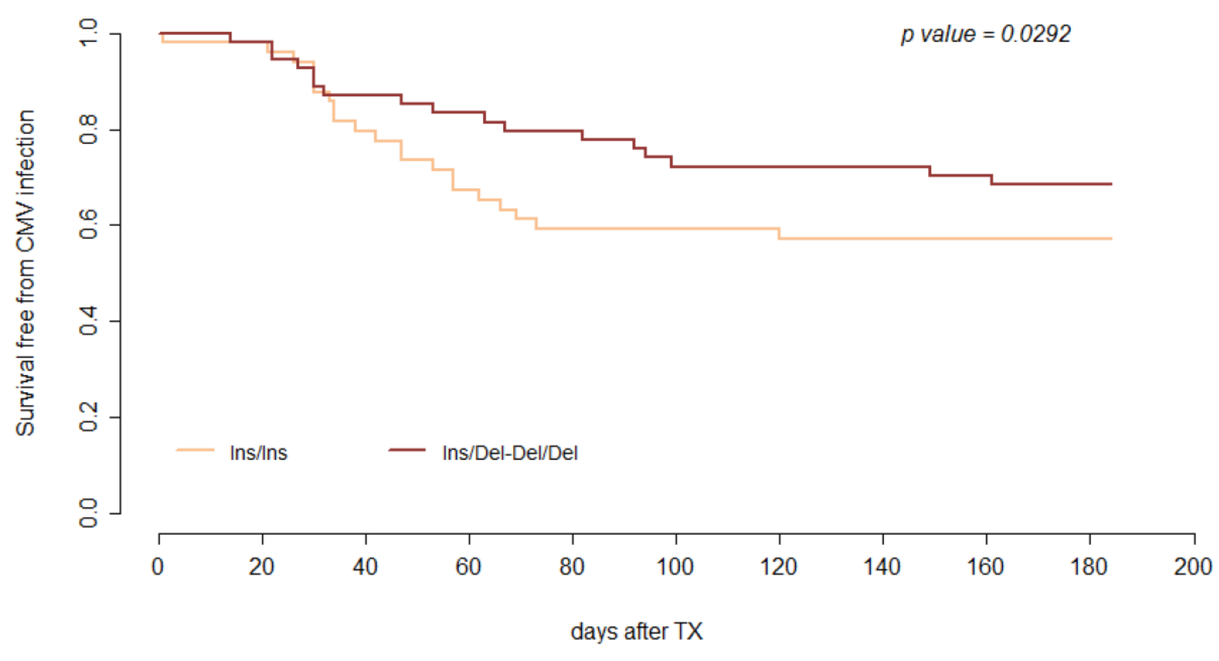
Using Cox regression and survival analysis we analyzed the association between the polymorphism and CMV infection in the first 6 months after transplantation.

RESULTS

We observed 45 CMV infections (42%). The genotyping frequencies of the polymorphism were: Ins/Ins: 53 KTR (50%); Ins/Del: 48 (45.3%); Del/Del: 5 (4.7%).

At multivariate Cox regression, Ins/Del genotype and/or Ins/Del and Del/Del KTR genotype showed a reduced risk of CMV infection after transplantation compared to Ins/Ins genotype (HR: 0.50, 95% CI 0.26-0.94; p = 0.03; 0.54, 0.29-0.98; p = 0.04, respectively) independently from age, sex, CMV serological status, DGF, acute rejection. Survival curves are shown in Fig. 1.

Figure 1. Survival free from CMV infection after Kidney Transplantation in Ins/Ins vs. Ins/Del-Del/Del patients.



CONCLUSIONS

THESE RESULTS SHOW THAT CMV INFECTION AFTER KIDNEY TRANSPLANTATION IS ASSOCIATED WITH FUNCTIONAL POLYMORPHISM IN THE PROMOTER OF NF-KB1 (-94INS/DELATTG).

PRE TRANSPLANTATION GENOTYPING COULD IDENTIFY KTR AT HIGH RISK FOR CMV INFECTION AND SO COULD HAVE IMPORTANT IMPLICATIONS FOR THE CHOICE OF ANTIVIRAL THERAPEUTIC STRATEGY AFTER RENAL TRANSPLANT.

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