

429 : INTERFERON-GAMMA INDUCIBLE PROTEIN-10 (IP10/CXCL10) IN KIDNEY TRANSPLANTATION

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INTRODUCTION

OBJECTIVES

- Acute T cell-mediated rejection (TCMR) remains a major determinant of renal allograft outcome [1,2].
- CXCL10 (or IP10: interferon gamma induced protein 10) is a member of the CXCR3 chemokine family that mediates inflammation by inducing chemotaxis of effector cells.
- Recent data have demonstrated that CXCL10 is a sensitive marker for both subclinical and clinical T cell-mediated rejection (TCMR) [3]. However, this association remains controversial by other authors.



- Our goal was to verify if elevated urinary CXCL10 levels could predict allograft damage in kidney transplantation.
- And if CXCL10 polymorphism has any impact in renal allograft outcome.

MATERIEL AND METHODS

88 urine samples were prospectively collected on:
Day 7 (D7), 1, 3, 6 months (M1, M3, M6) post-transplantation

Urinary CXCL10 measurements: ELISA (R&D systems®)

EDTA samples for molecular analysis

CXCL10 SNP (-872 G/A rs4256246): PCR-RFLP using NcoI: restriction enzyme

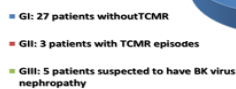


Figure 1 : Distribution of patients

- 35 patients
- Mean age = 37.91 years
- Sex ratio (Men/Women) = 2.88
- Categorized into 3 groups (G1, G2, G3) according to clinical surveillance, BK Virus Real-time monitoring and Banff biopsies criteria

RESULTS AND DISCUSSION

QUANTITATIVE STUDY

No association between elevated urinary CXCL10 levels and acute rejection was found



Studies of Raza et al. and Hirt-Minkowski et al. showed a statistically significant association between this biomarker and acute rejection [1,2].



A significantly higher concentration of urinary cxcl10 was observed in G3 compared to the two other groups (p=0.001) (Figure 2)

The area under receiver operating curve for the positivity of PCR BKV-DNA was 0.78 [0.66 – 0.90] (p = 66 x 10⁻⁵). This corresponded to a sensitivity-specificity of 0.65-0.81 for PCR BKV positivity at CXCL10 cutoff of 4.3 pg/ml (Figure 3).

Ho et al demonstrated that an active BKV infection induced an elevation of both urinary and serum CXCL10 levels in transplanted patients with normal histology [3]

Figure 2: Mean levels of CXCL10 in groups of patients

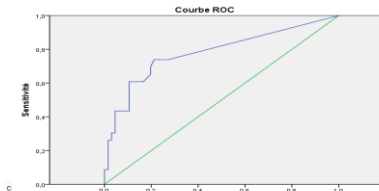
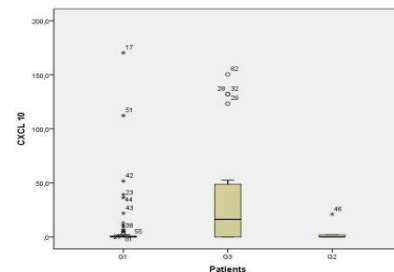


Figure 3: ROC curve study to evaluate the performance of urinary CXCL10 concentration in detecting PCR BKV positivity

MOLECULAR STUDY

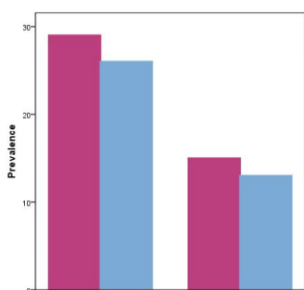


Figure 4: CXCL10 (-872) SNP in TCMR (+) and (-) patients

The frequencies of CXCL10 genotypes are similar in TCMR (+) group and TCMR (-) one (p = 0,56) (Figure 4)

Given the small number of patients, these results should be confirmed on a larger cohort.

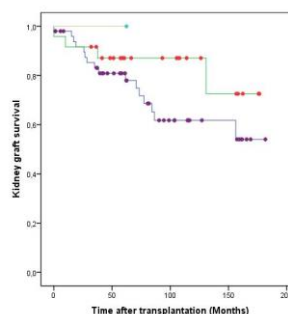


Figure 5: Kaplan-Meier actuarial curve

No impact of CXCL10 polymorphism in renal outcome was found (p = 0,35) (Figure 5)

It has been shown that genetic polymorphisms could affect the intensity of cytokine immune response [4].

CONCLUSION

REFERENCES

The above observations do not confirm that the noninvasive urinary CXCL10 quantification is a useful marker of acute rejection diagnosis in our population. Nevertheless, it could potentially be used to identify and to purser patients with suspicion of BK Virus nephropathy.

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3. Ho, J and al. (2017). Urinary CXCL10 chemokine is associated with alloimmune and virus compartment-specific renal allograft inflammation. *Transplantation*.
4. Nelson Leung-Sang, T and al. (2009) Genetic association between a chemokine gene CXCL-10 (IP-10, interferon gamma inducible protein 10) and susceptibility to tuberculosis. *Clinica Chimica Acta* 406 (2009) 98-102