IDENTIFCATION OF A NEW HAPLOTYPE OF RISK IN CFH GENE PREDISPONING TO DEVELOP A SEVERE THROMBOTIC MICROANGIOPATHY

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INTRODUCTION and OBJECTIVES

Growing evidences emerging from studies reported in literature demonstrated that some haplotypes of risk, found in gene coding for factors regulating alternative complement influenced the phenotype expression of diseases characterized by Thrombotic Microangiopathy (TMA), as Dense Deposit Disease (DDD), Atypical hemolytic-uremic syndrome (aHUS) Membrane-Proliferative Glomerulonephritis (MPGN), C3 glomerulophaty[1,2]. However, to date, there are no studies that have investigated the role of genetic background on TMA phenotype.

IN THIS STUDY WE EVALUATE THE ROLE OF HAPLOTYPES ON TMA PHENOTYPE

METHODS

In this retrospective study we enrolled 32 patients with TMA. In particular, 30/32 were affected by lupus nephritis, 1/32 by Moskowitz Syndrome and 1/32 by Dense Deposit Disease.

After extraction of DNA from venous blood, all patients were subjected to the genetic screening in genes of alternative complement pathway (CFH, MCP, CFI, CFB, C3, THBD) by gene sequencing, using primers yet described in literature[3].

RESULTS

The genetic analysis revealed in 6/32 patients the presence of a new haplotype in CFH gene: c.184G, IV2-18delTT, c.921A, c.1204T, c.1419A. We did not found mutations. Interestingly, we observed that the 6 patients were affected by a "severe" TMA, as they did not respond to the conventional therapy, all have multi-organ involvement and were subjected to the dialytic treatment. The remaining 26 patients did not show these findings.

CONCLUSIONS

Our results suggest that the new identify haplotype in CFH gene could be considered an haplotype of risk to develop a "severe TMA", independently from the disease by which the patient is affected. Therefore, the genetic screening could be helpful to establish a precocious, correct and focused therapy

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