

The Italian Registry of Membranoproliferative glomerulonephritis: an important tool for investigating the pathogenesis of a rare disease.


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MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

- MPGN is a rare kidney disease, with severe proteinuria and renal impairment, characterized by mesangial cell proliferation and increased mesangial matrix combined with thickening of the glomerular capillary wall
- Prevalence of primary forms in European Countries: 1-2 cases/10,000 inhabitants
- Different subtypes are recognized:
 - type I and III → immune complex mediated
 - type II → no immune complexes
 - GNC3 → GN with isolated C3 deposits

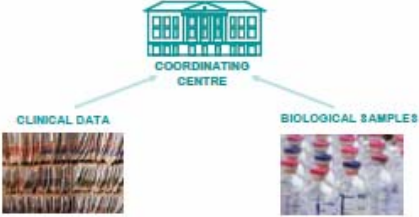
Type II MPGN: Dense Deposits Disease



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PURPOSE OF THE STUDY

In 2006 an Italian Registry of MPGN was established with the aim to collect clinical data and biological samples, and to perform biochemical and genetic complement analysis.



Methods: Complement profile assessment and sequencing of CFH, CFI, MCP, C3 genes.


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CASES REFERRED TO THE REGISTRY

76 MPGN patients: 35 females (2,6-70 y)
41 males (4-77 y)

- 23 patients → type I
- 22 patients → type II
- 2 patient → type III
- 5 patients → GNC3
- 16 patients → MPGN undefined

8 patients → MPGN associated with Hemolytic Uremic Syndrome (HUS)



Outcome:

- 19 patients → minimal urinary abnormalities
- 19 patients → nephrotic syndrome
- 21 patients → chronic renal failure
- 8 patients → dialysis
- 8 patients → functioning kidney transplant
- 1 patient → death

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COMPLEMENT PROFILE ASSESSMENT IN OUR COHORT

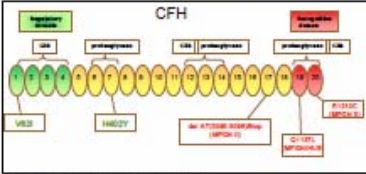
	CFH levels N=32	C3 levels N=51	C4 levels N=53
low	5	43	2
normal	27	18	51

C3NeF positive patients → n= 14 (out of 36)

In MPGN hypocomplementemia is a common finding due to complement hyperactivation, associated with presence of nephritic factors (C3NeF) or mutations in complement regulatory genes.

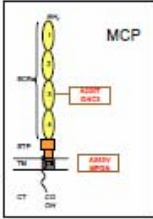
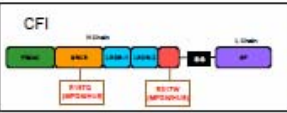

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COMPLEMENT GENE MUTATIONS IN OUR COHORT



Green polymorphisms Red mutations

VR22 and H402Y CFH variants analyzed in 36 patients:
- 24 homozygous and 12 heterozygous for VR22 variant
- 9 homozygous and 10 heterozygous for H402Y variant

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CONCLUSIONS

The Italian Registry of Membranoproliferative glomerulonephritis was exploited to gain new insight into the pathogenesis of this rare kidney disease.

Preliminary results of biochemical and genetic studies disclosed specific abnormalities underlying complement hyperactivation in MPGN.

Registry analysis will put the basis to better understand:

- clinical manifestations
- response to treatment
- long term outcome

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