Abstract: PO2336

Extensive Complement Analysis in a C3 Glomerulopathy Cohort of Dutch Children with Benign Outcome

Session Information

- Pediatric Nephrology: Glomerular Disease and Transplantation
  October 22, 2020 | Location: On-Demand
  Abstract Time: 10:00 AM - 12:00 PM

Category: Pediatric Nephrology

- 1700 Pediatric Nephrology

Authors

- Wijnsma, Kioa L., Amalia Children's Hospital, Radboudumc, Nijmegen, Netherlands
- Michels, Marloes, Amalia Children's Hospital, Radboudumc, Nijmegen, Netherlands
- Kurvers, Roel, Maastricht University Medical Center, Maastricht, Netherlands
- Van Wijk, Joanna, Emma Children's Hospital, Amsterdam University Medical Center, Amsterdam, Netherlands
- Bouts, Antonia, Emma Children's Hospital, Amsterdam University Medical Center, Amsterdam, Netherlands
- Gracchi, Valentina, Beatrix Children's Hospital, University of Groningen, Groningen, Netherlands
- Horuz-Engels, Flore, Maastricht University Medical Center, Maastricht, Netherlands
- Keijzer-Veen, Mandy G., Wilhelmina Children’s Hospital, University Medical Center Utrecht, Utrecht, Netherlands
- Dorresteijn, Eiske, Sophia Children's Hospital, Erasmus Medical Center, Rotterdam, Netherlands
- Volokhina, Elena, Amalia Children's Hospital, Radboudumc, Nijmegen, Netherlands
- Van den heuvel, Lambertus P.W.J., Amalia Children's Hospital, Radboudumc, Nijmegen, Netherlands
- Van De Kar, Nicole, Amalia Children's Hospital, Radboudumc, Nijmegen, Netherlands

Group or Team Name

- on behalf of the COMBAT consortium

Background

C3 glomerulopathy (C3G) is a rare renal disorder driven by dysregulation of the complement alternative pathway (AP) and characterized by predominant C3 depositions in the glomerulus.

C3G can be subdivided in dense deposit disease (DDD) and C3 glomerulonephritis (C3GN). Patient cohort studies including clinical features offer important data in rare renal diseases. Moreover, biomarkers are increasingly used to select patients for clinical trials with novel complement-targeted therapies. This retrospective study describes complement biomarker profiles and outcome of 29 Dutch children.

Methods

Patients with a C3G diagnosis from 5 Dutch university medical centers (1992- 2014) were included. Clinical, genetic, and laboratory findings were retrieved from patient files. Specialized biochemical assays were used to detect complement-directed autoantibodies and complement biomarkers.

Results

A total of 29 patients with DDD (n=19) and C3GN (n=10) were included. Median (IQR) follow-up was 51 months (26-90). Patients presented with proteinuria and hematuria (>90%) and low serum C3 levels (84%). Ten patients (35%; 8 DDD, 3 C3GN) presented with an impaired glomerulation filtration rate (GFR). DDD patients presented at younger age and with a lower GFR ($P<0.05$). C3 nephritic factors were found in 19 patients, and 3 patients carried rare genetic variants in AP genes. Elevated levels of the complement activation markers C3d, C3bBbP, and C5b-9, combined with lowered C3 and C5 levels, indicated AP activation in the acute phase. Taking longitudinal data into account, a linear mixed model showed that C3GN patients had higher C5b-9 and lower properdin levels than DDD patients ($P<0.05$). During follow-up, 13 (45%) patients experienced a relapse. No significant differences in clinical or laboratory features were observed between patients with and without a relapse and persistent renal sequelae. At last follow-up, only 4 patients (14%; all DDD) had a GFR below 60 ml/min/1.73m^2.

Conclusion

We present the extensive description of clinical, genetic, and biochemical complement features of a large pediatric C3G cohort. In most patients AP abnormalities were found. Overall, the outcome of the patients we described was relatively benign.