Follow the Experts – A review of Case Studies

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The Asian Pacific Society of Nephrology

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Bambino Gesù
OSPEDALE PEDIATRICO

- Presented by Sharon Ford on behalf of Marina Vivarelli

DISCLOSURES – Marina Vivarelli

- Consulting in the last 2 years for: Novartis, SOBI, Alexion, Santhera, Apellis, BioCryst, Bayer, Travere, Roche, Purespring, WebMD

- Sponsored lectures in the last 2 years for: Roche, SOBI, Novartis, Alexion, Travere

- Principal Investigator in clinical trials sponsored by: Alexion, Chemocentrix, Apellis, Chinook, Travere, Bayer, Novartis, received compassionate use of drugs from Vifor, Omeros, SOBI, Novartis, Alexion

Disclosures – Dr Sharon Ford

- Speaker: Abbot Laboratories, Boehringer Ingelheim, Novo Nordisk, Alexion, AstraZeneca
- Advisory Board Member: CSL Seqirus, Novartis, Novo Nordisk, Roche
- Steering Committee Member: Alexion, CSL Seqirus
- Honoraria paid to Austin Health

  - Principal Investigator: Apellis Study - Pegcetacoplan in C3G & IC-MPGN
  - Advisory Board Member: Novartis - Iptacopan, APPEAR C3G Study

A form of C3G with antiFH antibodies: rituximab?

10-yr old girl:

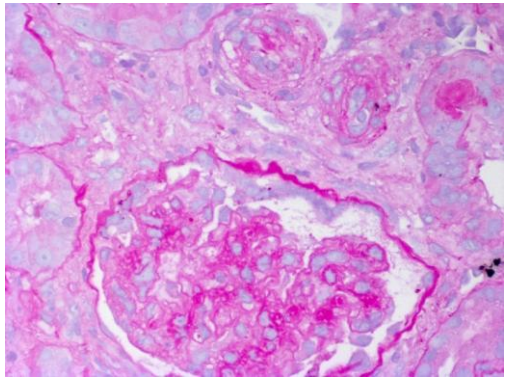
- proteinuria (protein/creatinine ratio 2.32 mg/mg), microscopic hematuria (60-150 blood cells per field)
- normal serum creatinine
- ↓ serum C3 and C4
- ↑ sC5b9 (2270 ng/ml)
- normal ANA and anti-dsDNA

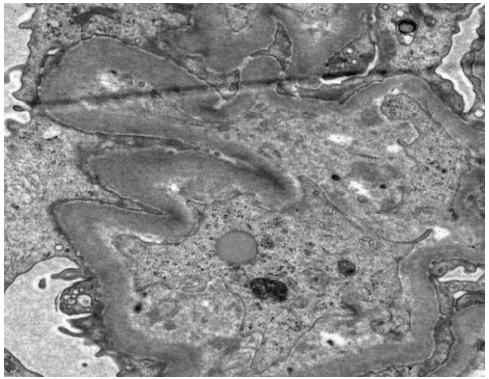
Kidney biopsy: membranoproliferative glomerulonephritis with mainly granular C3 by IF.
A low-salt diet, oral prednisone and mycophenolate were immediately started.
Treatment with 3 methylprednisolone pulses were added.

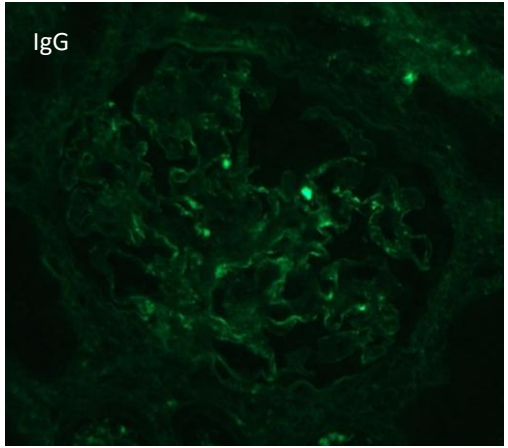
Screening for complement abnormalities: homozygous mutation in CFHR1-5. As expected, **Ab-FH (1069 AU/ml, upper limit of normal >127 AU/ml)** was found to be positive and Rituximab infusion (375 mg/m2) was administered. Interestingly, Ab-FH titer was not significantly reduced by Rituximab (739 AU/ml at 4 months) without any effect on proteinuria in the following months.

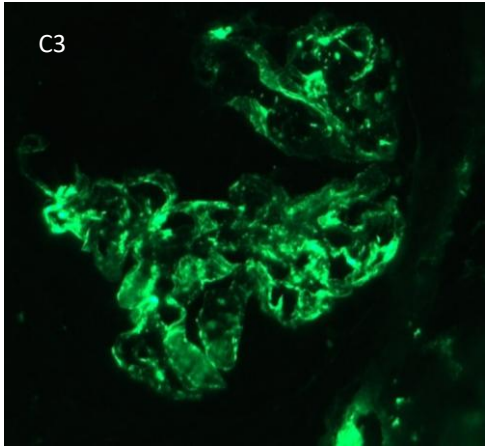
Ferri et al, Ped Nephrology 2024: 12 pts with anti-FH aHUS (4 no IS, 4 RTX, 4 MMF) no difference in decrease of anti-FH titers

Coexistence of C3G and aHUS





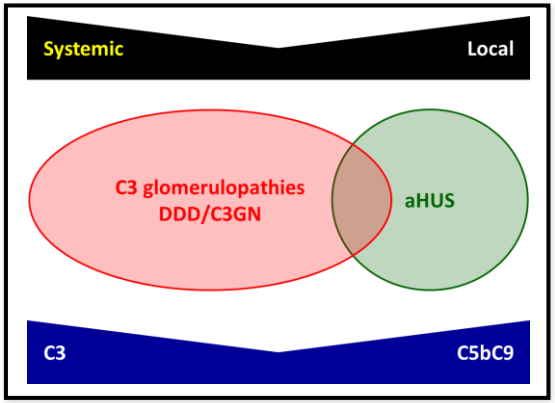




Courtesy of Dr F. Diomedi-Camassei

Male, 4 years old, aHUS
Nephrotic syndrome following recovery from anuric phase

Complete remission of proteinuria with eculizumab



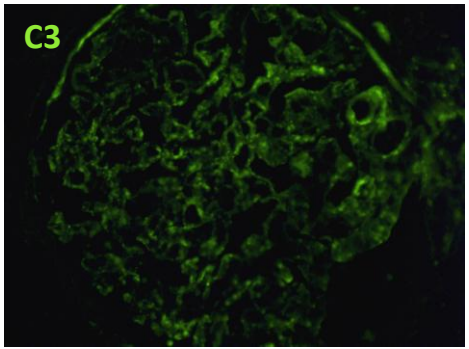
Busutti et al KI Reports 2020

A genetic form of C3G

Nine months old girl (2014):

- macroscopic hematuria
- normal kidney function (Cr 0.2 mg/dL)
- nephrotic syndrome with hypoalbuminemia, nephrotic proteinuria-to-creatinine ratio (UPCR 3.3)
- ↓ C3. Anti-FH antibodies and C3Nef were negative, and ↑ sC5B9 levels.

Kidney biopsy: mesangioproliferative glomerulonephritis with C3 deposits



Genetic testing: **heterozygous p.R127C variant in the CFH gene**,
pathogenic for C3G, which was also present in the patient's father (who also developed C3G at age 37)

Treatment: No response to prednisone, cyclosporine (CsA), and ACE inhibitor was initiated. **From February to August 2016, the patient received Eculizumab**, which was discontinued due to lack of therapeutic response. Since December 2023, renal function rapidly deteriorated and she was studied for a kidney transplant.

Giannini et al, manuscript in preparation

A genetic form of C3G

Due to

- Genetic familial form
- Persistently low circulating C3
- Young age and very limited tolerance of dialysis

the risk of relapse post-transplantation was considered extremely high.

LRKT form her mother, with **prophylactic pegcetacoplan**.

4 months post-kidney transplant:

- normal kidney function
- elevated C3
- no proteinuria
- no sign of relapse on protocol biopsy

Giannini et al, manuscript in preparation

Take-home messages

- Anti-FH antibodies do not appear to be modified by anti-CD20 monoclonal antibody-induced B cell depletion
- Terminal complement inhibition may be more effective in mixed C3//atypical HUS forms than in pure C3G
- Very rare genetic forms of C3G may be particularly challenging and represent forms with a particularly high risk of relapse post-transplantation

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The patients and their families

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