25th Hellenic Congress of Nephrology

‘Meet the expert’ session

Case presentation of C3 glomerulopathy

Clinic of Nephrology and Renal Transplantation

National and Kapodistrian University of Athens, Medical School

General Hospital of Athens ‘Laiko’

- C3 glomerulopathy is characterized by **predominant C3 glomerular deposition** and is associated with abnormal control of the alternative complement pathway

- ~ 40% of the patients progress to **advanced kidney disease**

- **Recurrence post-Tx** is observed in 67%–84% of the patients in a median time of 14–28 months

- Half of the patients with recurrent C3GN develop **allograft failure** within 10 years

Zand L. J Am Soc Nephrol. 2014 May;25(5):1110-7

Bomback AS. Kidney Int. 2018 Apr;93(4):977-985

Regunathan-Shenk R. Am J Kidney Dis. 2019 Mar;73(3):316-323

- **Case presentation:**

  Male, 22 years old

  Impaired kidney function, sCr: 2.54 mg/dl → eGFR: 36 ml/min/1.73m^2, CKD-EPI

  Proteinuria: 1.5 g/24h

  Hematuria

  Low serum C3 level

- **Family medical history**:

  Mother with hematuria and low C3 level

- **Kidney biopsy**:

  LM: 17 glomeruli, 64.7% globally sclerosed

  50% interstitial fibrosis/tubular atrophy

  Diffuse mesangial proliferation

  IF: dominant C3 staining (4+), C4,C1q (-), traces of IgG,IgA,IgM,κ- and λ- light chains

  EM: not available

  Diagnosis: C3 glomerulopathy with chronic lesions

- **Genetic testing**:

  Positive for the heterozygous sequence variation c.341G>A p.(Cys114Tyr)

  in the CFH gene

- **Testing for autoantibodies**: Negative for C3NeF, C4NeF, anti-CFH Abs

- **Conservative management** due to advanced chronic kidney disease

  RAAS blockade

  SGLT-2 inhibitors

  No immunosuppressive therapy

- The patient gradually progressed to **ESKD**

- (10/2022) Preemptive, ABO incompatible, **living-donor kidney transplantation**

  LD: Paternal aunt

  CDC and FXM: negative, no DSA

  Desensitization protocol due to ABO incompatibility: RTX + TPE + IVIG

- The patient underwent a **kidney graft biopsy** (post-Tx d25) due to unsatisfactory creatinine level decline (sCr: 1.82 mg/dl)

  LM: 15 glomeruli, no global glomerusclerosis

  diffuse **mesangial proliferation**

  15-20% interstitial fibrosis/tubular atrophy

  IF : dominant **C3 staining 4+**; C1q,IgM,κ,λ traces; IgG,IgA absent

  EM : electron-dense **mesangial** and **subepithelial** (humps) **deposits**

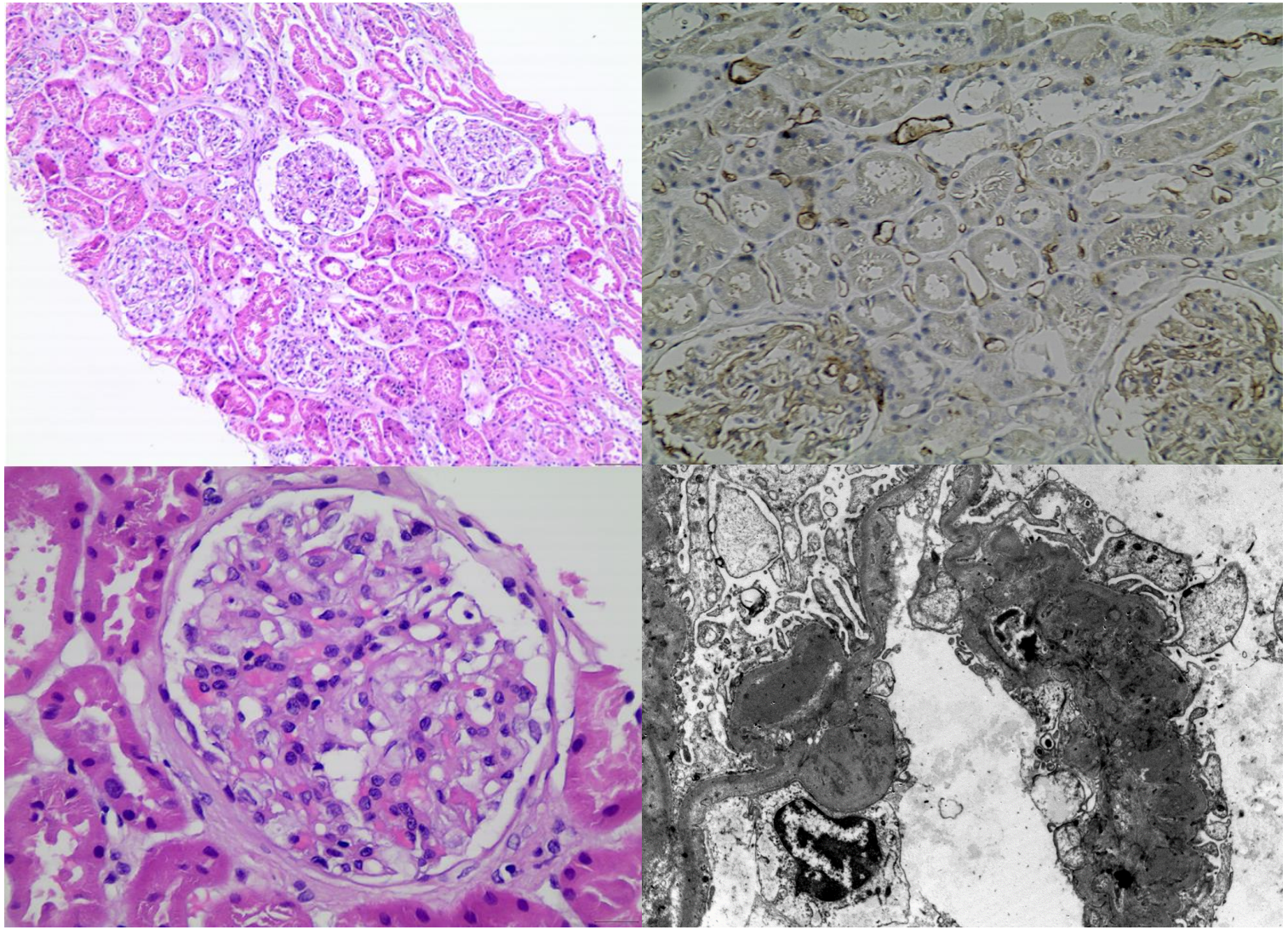
  Diagnosis: Post-transplant C3GN recurrence

- Low serum C3 levels 71.2 mg/dl (post-Tx d6)

- Urine protein level: 233 mg/24h

- Bland urine sediment

Kidney graft biopsy images



Courtesy of Dr. George Liapis, renal pathologist

ORIGINAL ARTICLE

Nephrol Dial Transplant (2018) 33: 2260–2265
doi: 10.1093/ndt/gfx369
Advance Access publication 23 January 2018

C3 glomerulonephritis secondary to mutations in factors H and I: rapid recurrence in deceased donor kidney transplant effectively treated with eculizumab

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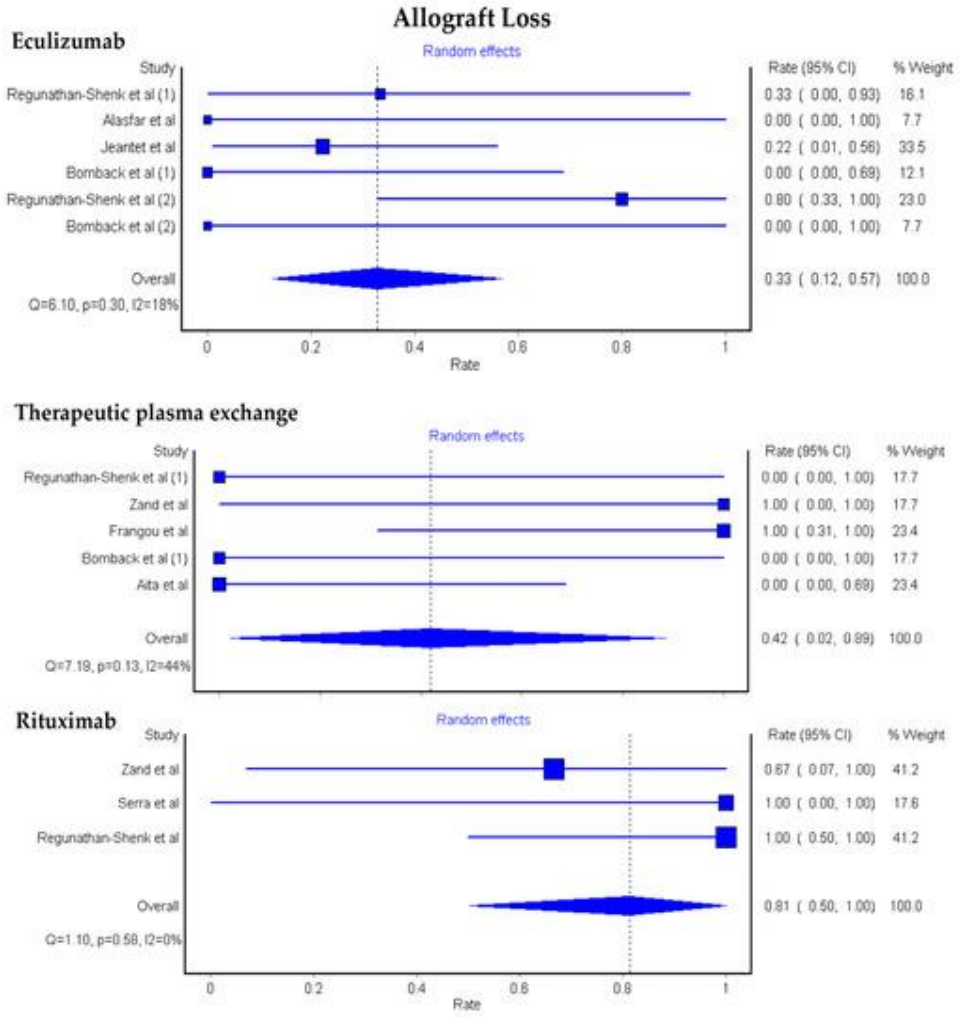
Treatment of C3 Glomerulopathy in Adult Kidney Transplant Recipients: A Systematic Review

by Maria L Gonzalez Suarez [1,2,*], Charat Thongprayoon [2,*], Panupong Hansrivijit [3], Karthik Kovvuru [4], Swetha R Kanduri [4], Narothama R Aeddula [5], Aleksandra I Pivovarova [1], Api Chewcharat [6], Tarun Bathini [7], Michael A Mao [8], Arpita Basu [9] and Wisit Cheungpasitporn [1,2,*]



The pooled estimated rates of **allograft loss** among KTx recipients with C3GN were

33% after **eculizumab**, 42% after **TPE** and 81% after **rituximab**

Gonzalez Suarez ML. Med Sci (Basel). 2020 Oct 21;8(4):44

- Due to the **early C3GN recurrence**, treatment with the anti-complement C5 agent, **eculizumab,** was decided

- **Therapeutic regimen**:
  900 mg per week for the first 4 weeks,
  1200 mg per 2 weeks afterwards

- Six months later the patient had a stable renal graft function (sCr: 1.87 mg/dl) without proteinuria

- (04/2023) A second **renal graft biopsy** due to **high-level BKV viremia** and **increased serum creatinine** (2.2 mg/dl) was performed:

  LM: 29 glomeruli, 7% global sclerosis

  Diffuse mesangial proliferation

  15% interstitial fibrosis/tubular atrophy

  IF : **dominant C3 staining (3+)**, C1q/IgA/IgM/κ/λ traces, IgG absent

  SV40 polyomavirus immunohistochemistry: positive

- Diagnosis : **BK Virus nephropathy PVN class 1** and **reccurent C3 glomerulonephritis**

- Management:

  Eculizumab cessation + **reduction of immunosuppression** + **IVIG**

- BKV clearance 3 mo later
- BKV viral load and renal graft function monitoring
- **Last follow-up visit** (05/2024):

  sCr: 1.82 mg/dl

  UPr: 240 mg/24h

  C3 level: 46 mg/dl

  Bland urine sediment

  Negative BKV viral load

What therapeutic steps should be taken next?

How would you approach this patient?