Case Presentation

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Particulars

- 24- year- old male, presented in Nov 2014

  with complaints of giddiness, nausea , dyspnoea on exertion, decreased appetite,

  generalised weakness ,with BP 160/100 mm of Hg,

- On presentation , Serum Creatinine was 4.0 mg/dl.
- USG of abdomen S/O bilateral small, shrunken kidneys (RK 7.5 x 3.5cm & LK 8.1 x 3.7cm) with loss of CMD.
- Diagnosed with chronic kidney disease stage V,

  ? Cause Unknown on conservative management.

- Presented in Jan 2015 with Serum Creatinine 9 mg/dl , Initiated on Hemodialysis.
- Patients was on maintanance Hemodialysis thrice a week
- Meanwhile was being worked up for renal transplant..
- His father undergo pre- operative transplant work up and found to be fit as donor.
- Underwent live related renal transplant on 08/06/2015
- No induction

- On Triple immunosuppresion therapy :

  Tacrolimus, Mycophenolate sodium, Corticosteroids.

- Discharged post op day 10 with baseline Serum creatinine of 1.1mg/dl.
- Patient was asymptomatic for next 2 years with stable creatinine and Tac levels

  & lost to follow up in next 6 months

- Presented in Feb 2018 with complaints of fever on & off, decreased appetite,

  generalised weakness since 15 days.

Examination – General

- Concious, Oriented
- PR- 84/min,
- B.P.- 140/80 mm Hg,
- RR-20/min,
- Afebrile
- No Pallor
- Edema – absent

Examination-Systemic

- CVS - S_1 S_2 Heard, No Murmur
- CNS - No Focal Deficit
- Respiratory System - B/L Normal Vesicular Breath Sounds
- P/A - Soft, Non tender,

  Transplanted kidney is palpable with scar mark seen in right illiac fossa.

Investigations-Urine

- Urine R/M-
- Protein-+++
- RBC-6-8/ hpf
- Pus cells-2-3/hpf
- UPCR- 3.0

Investigations-Routine

- Hb-12.5 gm%
- TLC-10000 cells/cumm
- Platelet-2.3 lakhs/cumm
- Blood Urea-**89 mg/dl**
- Serum Creatinine- **5.8mg/dl**
- Serum Na-142 mmol/l
- Serum K-4.2 mmol/l

Investigations

- Serum Uric acid – 7.8 mg/dl.
- Serum Phosphrous – 5.7 mg/dl.
- Serum Calcium- 7.6 mg/dl
- HIV, HBsAg, Anti HCV -Negative
- USG of Transplanted Kidney size : 11.4 x4.3 cm, CMD maintained, normal echogenecity.

- Blood C/S – no growth
- Urine C/S – no growth
- CMV load – negative
- B K Virus load – negative

Differential Diagnosis

- ? Chronic allograft nephropathy
- ? Recurrence of primary disease
- ? B K Virus nephropathy

- Patient underwent graft biopsy :

Light Microscopy

2H&E, 2 PAS, 1 Silver methanamine, 1MT, 1 GMS stained section of allograft kidney biopsy studied.

Kidney biopsy in single linear core reveal 11 glomeruli of which 2 glomeruli are globally sclerosed.

The remaining glomeruli show variable morphology in form of fibrous crescents in 2 glomeruli, segmental sclerosis in 1 glomerulus,

and remaining glomerular tuft show mild mesangial matrix expansion with mesangial hypercellularity.

No glomerulitis or chronic glomerulopathy seen.

No necrotizing lesion seen.

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Tubulointerstitial compartment show diffuse acute tubular injury
associated with moderate interstitial inflammation and interstitial edema.

No tubulitis seen.

Few small patches of tubular atrophy accompanied
with interstitial fibrosis are seen occupying 20-25% of the sampled cortex.

In addition, an occasional tubule show neutrophilic reaction to cast material.

Vascular compartment show no endothelitis (v0) or transplant arteriopathy .

Few arterioles show non-circumferential hylinosis.

No peritubular capillaritis is noted.

Few interstitial blood vessels show moderate medial thickening.

There is no morphological evidence of BKV nephropathy or CNI toxixity

Immunofluorescence: IF core reveals 5 glomeruli

IgG: Negative

IgA: 3+ granular in mesangium

IgM: Negative

C3: Negative

C1q: Negative

Kappa: 2+ granular in mesangium

Lambda: 2+ granular inm mesangium

C4d: Negative in peritubular capillaries (C4d0)

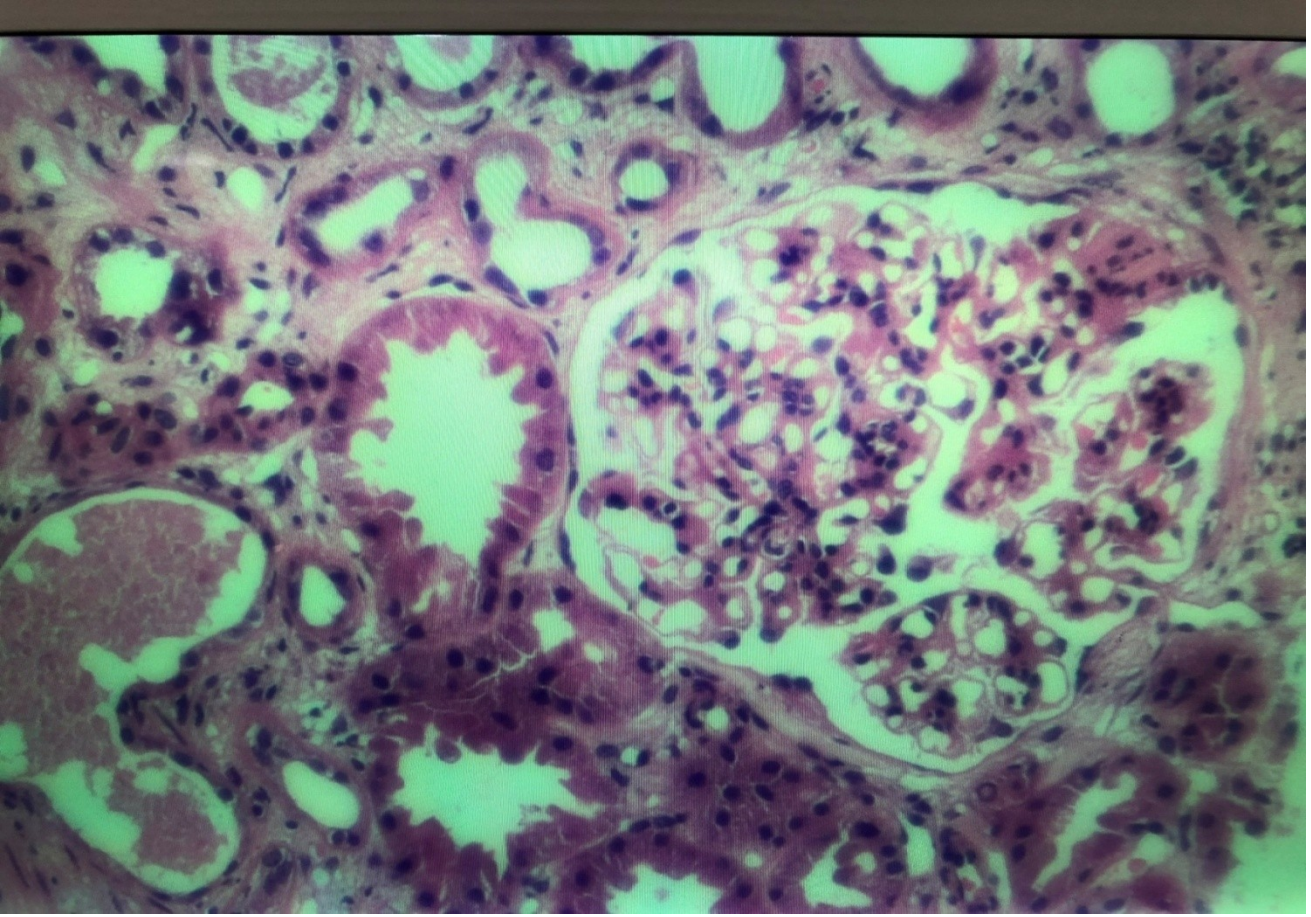
Immunohistochemistry:

SV40-Negative

Overall features are of IgA nephropathy (denovo/recurrent) with 18% glomerular crescents.

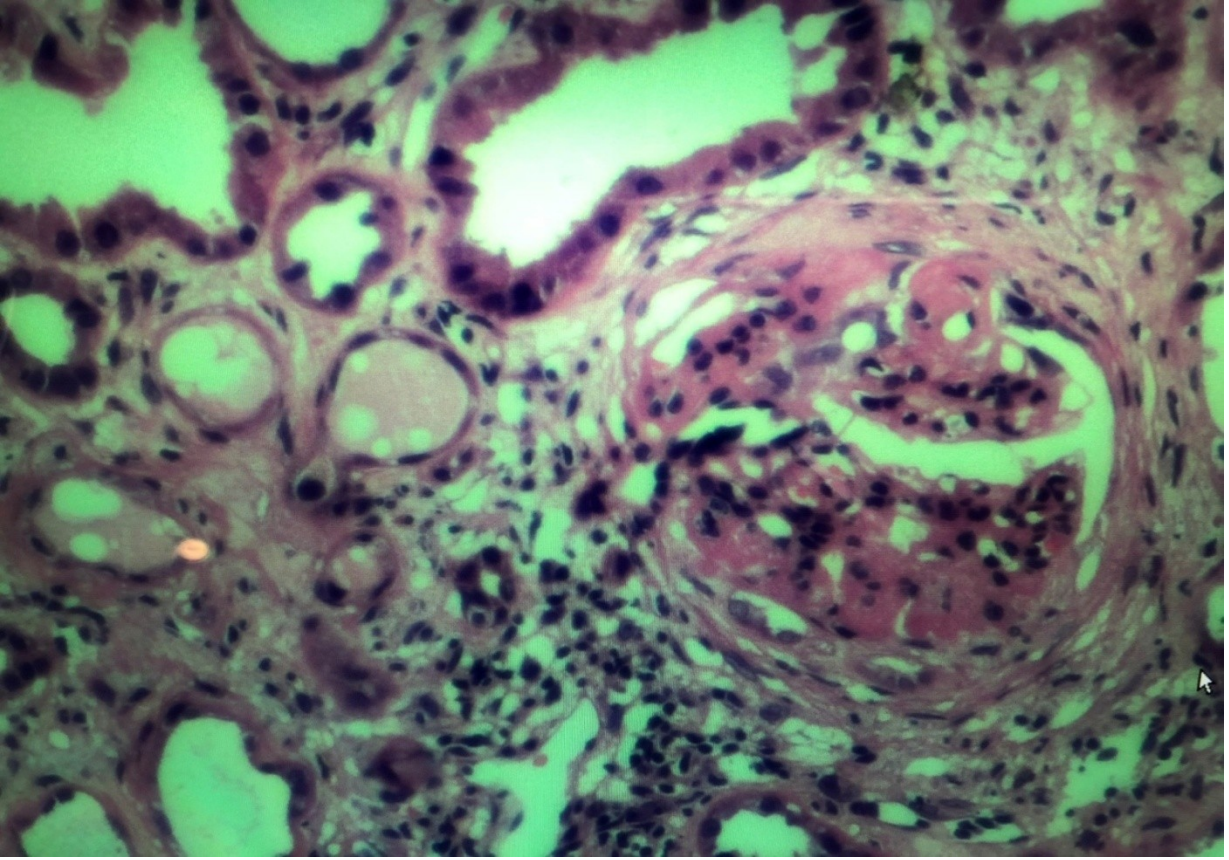
Diagnosis:

IgA nephropathy (denovo/recurrent) with 18% glomerular crescents.



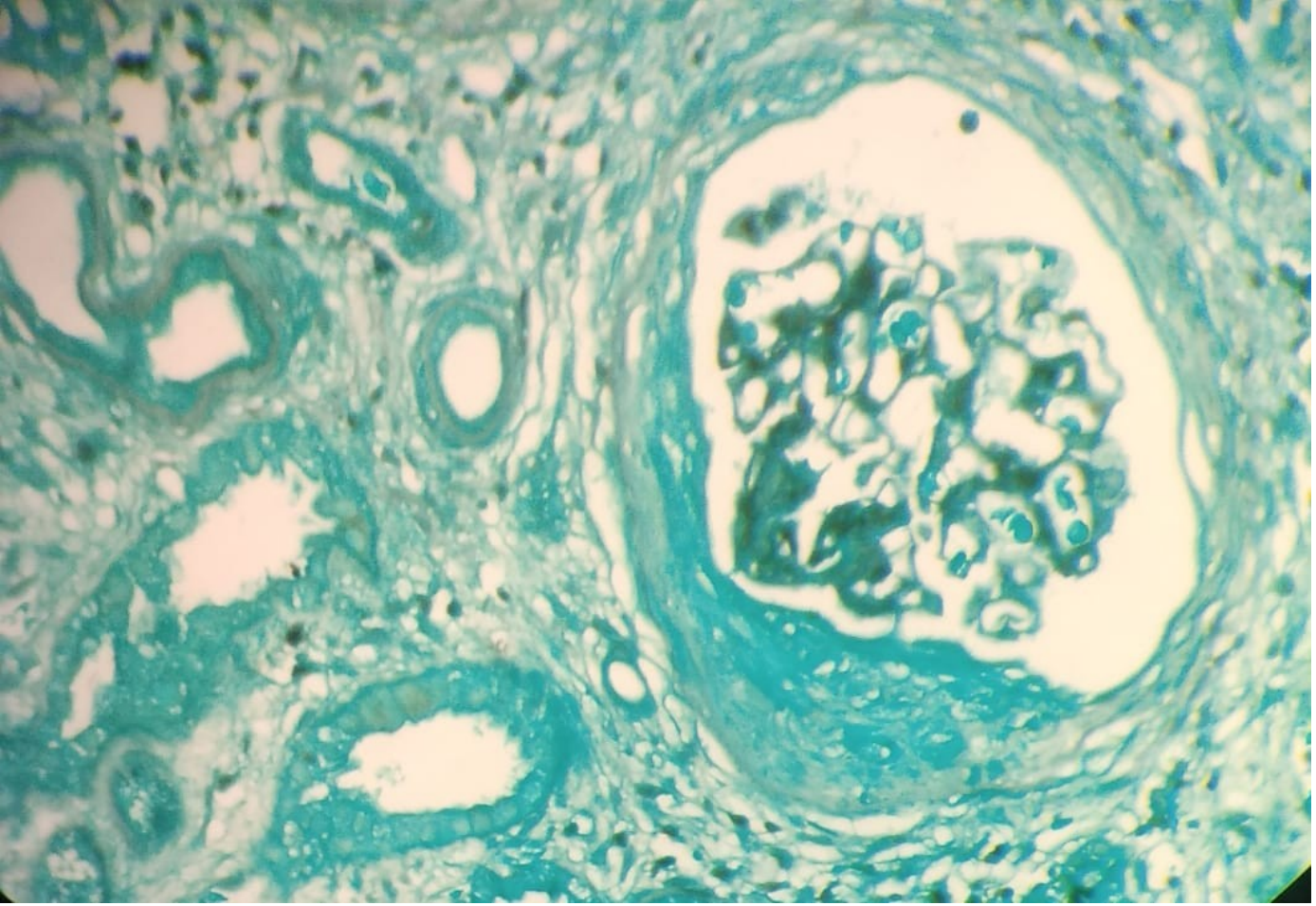
Mesangial proliferation and matrix expansion that can be focal, but more often seen diffusely.

H & E Stain



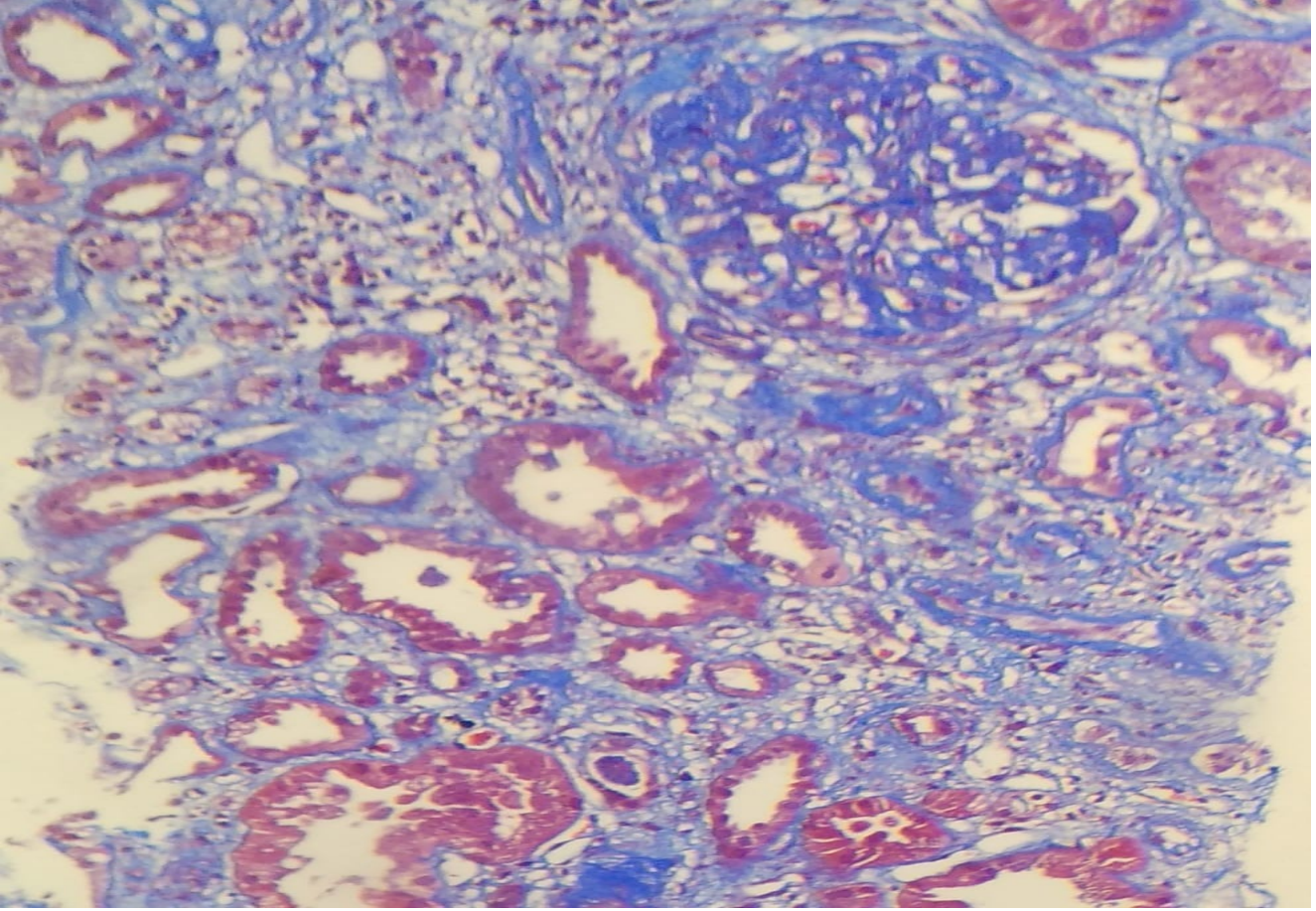
Cellular crescent with partial collapse of glomerular tuft.

H & E Stain



Mild to moderate mesangial hypercellularity can be seen.

GMS Stain



Transplanted glomerulopathy may show mesangial proliferation and matrix expansion.

MT Stain

Treatment

- IV Pulse therapy (methylpredisolone 1 gm) for 3 days , followed by oral steroids.
- Tripple immunosuppressants were continued.
- Patient underwent 4 cycles of Plasmapheresis and 3 dose of IV Cyclophosamide 500mg.
- Patient responded to given treatment .
- At Present , He is on regular follow up with Serum Creatinine of 2.8mg/dl.

Final Diagnosis

Graft Dysfunction/ Recurrence of IgA Nephropathy with Cresents.

Discussion

Introduction

- Immunoglobulin-A nephropathy (IgAN) is the most common primary glomerulonephritis worldwide [1] and 20–40% of patients progress to end-stage renal failure [2].
- For these patients, transplantation offers an excellent option for renal replacement therapy.
- However, immunohistological recurrence develops in as many as 60% of allografts by 10 years after engraftment [3].

1.Levy M, Berger J. Worldwide perspective of IgA nephropathy. Am J Kidney Dis 1988; 12: 340–347
2.Radford MG Jr, Donadio JV Jr, Bergstralh EJ, Grande JP. Predicting renal outcome in IgA nephropathy. J Am Soc Nephrol 1997; 8: 199–207
3.Odum J, Peh CA, Clarkson AR *et al*. Recurrent mesangial IgA nephritis following renal transplantation. Nephrol Dial Transplant 1994; 9: 309–312

IgAN

- IgAN is a primary GN characterized by the dominant or co-dominant diffuse mesangial deposition of IgA, usually IgA1.
- The deposits consist of an aberrant galactose-deficient form of IgA1 and IgA or IgG autoantibodies to the aberrantly glycosylated IgA1.
- Recurrences of IgAN can be “immunopathologic” only.
- Clinical recurrence of IgAN may occur immediately after transplantation, but on average the diagnosis is made approximately 3 years after transplantation (1,2) and is usually presented by hematuria and low-grade proteinuria.
- Recurrence tends to occur more frequently in younger patients and in those with a rapid progression of the original disease

1. Ponticelli C, Traversi L, Banfi G: Renal transplantation in patients with IgA mesangial glomerulonephritis. *Pediatr Transplant 8: 334–338, 2004*
2. Suzuki K, Honda K, Tanabe K, Toma H, Nihei H, Yamaguchi Y: Incidence of latent mesangial IgA deposition in renal allograft donors in Japan. *Kidney Int 63: 2286–2294, 2003*

- An analysis of the Eurotransplant registry data reported the outcome of 1207 patients with IgAN and 7935 other renal transplant recipients.
- The 10-year death-censored graft survival was identical in the control group with and without the HLA-B8, DR3 haplotype but significantly worse in IgAN patients carrying the HLA-B8, DR3 haplotype than in patients without it, suggesting that this HLA haplotype may represent a risk factor for transplant recipients with IgAN (1).
- A review of the data collected by the Australia-New Zealand registry reported that biopsy-proven IgAN recurrence was significantly more frequent in zero HLA-mismatched living donor grafts (2).

1. Andresdottir MB, Haasnoot GW, Persijn GG, Claas FH: HLA-B8, DR3: A new risk factor for graft failure after renal transplantation in patients with underlying immunoglobulin A nephropathy. *Clin Transplant 23: 660–665, 2009*
2. McDonald SP, Russ GR: Recurrence of IgA nephropathy among renal allograft recipients from living donors is greater among those with zero HLA mismatches. *Transplantation* 27, 759–762, 2006

- No specific therapy for recurrent IgAN is currently available.
- A review of the U.S. Renal Data System examined the effect of immunosuppressive medication on allograft failure due to recurrent GN.
- After adjusting for important covariates, the use of cyclosporine, tacrolimus, azathioprine, mycophenolate mofetil, sirolimus, or prednisone was not associated with graft failure due to recurrent GN for any type of GN, including IgAN (1).
- Angiotensin converting enzyme inhibitors (ACEIs) may be prescribed because a study showed that their use could reduce proteinuria and blood pressure in transplant recipients with IgAN (2), but may be associated with significant decreases in GFR (3).

1. Mulay AV, van Walraven C, Knoll GA: Impact of immunosuppressive medication on the risk of renal allograft failure due to recurrent glomerulonephritis. *Am J Transplant*9: 804–811, 2009
2. Oka K, Imai E, Moriyama T, Akagi Y, Ando A, Hori M, Okuyama A, Toki K, Kyo M, Kokado Y, Takahara S: A clinicopathological study of IgA nephropathy in renal transplant recipients: Beneficial effect of angiotensin-converting enzyme inhibitor. *Nephrol Dial Transplant 15: 689*–695, 2000
3. Hiremath S, Fergusson D, Doucette S, Mulay AV, Knoll GA: Renin angiotensin system blockade in kidney transplantation: A systematic review of the evidence. *Am JTransplant 7: 2350–2360, 2007*

- Tonsillectomy has been suggested to be of benefit by Japanese investigators.
- In the rare cases of recurrent IgAN associated with a rapidly progressive course and crescents at biopsy, a trial with high-dose corticosteroids, cyclophosphamide, and plasmapheresis may be attempted, although the results are usually poor.

Thank You