The first case is often a hard case-the first treatment of Antibody-mediated rejection with immunoadsorption and alemtuzumab in Hungary

A case from Debrecen, Hungary

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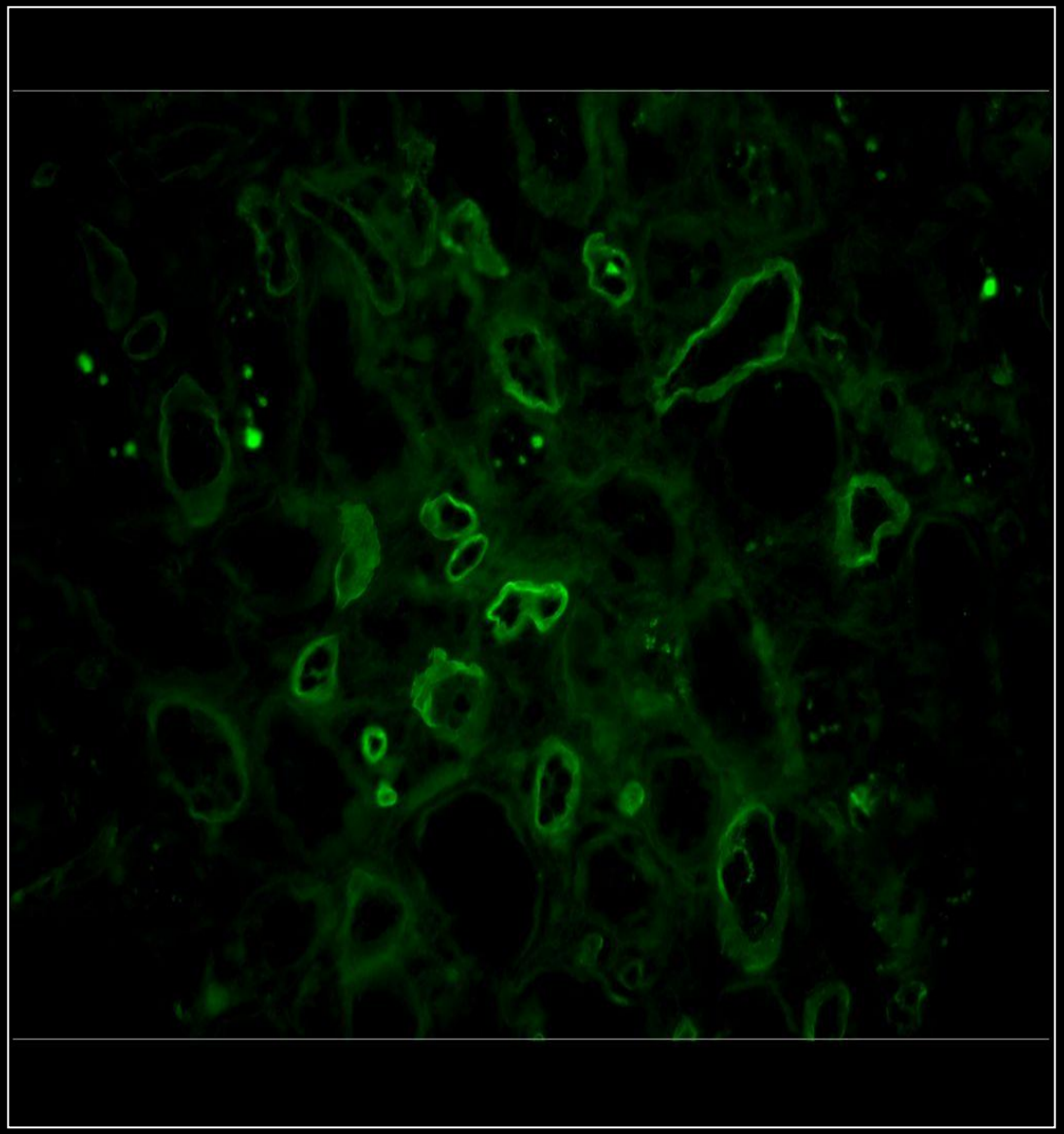
History and early Course

- 51 y/o Hungarian male with ADPKD, HTN and no major comorbidities
- ESRD on maintenance dialysis starting in 2006
- Cadaveric renal transplantion in August, 2007 with primary non-function
- Graftectomy in October 2007-histology showing acute humoral and cellular rejection
- Re-transplant July 2014: 55 y/o heartbeating donor with HTN history and 1+ proteinuria not quantified, se creatinine 26.5 mcmol/L- from Germany
- CIT 22 h 17 min, HLA matching: 2A 1 B 1 DR, CMV d-r+
- Induction with Thymo 1,5 mg/kg/d for 5 days, MMF 2x1000 mg, Prograf 10-13 mcg/L initial target
- Oliguric until day 4 /residual uo 500 ml/d/ then graft function improves with urine output over 2000 ml/day

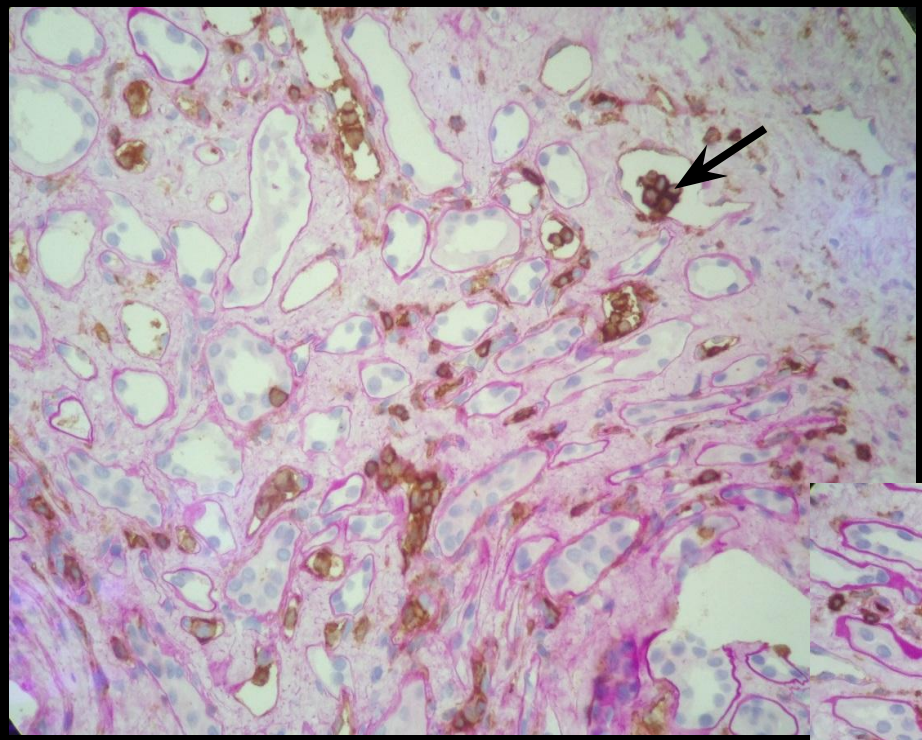
Early Course 2

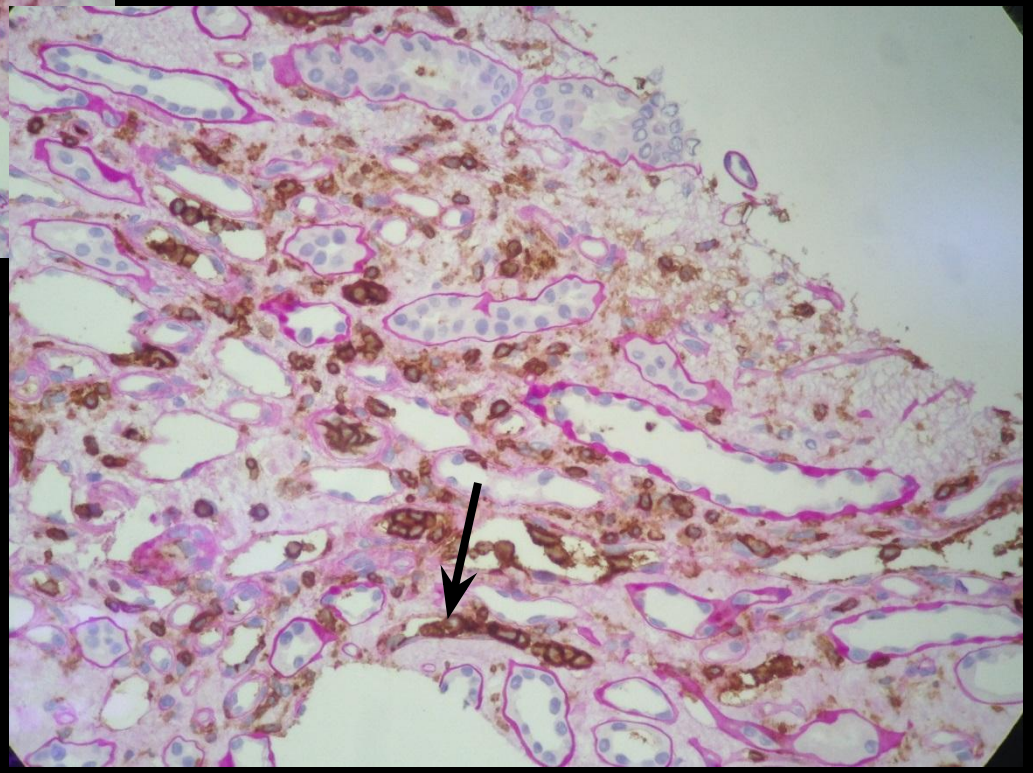
- At discharge, Se creat 200-220 mcmol/L, U alb/creat 17.9 mg/mmol, early DSA: HLA B44 MFI 2529 day 15 decreased then completely disappeared on subsequent follow up /October 2014, month 3/-Pt refusing biopsy
- RI 0,7 normal renal sizes, cortical thickness and parenchyma
- First 4 months: se creat 190-230 mcmol/L, proteinuria 19-33 mg/mmol, BP and volume status well controlled
- November 2014: Admission for signs of nephrotic syndrome, proteinuria 360 mg/mmol, se creat rising, DSA: DP13 6900 MFI **/appearance of multiple DP antibodies and consequent request for donor DP typing not previously done!/**
- Renal biopsy done

Initial Biopsy showing C4d deposition at PTC BM



Peritubular capillaritis (ptc3) (PAS-LCA)

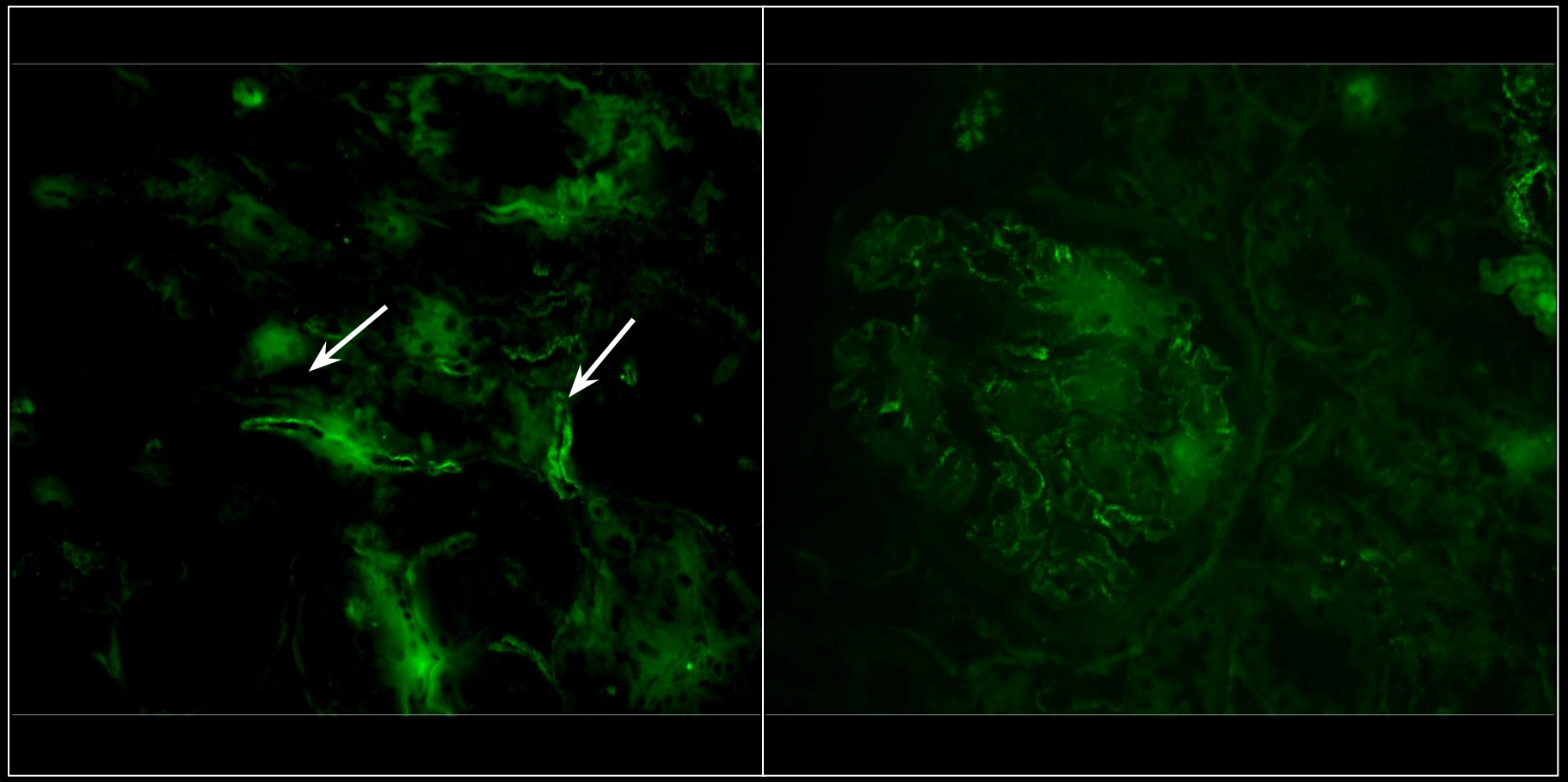




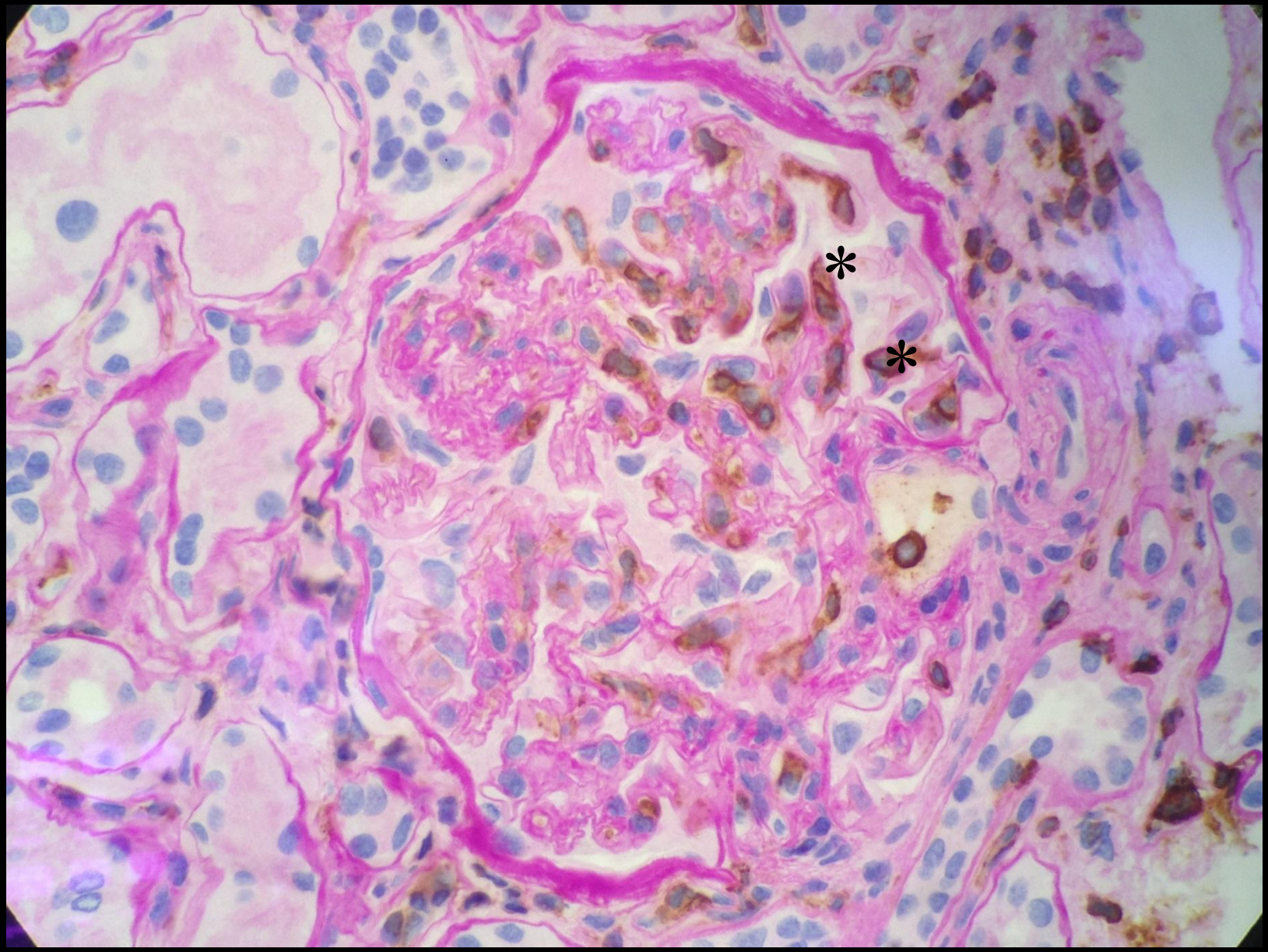
Summary of Treatment and Early Response-1

Treatment	initial	Follow up	Side efect-1	Side effect-2
Immunoadsoprtion *	3 sessions daily	Thrice weekly	Hypogamma globulinemia /1,23 g/L/	Generalized weakness, shivering
Steroid bolus				
HD started due to hypervolemia and creatinine rising to 500-600 mcmol/L				
Repeat biopsy in 1 week as creatinine was rising				
*Plasmaflux Globaffin-Potein A, 6150 ml plasma volume/session, TBV 28 L				

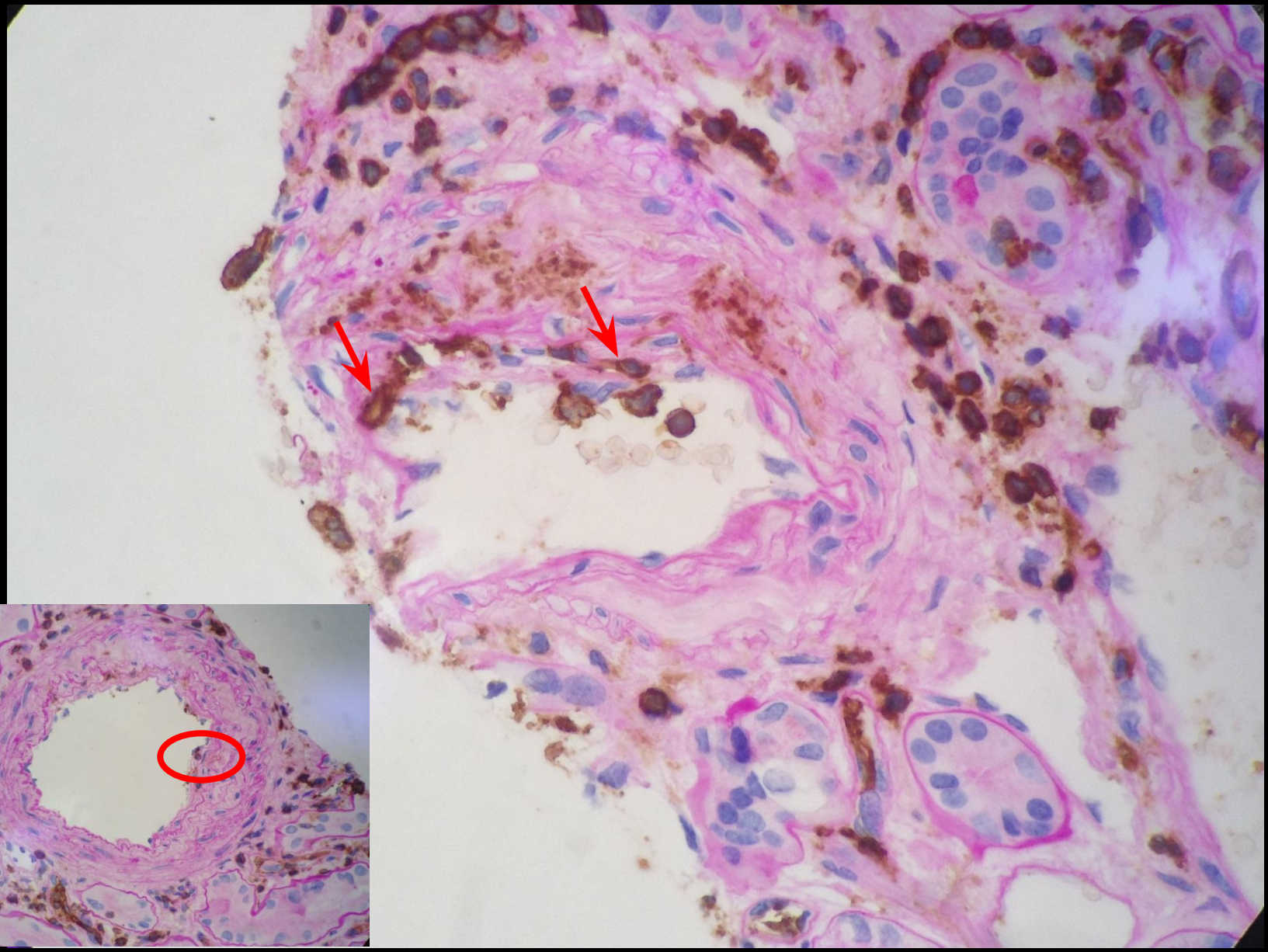
Only focal /<10%/ C4d deposition at PTC BM



Ischemic wrinkling of the GBM, g3



Endothelialitis, v1 (PAS-LCA)



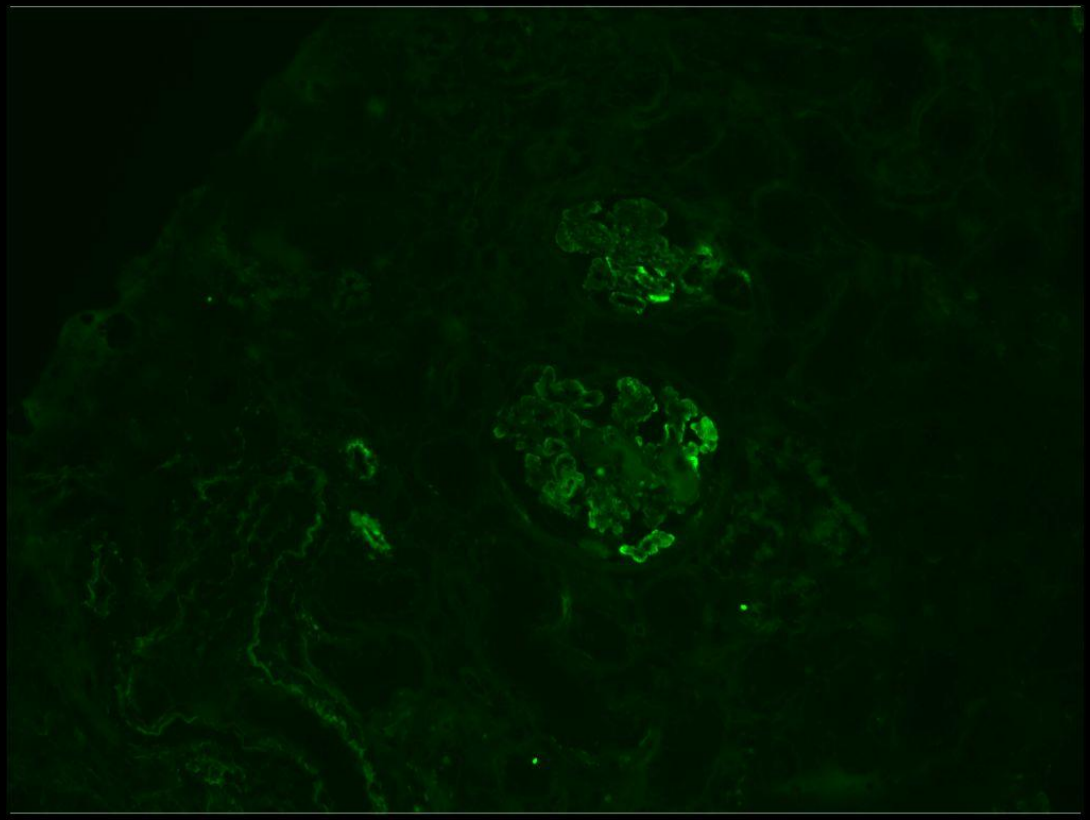
Summary of Treatment and Early Response-2

Treatment				
Thymoglobulin started /1,5 mg/kg/d x6 days/				
Repeat DSA: DP 13 MFI 3564, Proteinuria <1 gm/day, Se creat stabilized around 250-290 mcmol/L Rituximab 500 mg x1 **Maintenance regimen at discharge:** Methylprednisolone, tacrolimus; MMF temporarily converted to mTor due to persistent leukopenia				

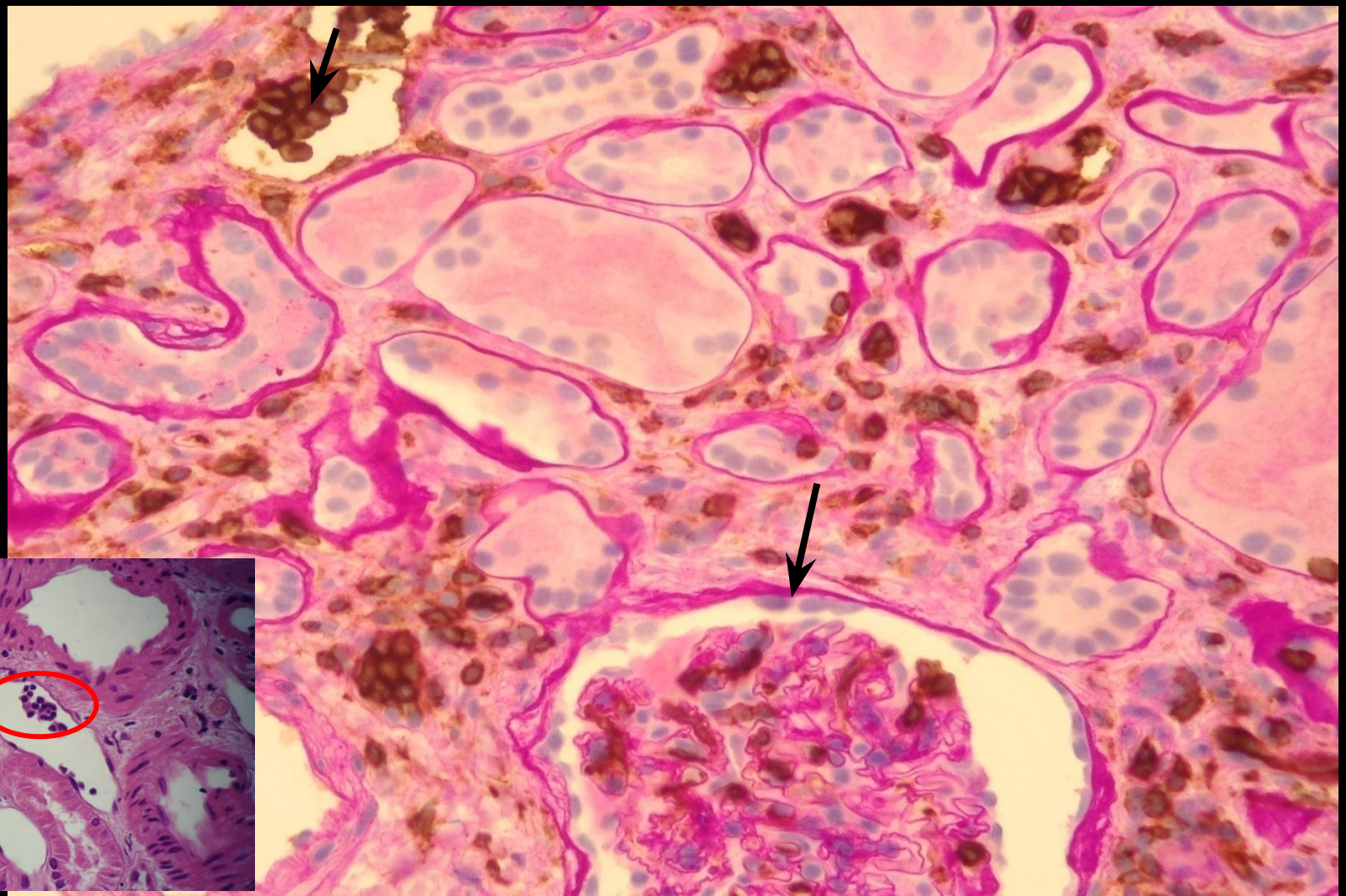
One month later….

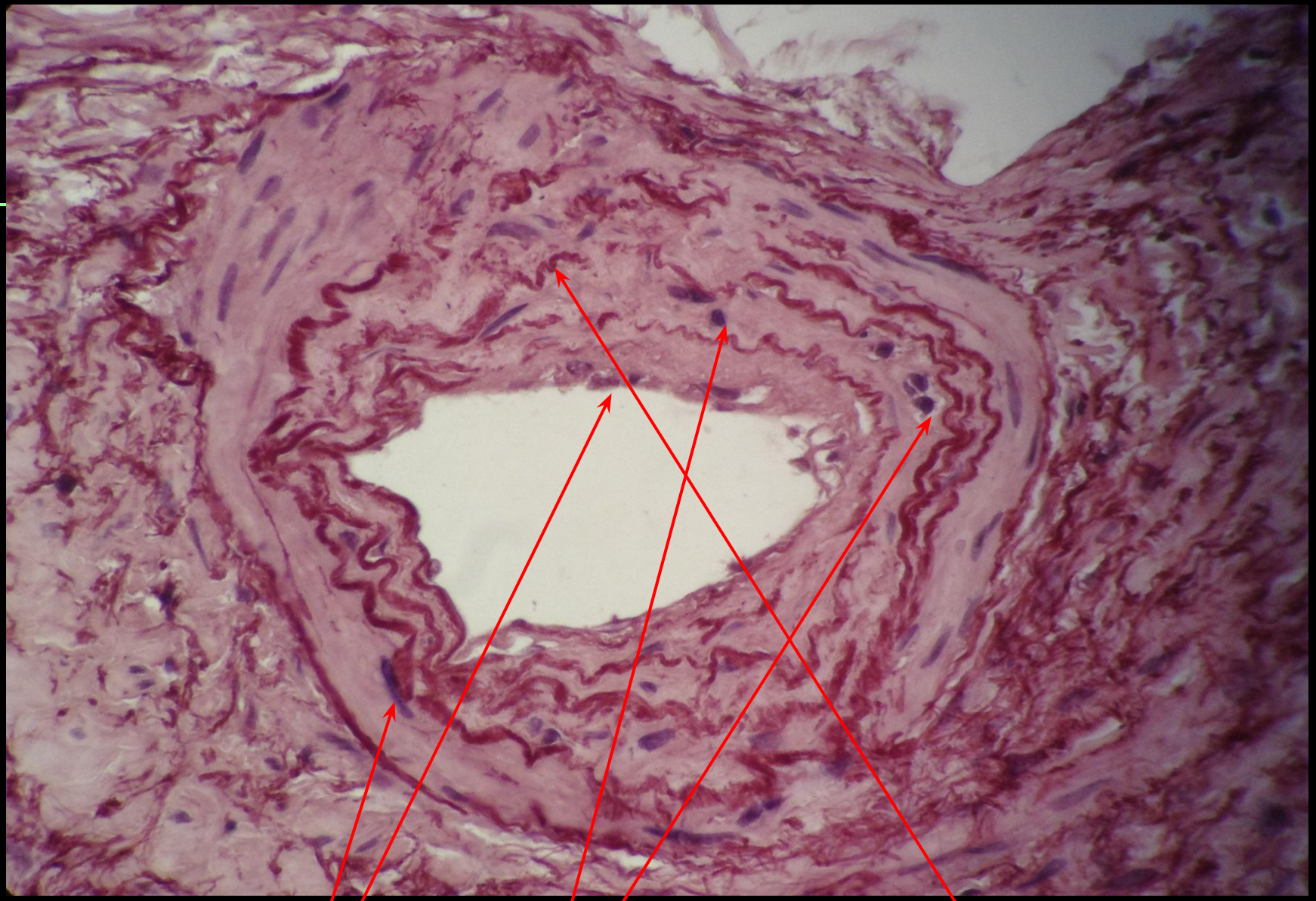
- Re-admitted due to proteinuria exceeding 3 gm/d, se creat 378 mcmol/L and rising, DSA /DP13/ 6405 MFI
- Renogramm /dynamic flow/ showing ATN
- Started on hemodialysis for oliguria, hypervolemia and creatinine rising >600 mcmol/L
- Repeat biopsy done

PTC BM: C4d negative

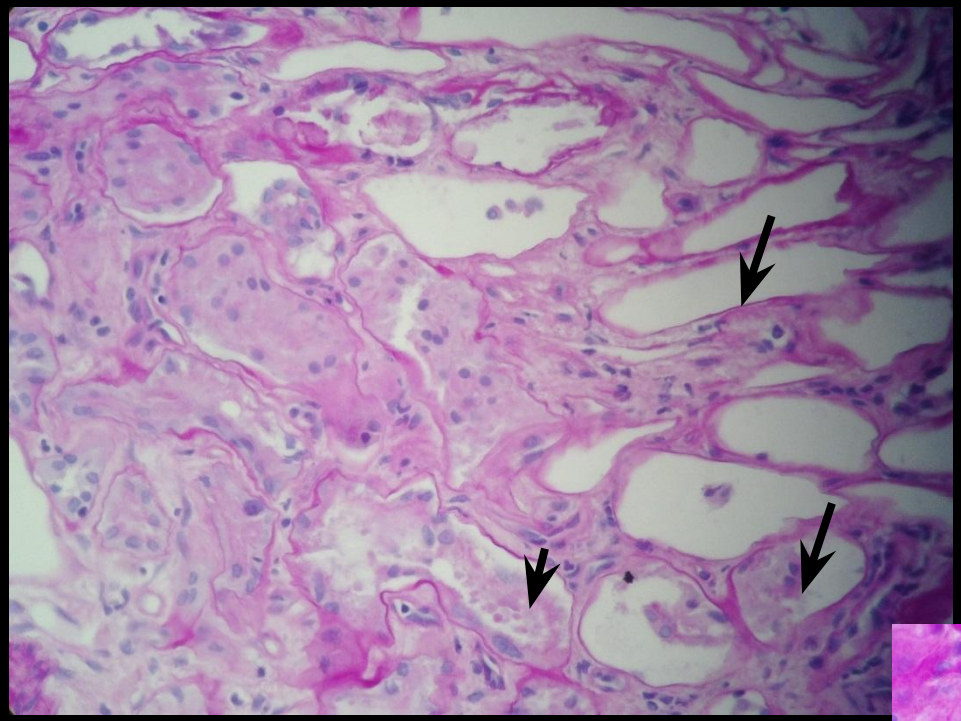


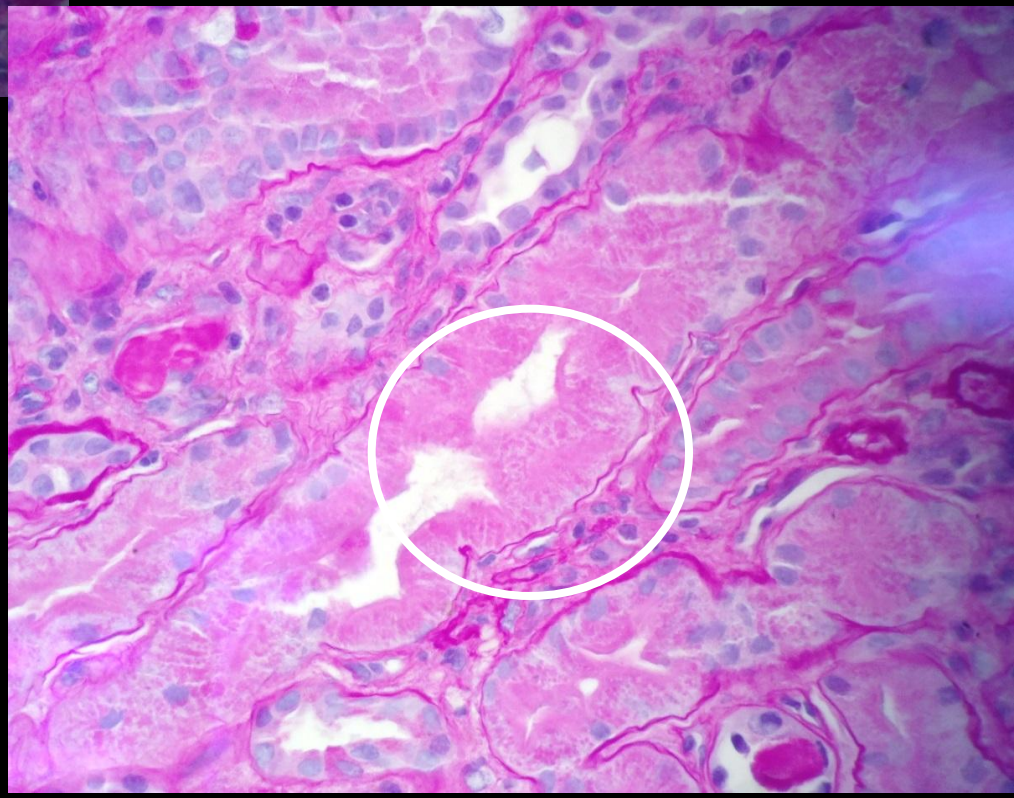
Repeat Biopsy: ptc3, g3 /PAS-LCA/





intimalis fibroelastosis with multilayering, injured lamina elastica, mild initimal fibrosis, lymphocytic infiltration /CD3 positive/





Focal signs of tubular necrosis:

- Desquamation of cells
- Denuded tubular BM
- Focal absence of nuclear staining

Treatment and Partial Recovery

- 4 sessions of Immunoadsorption followed by 30 mg Alemtuzumab given
- Pancytopenia requiring Neupogen x2
- Persistent hypogammaglobulinemia, 0.5 g/kg IVIGx1
- Proteinuria-partial remission /1.5 gm/day/
- Hemodialysis stopped because of recovery of renal function
- DSA halved
- RLL pneumonia-resolved
- Discharged home-clinically improving

DSA, Proteinuria, se creatinine- summary

	DSA	se creat	prot/creat
Week 2:	0	220	17.9
Month 4:	6900	5-600 /HD/	360
IA, thymo			
Month 5:	3564	250	70
RTX			
Month 6:	6405	>600 /HD/	318
IA, alemtuzumab			
Month 7:	3578	318	159

What have we learned from this case?

- DSA: ask for DP haplotype in donor-as this is not routinely done in all Eurotransplant centers and may lead to delayed recognition of DSA
- Immunoadsorption+hypogammaglobulinemia: a learning curve: replacement with IVIG?-Let us discuss!
- Alemtuzumab-is it justified? Known rebound in 5-6 months, yet for now seems to work in this particular case
- Early mTor conversion in case of poor tolerance of MMF-is it an option?
- More questions than answers…a case for continued discussion

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