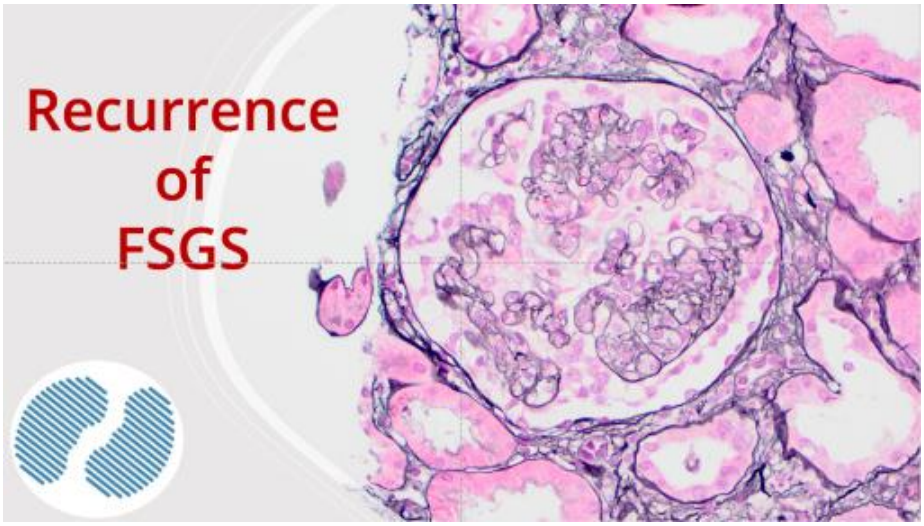
📣 Hello, #MedTwitter

⚡This month's @ASPNeph Renal Pathology Webinar was all about 🌟#Recurrent Focal Segmental Glomerulosclerosis (FSGS)
Here are some important "facts" I learned!

#Medtweetorial
#Nephtwitter

Tweetorial Alert



1/ let's start with an important question
What is the incidence of primary FSGS recurrence in children after kidney transplantation (KT)?

A. No risk
B. <20%
C. 20-30%
D. 40-60%

2/ Ans: D.
The incidence of primary FSGS recurrence after KT varies between 40- 60% .

Ref: https://www.frontiersin.org/articles/10.3389/fimmu.2019.01669/full

It may be important to point out somewhere in this thread that high index of suspicion, consecutive checks of urine protein, and serum albumin post-transplant in a patient with FSGS is used for diagnosis. PLEX needs to be initiated immediately once proteinuria and hypoalbuminemia is seen, sometimes even without waiting for biopsy.

3/ 🌟What do you expect in early allograft biopsies in FSGS recurrence?

- The only initial finding in allograft biopsies is diffuse podocyte foot process effacement on electron microscopy.

recurrence occurs in the first 2 years following kidney transplantation

4/ ✵All of the risk factors are a/w FSGS recurrence except

A. Prior graft loss due to FSGS recurrence
B. Living-related kidney donation
C. Young age
D. Black race

5/Ans D
Check out the following table
https://doi.org/10.1093/ndt/gfp538

Factors influencing the risk of recurrence of FSGS

Factors associated with increased risk of recurrence	**Factors associated with low risk of recurrence**
Second transplant after loss from recurrence	Familial FSGS
Childhood	Sporadic form with podocin mutation
Rapid progression to uraemia	Slow progression to uraemia
Mesangial proliferation in native kidneys	Non-nephronic proteinuria in the original disease
Living donation	
White race	
Elderly donor	

6/- Ever wondered what could be the outcome of FSGS recurrence post-KT?

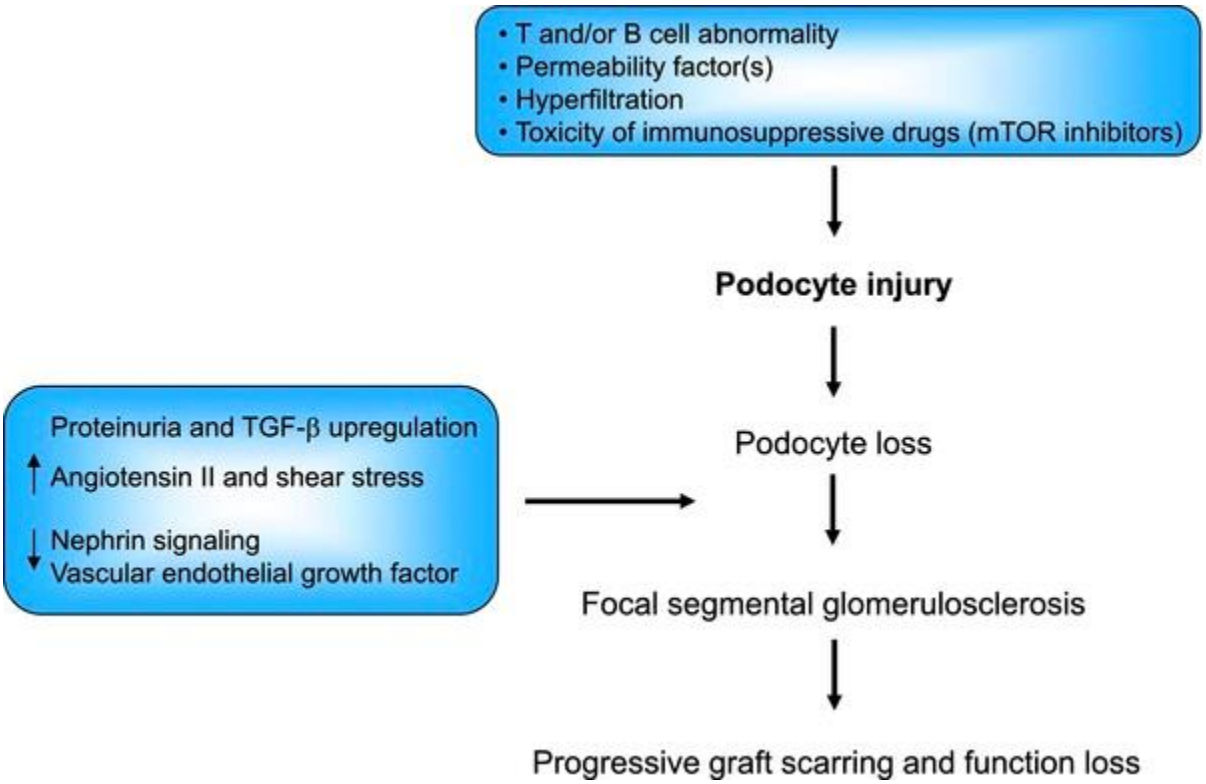
- Graft losses occur during the first 2 years after disease recurrence in the majority of cases.
- Higher chances of delayed graft function
- ? more biopsy-proven AR
- Increased exposure to procedures (catheter placement for PLEX if someone was on PD or pre-emptive transplant) and more immunosuppressants
- Development of PRA after loss of the 1st transplant causing longer wait times for 2nd transplant.

Ref: https://www.frontiersin.org/articles/10.3389/fimmu.2019.01669/full#B8

7/- QUE: What are the postulated permeability factors associated with FSGS recurrence?

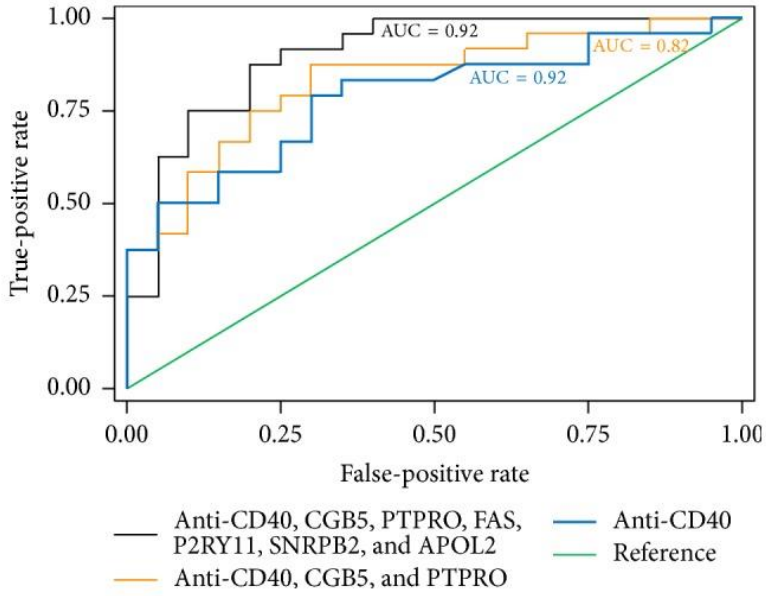
A. Soluble urokinase-type plasminogen activator receptor (suPAR)
B. Cardiotrophin-like cytokine factor 1 (CLCF-1)
C. Anti-CD40 antibodies
D. All of the above

8/- Ans: D
Although experimental research has proposed multiple circulating permeability factors in FSGS, the causative role could not be validated yet.



https://pubmed.ncbi.nlm.nih.gov/23312002/

9/- Are there any biomarkers predicting recurrence?
Other than circulating factors, assessment of podocyte changes in response to suspicious factor(s) is ongoing. Vasodilator-stimulated phosphoprotein (VASP) in human podocytes has been shown to be phosphorylated in response to plasma from patients with post KT recurrence



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4860214/

10/ What are the rate of FSGS recurrence in pts who had a prior h/o graft loss due to FSGS recurrence?

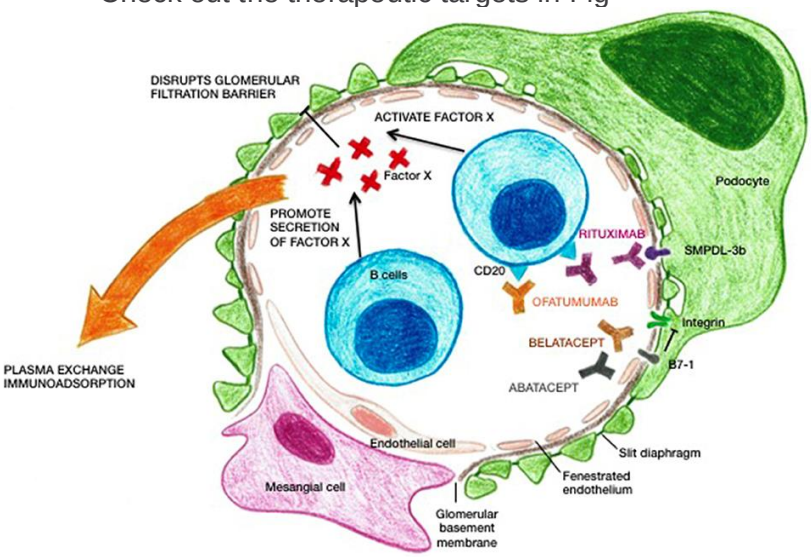
A. 10-20%
B. 20-50%
C. >80%
D. NO risk

11/ In pts who have lost their first allograft due to recurrent FSGS, kidney retransplantation is associated with recurrence rates > 80%
https://www.frontiersin.org/articles/10.3389/fimmu.2019.01669/full#B8

12/- Now let's talk about treatment

Rx is challenging as

- lack of RCT
- Only small study cohorts case series, and case reports are available
- Check out the therapeutic targets in Fig



https://www.frontiersin.org/articles/10.3389/fimmu.2019.01669/full#:~:text=Most%20commonly%2C%20recurrence%20occurs%20in,in%20patients%20without%20FSGS%20recurrence.

Mainstay of Rx: Plasmapheresis (PLEX) /immunoadsorption to remove circulating factor(s)

13/-Regimens like : PLEXPlex and cyclophosphamide to supplement usual Post KT immunosuppression with calcineurin inhibitors and steroids has been tried with variable success.
Ref:https: bmcnephrol.biomedcentral.com/articles/10.1186/s12882-022-02768-w

14/- Some studies has advocated the combination of pulse methylprednisolone infusions with cyclosporine-based immunosuppression
Success rate reported in 70% of cases.
Ref: https://doi.org/10.1111/ctr.12079

15/- Use of Rituximab

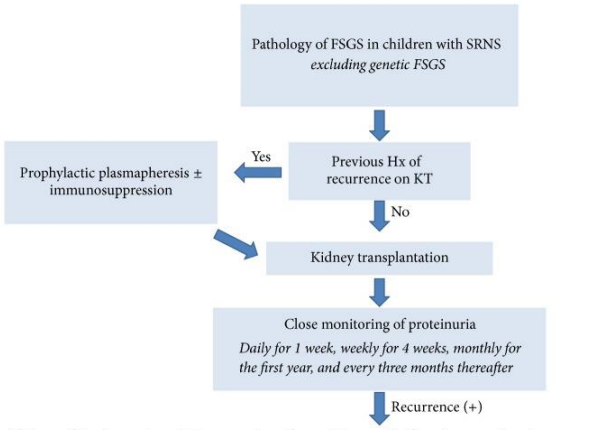
- Some studies showed response rate of 79%
- Dosing: Unclear
- 375 mg/m2 up to 6 doses or a single dose of 1000 mg
- MOA: eradication of B cells or binding to sphingomyelin phosphodiesterase acid-like 3b [SMPDL-3b] on podocytes

16/- Other therapeutic agents awaiting validation are

- CTLD4-Ig, abatacept
- anti-TNF-*α* (based on the upregulation of TNF-*α* mRNA)
- ACTH gel
- Allogeneic mesenchymal stem cells
- LDL Apheresis

17/ 🔥🔥Let's summarize,

- Recurrent FSGS affects up to 60% of 1st kidney grafts
- Exceeds 80% in pts who have lost their first graft due to recurrent FSGS
- Main pathogenic hypothesis: circulating permeability factor
- Rx is unclear but PLEX and B-cell depleting Ab (rituximab, ofatumumab) can be tried



(i) Immediate plasmapheresis/immunoadsorption until normalization of serum albumin
(ii) Methylprednisolone pulse 30 mg/kg up to 1 g per day, 3 days
(iii) Calcineurin inhibitor tacrolimus trough 12~15 ng/mL or cyclosporine trough 120~150 ng/mL
(iv) Rituximab 375 mg/m^2, till CD19 = 0

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4860214/

18/ That's all folks!
For a case-based clinical discussion with a radiology expert login to @ASPNeph website, March webinar #Membereducation

Special thanks to Swasti, Roshan, Abdul & Sudha and #ASPNFOAM group

Until next time…