

CASE OF THE WEEK 1

Clinical Presentation:

A 17 year old Indian boy presented with anasarca, decreased urine output and episodes of nausea and vomiting over the last three weeks. No h/o joint pains, fever, sore throat, skin rashes or macroscopic hematuria. No significant drug/therapeutic history. No previous personal /family history of tuberculosis or other systemic ailments

Physical Examination:

Pallor+, Anasarca ++, Healed scar in axilla
Abdominal distension and ascites +, BP 160/100 mm Hg (not on drugs)
Rest of physical examination (CVS, Respiratory system, CNS: WNL)

Investigations:

Urea 56 mg%, Creatinine 2.4 mg%, Urine Albumin 3+, RBC 10-12/hpf (15% dysmorphic), 24 hours urinary protein excretion 3.8 gms .
ANA/pANCA/cANCA/anti GBM antibodies/ANA/anti dsDNA- negative,
HIV/HBsAg/HCV- negative, Serum C3: 58 mg% and C4- within normal limits, ASO- normal

Clinical Impression: Nephrotic- nephritic syndrome ? MPGN, ? IgA nephropathy

A renal biopsy was performed.
Representative images from various areas of biopsy core are provided.
DIF studies did not reveal significant immune deposits

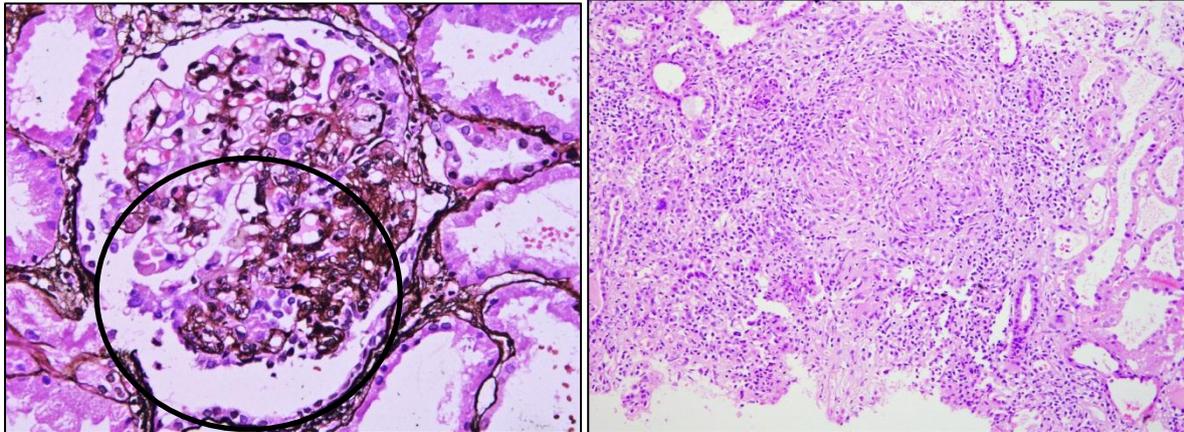
MICROSCOPIC EXAMINATION:

Upto 17 glomeruli were seen, none globally sclerosed. The provided images reveal two distinct lesions; glomerular and tubulointerstitial.

Glomerular lesions: There were areas of segmental endocapillary cellularity with capillary closure, sclerosis and few intracapillary neutrophils and foam cells, consistent with cellular lesions of FSGS; however few other glomeruli exhibited segmental collapse of the capillary tufts with remarkable hyperplasia and hypertrophy of visceral epithelial cells which possessed enlarged nuclei and voluminous cytoplasm with PAS positive resorption droplets. There was no evidence of parietal epithelial cell proliferation or tuft necrosis. Overall 5 glomeruli (29.4%) showed FSGS lesions.

The findings were consistent with “Collapsing variant of FSGS” or “Collapsing glomerulopathy”

Tubulointerstitial lesions: Discrete foci of interstitial epithelioid cell granulomas with no definite evidence of necrosis and associated mild chronic interstitial inflammation were seen (Granulomatous interstitial nephritis). In addition there were features of acute tubular injury and focal interstitial edema.



Final Diagnosis:

Collapsing glomerulopathy (collapsing variant of FSGS) with granulomatous non-necrotizing epithelioid cells granulomas (granulomatous interstitial nephritis)

Follow up:

- The patient was evaluated further and during the course of investigations developed small posterior triangle cervical lymph nodes which on FNAC revealed necrotizing granulomatous inflammation. ZN stain was positive. On further query he revealed that axillary scar resulted from a swelling which was first noted about 3 months back, had spontaneously ruptured and was managed with local application of traditional medications.
- The patient was severely malnourished: BMI <16 kg/m² and had marked hypoalbuminemia (0.8 g %) at presentation. He was given adequate nutritional support, treated with a combination of steroids and anti-tubercular therapy (ATT), and achieved remission of proteinuria and resolution of creatinine levels to 1.1 mg% on a follow up visit one month after initiation of treatment. The ATT (12 months) was completed and complete regression of enlarged lymph nodes was noted.
- Serum C3 levels tested at one month follow up (and on two subsequent occasions) were within normal limits.
- During a follow up of 2 years, he has had one relapse of nephrotic syndrome for which oral steroids were administered for 4 weeks with remission of proteinuria.

Discussion:

- Collapsing glomerulopathy (CG) is recognized as an unusually aggressive variant of focal and segmental glomerular sclerosis characterized histologically by hyperplasia and hypertrophy of visceral epithelial cells overlying wrinkled or collapsed capillary loops. The lesions can be segmental or global in distribution.
- CG was initially described in association with HIV infection ¹ but now several other causes including non-viral infections, drugs etc. are identified. A classification of CG recognizes Idiopathic, Genetic (syndromic and non-syndromic) and reactive forms.²
- Amongst the non-viral etiologies of CG, infections with Loa Loa, leishmaniasis, filariasis and mycobacterium tuberculosis have been reported. ²
- In the present case, the glomerular pathology and interstitial granulomatous lesions are possibly etiologically linked to tubercular infection as evidenced by response to specific treatment, in spite of unfavourable histology (collapsing glomerulopathy) and severe clinical presentation. Cases tuberculosis associated CG responding well to ATT and corticosteroids have been published ³⁻⁴.
- The low serum C3 at presentation was possibly a result of severe malnutrition status and normalized with remission of disease and improvement in nutritional status.

Key points:

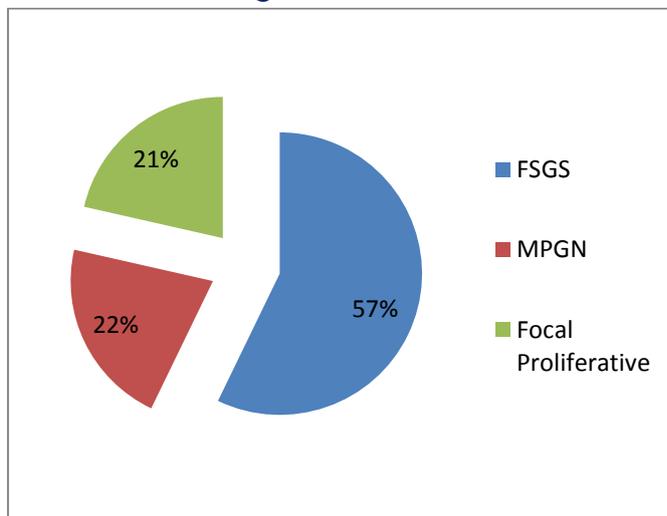
- Amongst infection related CG, tubercular infection is possibly unique, in being associated with a more favourable clinical course, as suggested by small volume of available literature.
- Strict and uniform criteria for histological diagnosis of CG should be applied. The algorithmic approach in the Colombia classification of FSGS ⁵ is a good guide.
- Awareness regarding causes of low C3, unrelated to immune complex formation is useful: The following etiologies have been described in this context:⁶
 - Atheroemboli
 - HUS/TTP
 - severe sepsis
 - Severe malnutrition
 - Hepatic failure
 - Acute pancreatitis
 - Inherited abnormalities of complement pathway components

References:

1. Weiss MA, Daquiaoag E, Margolin EG, Pollak VE: Nephrotic syndrome, progressive irreversible renal failure, and glomerular “collapse”: a new clinicopathologic entity? *Am J Kidney Dis* 1986; 7: 20-28.
2. Albaum M, Barisoni L. Current views on collapsing glomerulopathy. *J Am Soc Nephrol* 2008; 19:1276-1281.
3. Coventry S, Shoemaker LR. Collapsing Glomerulopathy in a 16-Year-old Girl with Pulmonary Tuberculosis: The Role of Systemic Inflammatory Mediators. *Pediatric and Developmental Pathology* 2004; 7:166-170.
4. Camila E. Rodrigues, Luís H.B.C. Sette, Juliana Torritani, Denise M.A.C. Malheiros, Sílvia M. Titan, Rui T. Barros, and Viktoria Woronik. Tuberculosis-Associated Collapsing Glomerulopathy: Remission after Treatment. *Renal Failure* 2010;32:143-146.
5. D'Agati VD, Fogo AB, Bruijn JA, et al. Pathologic classification of focal segmental glomerulosclerosis: a working proposal. *Am J Kidney Dis* 2004; 43:368–382.
6. Herbert LA, Cosio FG, Neff JC. Diagnostic significance of hypocomplementemia. *Kidney International* 1991; 39:811–821.

SUMMARY OF SUBMITTED DIAGNOSIS

Overall Diagnosis



Distribution of responses as per FSGS subtypes

