

CASE OF THE WEEK 8

CLINICAL HISTORY:

A 61 year old Indian lady, previously in good health presented with swelling over face and feet since three months and a recent rapid rise in serum creatinine from 1.0 mg% (recorded three weeks back) to current value of 4.8 mg%. No previous co morbidities. No past history of tuberculosis or NSAID intake.

EXAMINATION:

Facial and pedal edema +, BP 140/80 mmHg, Systemic examination- unremarkable except for edema and mild abdominal shifting dullness. No finger clubbing/cyanosis.

INVESTIGATIONS:

Urine - Albumin 3+, RBC 25-30/ hpf (40% dysmorphic), WBC 8-10/hpf. Urine culture- sterile
Haematological profile - Hemoglobin 11 g% (110 g/L), Total leukocyte count 14,800/ mm³,
Differential: 70% polymorphs, platelets adequate, ESR 35 mm/ 1st hour.

Urea: 78 mg% (27.84 mmol/L), Creatinine 4.8 mg% (424.3 µmol/L)

Cholesterol 138 mg% (3.57 mmol/L), 24 hours urinary protein 12.4 gms (urine volume 2800 ml)

ANA, anti dsDNA, pANCA, cANCA, anti GBM antibodies, ASO titres- negative.

Serum C3 & C4 levels: WNL, cryoglobulins- negative, HBsAg/HIV/HCV- negative

Serum electrophoresis- no "M" band, serum free light chain ratio- WNL

USG abdomen: Bilateral enlarged kidneys (13.1 AND 12.9 cms), raised cortical echogenicity.

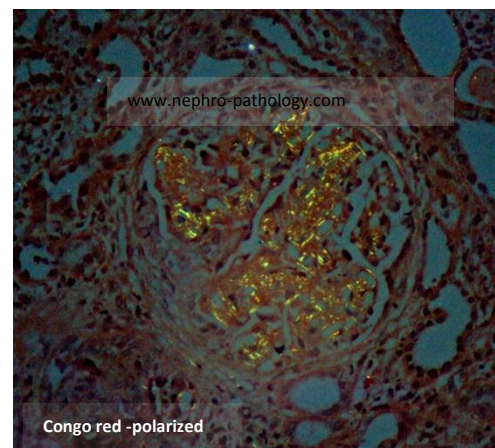
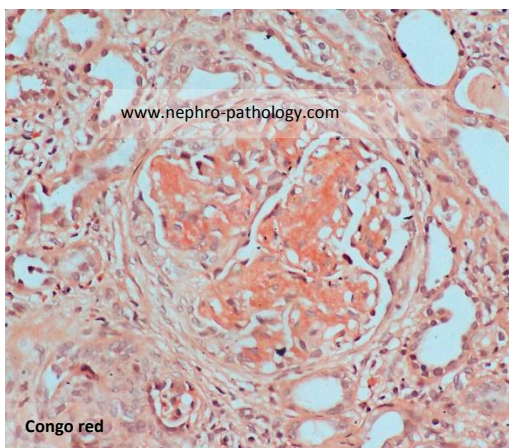
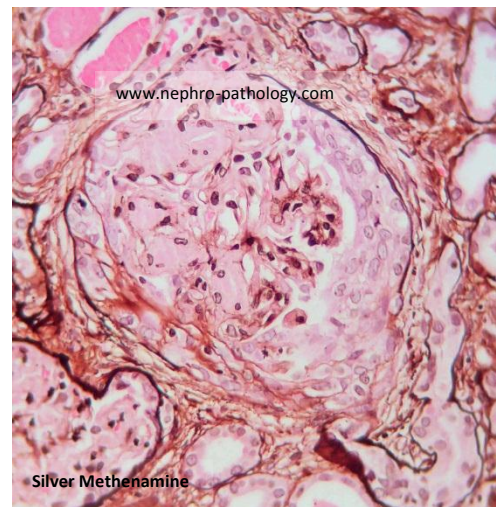
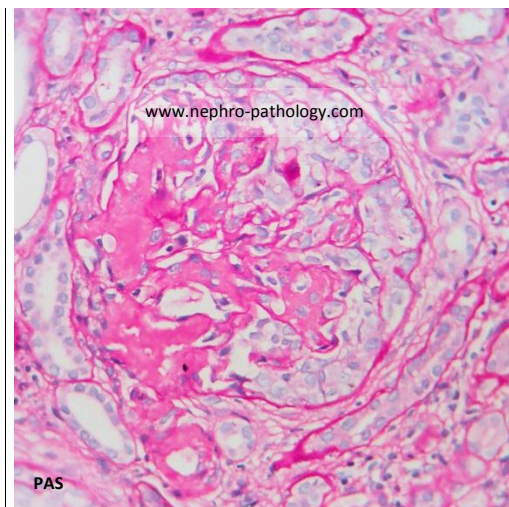
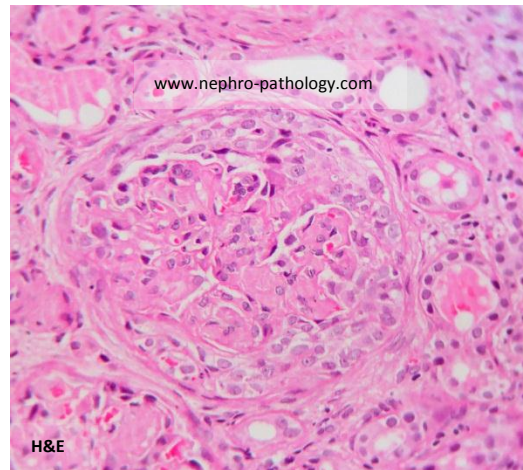
A renal biopsy was performed in view of rapidly progressive renal failure associated with significant proteinuria and negative serological profile

DIF studies showed non- specific segmental glomerular mesangial staining for IgM, and negativity for IgA, IgG, C3, C1q and kappa & lambda light chains.

MICROSCOPY:

Biopsy included about 23 glomeruli, three among which were globally sclerosed. All the viable glomeruli showed irregular mesangial matrix expansion with variable paramesangial extension, due to deposition of a material that was negative with PAS and Silver methenamine stains, showed congophilia and exhibited greenish birefringence in Congo red stained sections viewed under polarized light. Features were consistent with renal amyloidosis. Additionally, extracapillary proliferation and cellular / fibrocellular crescents

were seen in 16/23 (69.56%) glomeruli. Focal intracrescentic inflammatory cell infiltrate and fibrin deposition was noted. There were features of acute tubular injury with tubular lumina containing granular casts, and few large RBC casts. Immunohistochemistry for serum amyloid associated protein (SAA) showed strong positivity in areas of amyloid deposition.



Diagnosis:

Renal (AA) amyloidosis with a crescentic presentation (crescentic glomerulonephritis)

Follow up: Serum rheumatoid factor (RA) assay was negative. Patient continues to be dialysis dependent three months after the diagnosis.

DISCUSSION:

The most common renal manifestation of amyloidosis is nephrotic syndrome due to glomerular amyloid deposition. Extracapillary proliferation and crescent formation associated with the clinical syndrome of rapidly progressive renal failure is a rare but well recognized phenomenon in amyloidosis. Many of the cases reported had an underlying rheumatoid arthritis (RA) and presented clinically with RPRF [1]. In addition to RA crescentic presentation of renal amyloidosis has also been reported with primary (AL) amyloidosis [2] and Waldenstroms macroglobulinemia [3].

Schafernak et al.[4] have summarised 12 previous case reports of crescentic rapidly progressive glomerulonephritis associated with amyloidosis, 11 in the setting of AA amyloidosis and one in the setting of Waldenstroms macroglobulinemia.

The pathogenesis of crescent formation in renal amyloidosis is not fully understood, but appears to involve mesangial cell dysfunction due to nodular expansion and amyloid fibril-induced capillary loop rupture with fibrin entering Bowman's space and initiating the process of extracapillary cell proliferation. Watanabe and Nagata [5] suggest that rupture of the fragile glomerular basement membrane by amyloid deposition, as revealed by immunostaining and electron microscopy may be the mechanism of crescent formation.

This is supported by a spatial co-existence of amyloid deposits and crescents on light and electron microscopy and glomerular basement membrane rupture associated with amyloid

fibrillary deposition. Upregulated cell mediated immunity in patients with amyloidosis and glomerular crescent formation has been noted [6].

A retrospective analysis by Nagata et al. [7] of 44 renal biopsies and 61 autopsy specimens with a diagnosis of renal Amyloidosis revealed that 14/105 specimens analysed demonstrated between 5% and 77% crescents. Of the specimens demonstrating crescents, eight were autopsy specimens, and six were ante mortem renal biopsies. In 12/14 cases, there was AA amyloid deposition, the majority of which was secondary to rheumatoid arthritis. In 2/14 of these cases, crescents were observed in association with AL amyloidosis.

It is important to be aware of crescent formation in renal amyloidosis as such cases portend a poorer progression. As crescent formation may be focal in a given biopsy sample, a careful morphological observation is warranted.

References:

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3. Ogami Y, Takasugi M, Soejima M, et. al. Waldenström's macroglobulinemia associated with amyloidosis and crescentic glomerulonephritis. [Nephron. 1989;51\(1\):95-8.](#)
4. Schafernak KT, Chugh SS, Kanwar YS. Co-existent crescentic glomerulonephritis and renal amyloidosis: a case report and literature review. *J Nephrol.* 2005;18(5):616-22.

5. Watanabe T, Toyoshima H, Nagafuchi Y, Yoshikawa Y. Renal amyloidosis with crescents. [Hum Pathol. 1984 ;15\(7\):684-6.](#)
6. Masutani K, Nagata M, Ikeda H et. al. Glomerular crescent formation in renal amyloidosis. A clinicopathological study and demonstration of upregulated cell-mediated immunity. [Clin Nephrol. 2008 Dec;70\(6\):464-74.](#)
7. Nagata M, Shimokama T, Harada A et. al. Glomerular crescents in renal amyloidosis: An epiphenomenon or distinct pathology? [Pathology International 2001;51\(3\): 179-186.](#)