CASE OF THE WEEK 6

CLINICAL HISTORY:

A 35 year old lady of Asian origin, presented with edema feet and facial puffiness. She gave history of persistent proteinuria since last one and a half years, which was initially sub nephrotic but had gradually increased to 6.2 gms/24 hours at last evaluation about three months back. There was no history of joint pains, skin rashes, oral ulcers, alopecia or any other signs suggestive of connective tissue disorder.

EXAMINATION:

Pedal edema and facial puffiness +, BP 146/88 mmHg (supine), Systemic examination- NAD

INVESTIGATIONS:

Urine – Albumin 4+, no hematuria, 24 hours urine protein 8.3gms

Serum ANA, anti dsDNA, ANCA, HIV, HBsAg, anti HCV- negative

Serum complement levels (C3 and C4) –WNL, Haematological profile -WNL

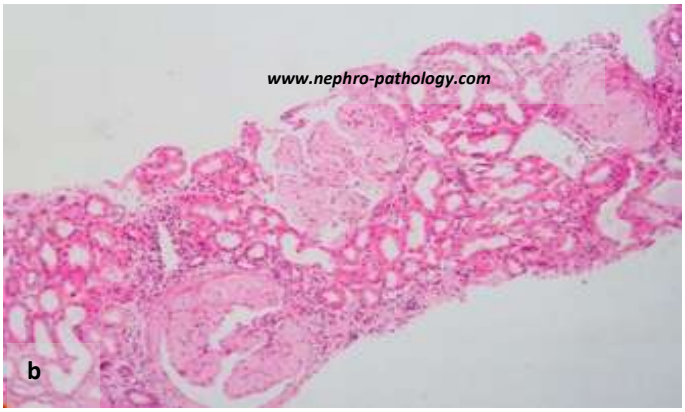
Urea: 44 mg% (15.7 mmol/L), Creatinine 1.4 mg% (123.76 m mol/L), Cholesterol 236 mg% (6.1 m mol/L)

USG abdomen: Mild ascites +, bilateral normal sized kidneys with well-maintained cortico medullary differentiation (CMD), no hydronephrosis

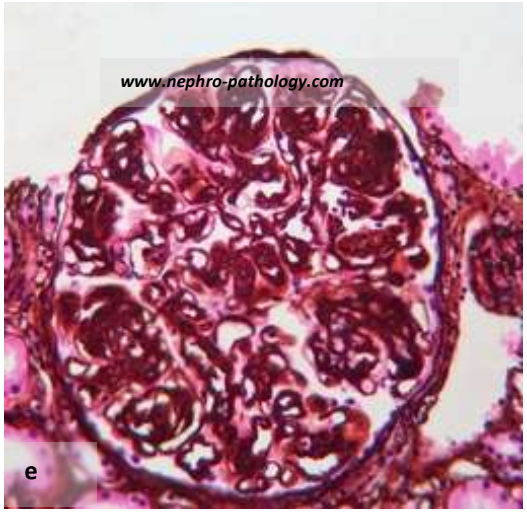
In view of persistent progressive proteinuria of adult onset, a renal biopsy was performed.

DIF studies: Glomeruli showed segmental minimal mesangial staining for IgM and were negative for IgA, IgG, C3, C1q and kappa & lambda light chains.

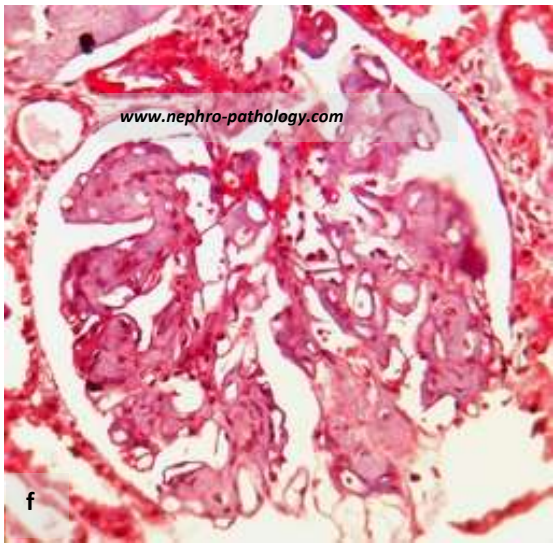
MICROSCOPY:

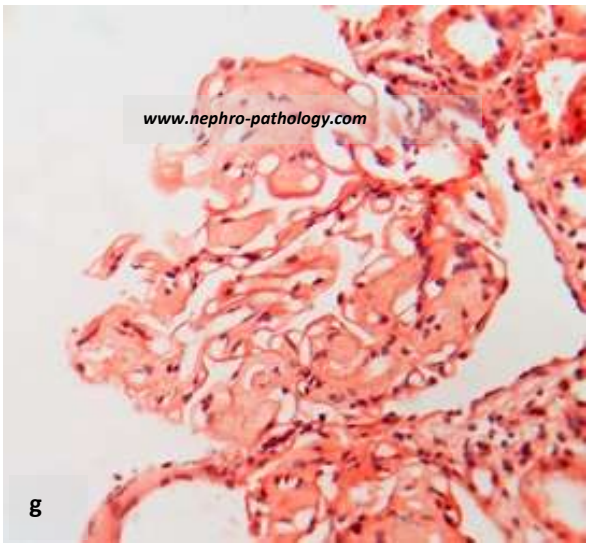


H&E stained sections (Fig a &b) show enlarged “pale” appearing glomeruli which exhibit a nodular configuration and variably sclerosed/solidified mesangial areas.



The enlarged pale glomerular mesangial areas/nodules were negative with PAS stain (Fig c &d) and were intensely argyrophilic (Fig e). The peripheral capillaries were variably thickened and showed focal “splits” or “double contours” in silver methenamine stained sections (membranoproliferative or mesangiocapillary pattern).Significant increase in mesangial cellularity was not observed.





The nodules stained blue with MT (Fig f) and were non congophilic (Fig g)

DIF studies did not show significant immune deposits.

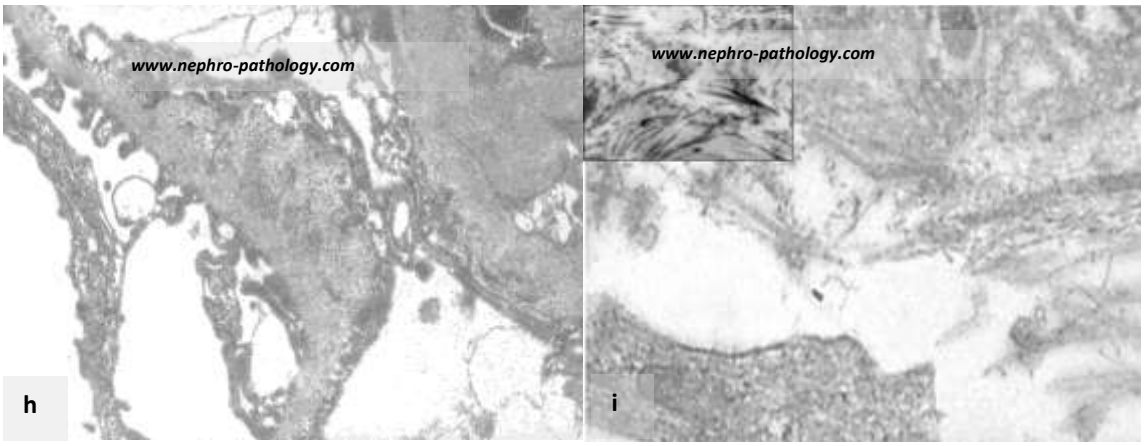
Summary of morphological features:

- Nodular glomerular sclerosis
- Thickened glomerular capillaries with a focal membranoproliferative pattern
- Lack of significant mesangial cellularity
- Mesangial nodules were pale on H&E stain, PAS negative, Argyrophilic, MT blue and non congophilic

Considering the absence of immune deposits in DIF studies the following differentials were considered

- Collagenofibrotic glomerulopathy
- Chronic Thrombotic microangiopathy

However, there was no evidence of thrombotic vascular lesions in the biopsy.



Ultrastructural studies revealed thickened capillaries with widened subendothelial areas and deposition of abnormally oriented collagen fibrils with a periodicity of about 60 nm in glomerular subendothelial spaces and focally in the mesangium (Fig h,i)

DIAGNOSIS:

Collagenofibrotic glomerulopathy

DISCUSSION:

Collagenofibrotic glomerulopathy is a rare condition characterized by deposition of abnormal Type III collagen fibres in the subendothelial space and mesangium of the glomerulus [1–7]. It was initially thought to be a variant of the nail–patella syndrome sans the skeletal abnormalities [8,9]. Later research revealed that CG was a novel type of hereditary glomerulopathy [10].

Less than 50 cases of this entity have been reported in the literature. In the described cases, the patients ranged from 2–66 years of age, with no definite gender predilection. The most common clinical presentation was proteinuria with or without associated nephrotic syndrome, and minimal/mild alterations in renal function [4, 5].

The exact etiopathogenesis of this disease is not clear; however the regional clustering of cases from Asia and occurrence of disease in siblings point towards role of environmental as well as genetic factors respectively [6]. Several patients with CG were detected with elevated levels of serum procollagen III peptide, which is considered a marker of renal fibrosis and is elevated in patients with ESRD and widespread renal fibrosis.

Histopathological features include lobular accentuation or a nodular glomerulosclerosis pattern due to global expansion of the mesangium with thickening of the peripheral capillary walls. Mesangial cellularity however is usually insignificant /minimal. The expanded mesangium is weakly eosinophilic, PAS negative and non Congophilic.

On Masson's trichrome stain, the deposited material reveals blue staining and is variably but usually intensely argyrophilic (in contrast to amyloid). The capillary walls are thickened and show focal to widespread reduplication mimicking the MPGN pattern of injury. Usually, no endocapillary or extracapillary proliferation is seen in CG.

Staining for immunoglobulins and complement components is generally negative, though a single case of CG associated with immune complex deposits has been reported [11].

Electron microscopy is essential to establish a definitive diagnosis of CG .There is massive accumulation of banded collagen in mesangial and sub-endothelial areas. The collagen fibrils are arranged in irregular bundles, show a distinct periodicity of 43–65 nm and appear curved, frayed, and worm and comma shaped when sectioned transversely [12-15]. Owing to their peculiar size and disposition these collagen linear arrays) and other types of organized glomerular deposits, including amyloid, cryoglobulins, fibrillary glomerulonephritis and immunotactoid glomerulopathy [16].

Currently no specific treatment is available for the disease. There is limited experience of renal transplantation in patients with Collagenofibrotic glomerulopathy, however the outcome has been favourable in the reported cases [17].

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