

## **CASE OF THE WEEK 2**

### **CLINICAL HISTORY:**

A 60 year old man, previously in good health presented with nausea, vomiting , mild pedal edema for 2 weeks  
Palpitations with compressive chest pain for 2 days  
No h/o joint pains, recent fever, sore throat, skin rashes or macroscopic hematuria.  
No significant drug/ therapeutic history, no history of previous cardiovascular events/ surgeries.

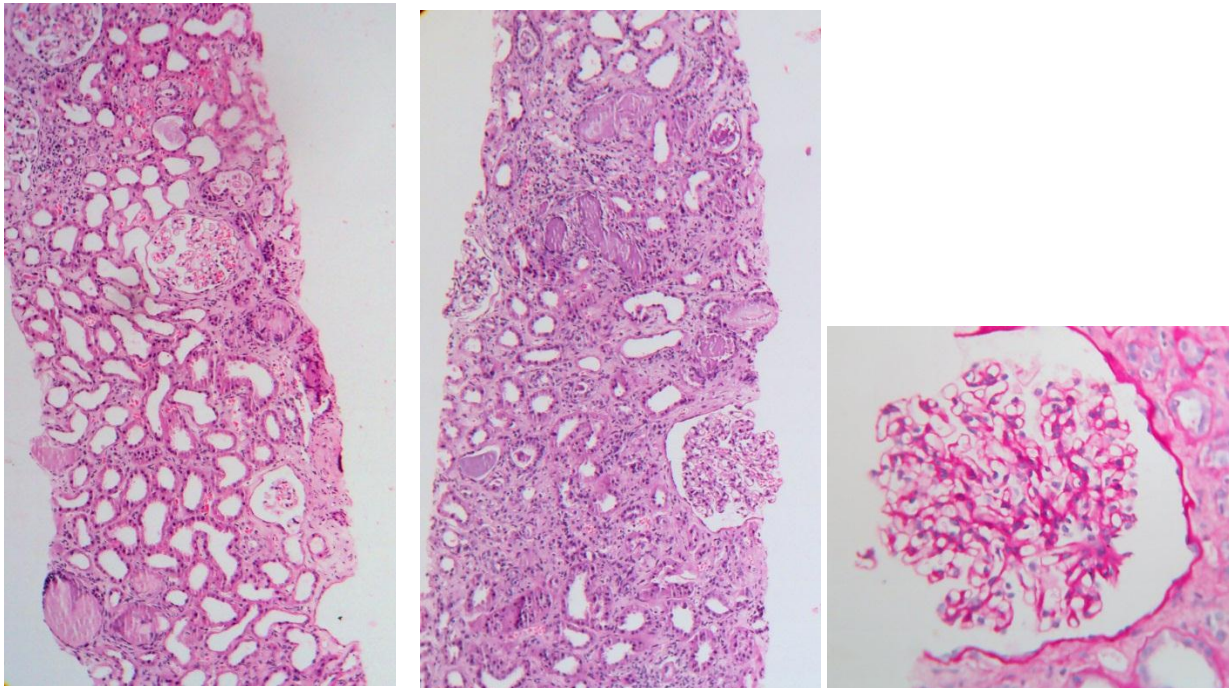
### **EXAMINATION:**

Pallor +, mild pedal edema + BP 140/ 80 mm Hg (not on drugs)  
Systemic examination: Chest - Mild Rt. sided pleural effusion

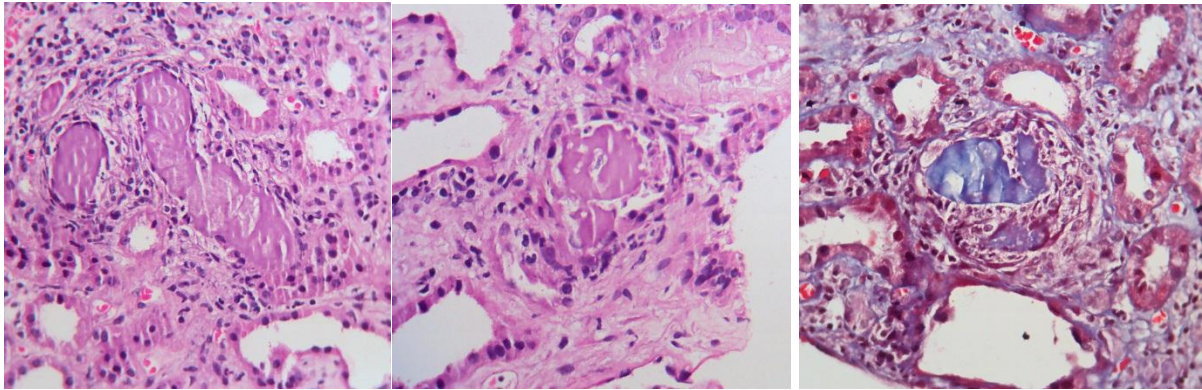
### **INVESTIGATIONS:**

Urine Albumin 1+, Sugar Nil, RBC occasional, Pus cells 10-15/hpf, Casts: Granular /WBC casts ++  
Urine Protein creatinine ratio: 1.2.  
24 hours protein: 1.0 gms  
Urea: 128 mg%, Creatinine: 11.2 mg%  
Cholesterol: 128 mg%, HIV/HBsAg/HCV/ANA/anti dsDNA/ANCA/anti GBM antibodies: Negative  
Total protein/Albumin/Glob: 7.1/3.5/ 3.6 g%  
Complement C3: 70 mg% , C4: 38 mg%  
USG abdomen: B/L normal sized kidneys, Increased cortical echogenicity  
ECG and ECHO: Anterior wall myocardial infarction  
eGFR (MDRD): 34 ml/min  
Hemoglobin:8.2 g%, TLC:11600/mm<sup>3</sup>, DLC: P70 L27 E1 M2, Platelets: 2.9 lakh/mm<sup>3</sup>, ESR 90 mm/1st hour  
PS examination: Normocytic normochromic

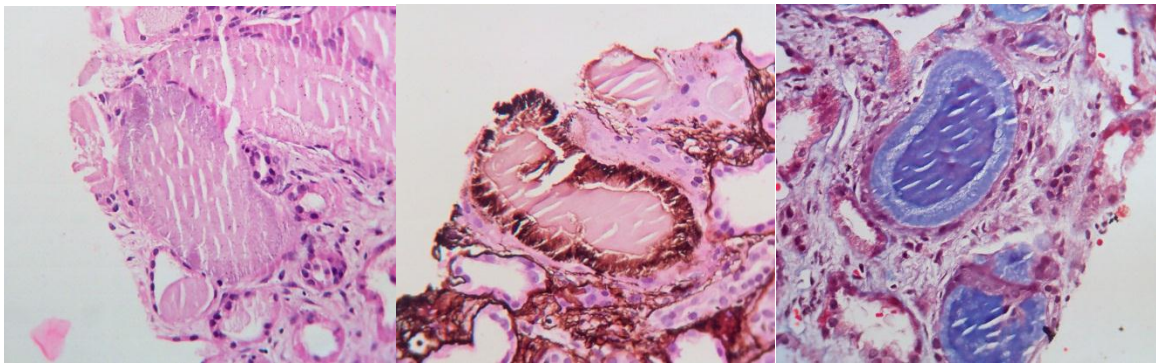
## **MICROSCOPIC EXAMINATION**



Low magnification views showing acute tubular injury (epithelial simplification, loss of brush borders), focal chronic interstitial inflammation and several atypical appearing intratubular casts. Higher magnification image shows a normal appearing glomerulus.



Higher magnification of atypical “brittle” casts with pale eosinophilic appearance, “fracture” planes and surrounding epithelial cell and inflammatory reaction, suggestive of myeloma cast nephropathy.

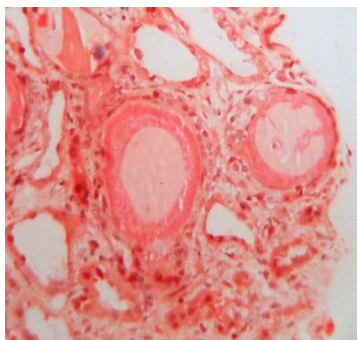


a

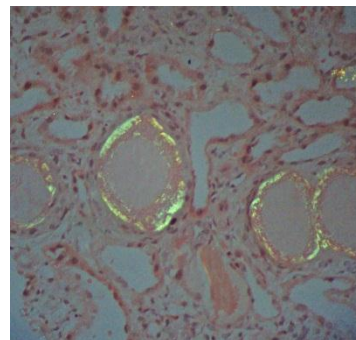
b

c

The other type of casts had a central pale area (nidus) and spiculated periphery which was PAS positive, argyrophilic (b) and blue with MT stain (c)



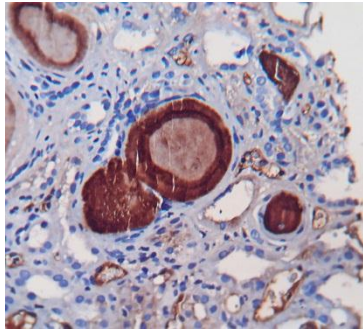
Congo red



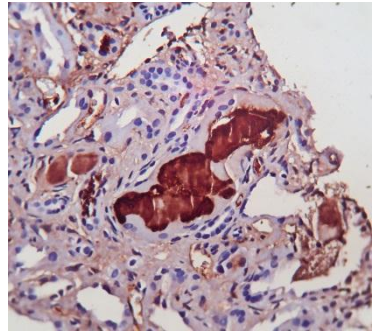
Congo red -polarizing light

Peripheral spiculated area was congophilic and exhibited greenish birefringence on examination under polarizing microscope, suggestive of amyloid (intratubular amyloidosis)

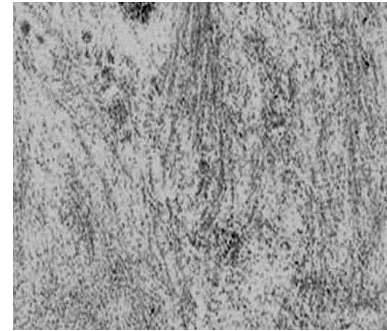




(a) Amyloid casts



(b) Myeloma casts



(c) Amyloid fibrils (EM)

Lambda light chains (immunohistochemistry)

Both intratubular amyloid casts (a) and the conventional myeloma casts showed lambda light chain restriction on immunohistochemistry. Paraffin embedded tissue was reprocessed for ultrastructural studies and though preservation was suboptimal, randomly branching fibrils of amyloid were identified.

### CLINICAL COURSE:

The patient was further investigated and showed

- “M” band on serum electrophoresis,
- Bone marrow plasmacytosis (30%), No amyloid in bone marrow, Lambda restriction +
- Serum free light chain (lambda ): 79.5 mg/L,
- Serum free light chain kappa/lambda ratio: 0.03
- No bony lytic lesions were detected

### DIAGNOSIS:

Coexisting Myeloma cast nephropathy and intratubular light chain amyloidosis.

No glomerular or vascular deposition of amyloid was seen.

### DISCUSSION:

- In renal amyloid deposition associated with plasma cell dyscrasias (AL amyloidosis), glomerular deposition is commonest followed by vascular and tubulointerstitial deposits.
- Intratubular amyloid in absence of glomerular involvement is rare
- Differential diagnosis of casts in a setting multiple myeloma includes: 1. Myeloma casts, 2. Hyaline casts, 3. Tamm Horsfall protein casts, 4. Light chain crystal casts, and 5. Light chain amyloid casts
- Pathophysiology behind tubular amyloid formation is unclear as fibrils are large and unlikely to filter across the glomerular filtration barrier. Presumably these form either from proteins secreted by tubules or from the light chains filtered across the glomerulus.

## KEY POINTS:

- Careful search for amyloid casts should be made in cases of myelomas cast nephropathy
- Amyloid light chain casts can show PAS and silver positivity and have a characteristic spiculated appearance at periphery

## REFERENCES:

1. Melato M, Falconieri G, Pascali E, Pezzoli A: Amyloid casts within renal tubules: A singular finding in myelomatosis. *Virchows Arch A Pathol Anat Histol* 1980; 387:133-145.
2. El-Zoghby Z, Lager D, Gregoire J, Lewin M, Sethi S: Intra-tubular amyloidosis. *Kidney Int* 2007;72:1282-1288. Full text link
3. Friman C, Tornroth T, Wegelius O: IgD myeloma associated with multiple extramedullary amyloid-containing tumours and amyloid casts in the renal tubules. *Ann Clin Res* 1970; 2:161-166.
4. Sethi S, Hanna MH, Fervenza FC: Unusual casts in a case of multiple myeloma. *American Journal of Kidney Diseases* 2009; 54(5): 970-974.

## SUMMARY OF SUBMITTED DIAGNOSIS

